A STUDY OF SOME ASPECTS OF THE TOXAEMIAS OF LATE PREGNANCY IN THE CITY OF CAPE TOWN :

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by

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A BRIEF SUMMARY OF THE THESIS ENTITLED
"A STUDY OF SOME ASPECTS OF THE TOXAEMIAS
OF LATE PREGNANCY IN THE CITY OF CAPE TOWN"
by L. v.R. Oosthuysen.

The General Introduction in Section 1, Page 1 describes briefly the scope of the work in this thesis.

Section 2 deals with the Historical facts with emphasis on the History in South Africa which has never been published previously. In addition the general history as well as the literature concerning the Etiology, Pathogenesis and follow up studies is summarised.

Section 3 is a study of the incidence of the Toxaemias of late pregnancy within the municipal boundaries of the city of Cape Town and the Langa Native Township, and their racial grouping. A separate introduction on page 38 as well as the problems investigated on page 48 and the standards employed on page 49 as well as the methods and material on page 50 indicate how this problem was investigated. The conclusions of this aspect of the study are summarised on page 85.

Section 4 deals with follow up studies of 100 cases of non-convulsive toxaemia and 100 cases of eclampsia, and the material and methods are described on pages 88 and 94 respectively.

Section 5 portrays the results of the follow up studies and the conclusions reached in this regard. In addition fields for further investigation are suggested on page 229.

Section 6, the Appendix, gives additional case history information and Section 7 reproduces the Bibliography used.

P R E F A C E.

I am greatly indebted to Professor J.F. Brock for having stimulated my interest to undertake a study of the toxaemias of late pregnancy. It is with particular pleasure that I thank him for his enduring encouragement, criticism and guidance, and allowing me the use of the amenities of the Department of the Practice of Medicine.

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I N D E X:

SECTION I.

INTRODUCTION.

I N T R O D U C T I O N:

It has been stated for years to medical students and those specially interested in obstetrics and its medical problems, that there is a strong impression that in Cape Town eclampsia and toxaemias of late pregnancy have a high incidence. (Crichton 1935 and 1949, Brock and Rollo 1949).

This idea acted as a stimulus to consider this as a subject for further study especially as a detailed enquiry into the toxaemias of late pregnancy has never been made in Cape Town. There are no accurate figures with regard to the incidence of toxaemias amongst the various races, but hospital figures have been analysed and elsewhere in the world work in this direction has been done. Cape Town presents a unique opportunity for studing the incidence of the toxaemias amongst the different racial groups, because of its multi-racial population. A critical analysis of all statistical and other available data will be made in order to reach some definite conclusions.

Although, a great deal of research and follow-up study has been done in the last 80 years, there is still a marked controversy and difference of opinion amongst the various authors as to the effects of the toxaemias in general, and the permanent cardiovascular and renal damage, if any, that may result amongst parous women. Statistical and other studies from all over the world can be quoted to confirm or disprove almost any view held. Further follow-up study should contribute to the accumulative general knowledge on the subject thus increasing the understanding and improving the management of the various toxaemias of late pregnancy. This is the second objective of this thesis. Data obtained from an exhaustive study made will aid in determining the incidence and type of post-toxaemic vascular and renal complications. The method used towards the second main objective of the present study, was a follow-up of eclampsia and other severe non-convulsive toxaemia cases subjected to attacks five years previously or longer, so as to throw further

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light on the much discussed question as to whether or not they leave irreparable vascular and renal damage and are causative factors in subsequent hypertensive cardiovascular disease.

Attention was paid to the present and past state of health, the health during pregnancy, the number of pregnancies and the offspring in order to compare the findings with those of other observers. In addition the family history of a hypertensive and epileptic tendency was noted amongst the relatives to see what part, if any, it plays. There still appears to be a place for fresh contributions, not only to the above aspects, but also with regard to the effects of repeated pregnancies, especially amongst the non-Europeans, as well as the effects of dietetic, hygienic, climatic, economic, psychological and hereditary factors. The vast literature on the subject indicates that these factors may play a part in the etiology of this group of diseases which seems to have a multiple etiology.

By initiating clinical and statistical study, and with the recent establishment of a toxaemia ward, it is hoped that a foundation will be laid for further research work into the many avenues of the controversial aspects of this group of diseases.

As with all clinical problems investigated, one can usually only produce a partial solution. The rest will ultimately have to be proved by laboratory and other studies. Brock (1939).

A knowledge of the history and a review of the literature of the toxaemias of late pregnancy are essential to understand the problems, and although little original work has been done in South Africa, the knowledge gained locally and written about has been summarised.

In order to limit the extent of this thesis no special investigation was done into cases of "Toxaemic Accidental Haemorrhage" This is a controversial subject due to several etiological factors, unrelated conditions, and causes unknown, that need further investigation. (O. Browne 1952). An urgent problem that in itself

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is a suitable subject for a thesis. (Editor B.M.J. 1952).

S E C T I O N II.

THE HISTORY OF THE TOXAEMIAS OF LATE PREGNANCY AND A REVIEW OF THE LITERATURE CONCERNING THE ETIOLOGY AND THE REPORTED FOLLOW-UP STUDIES.

CHAPTER 1.

THE GENERAL HISTORY OF THE TOXAEMIAS OF LATE PREGNANCY.

The word eclampsia is derived from the Greek word "ἐκλάμπειν," and means a flash or shining forth, and is indicative of the fulminating character of the disease which has come to be generally known as eclampsia.

Apparently Hippocrates first used the word Eclampsia to designate a fever of sudden onset, and not for Toxaemia and convulsions during pregnancy (Stander 1936).

However, Hippocrates 460-375 B.C. stated that headaches, drowsiness and convulsions were of serious significance in pregnant women, so that the entity later termed eclampsia was recognised by him.

There is no direct Biblical reference to eclampsia, although epileptiform seizures are well described in Luke Chapter 9 verse 39, and in Numbers, Chapter 24 verse 4 (Weinbren and Bosman 1936).

The literature of the ancient Chinese, Egyptians and Greeks mentions the dangers of convulsions in pregnancy (Wong Wu Lien-Teh, 1936, and Logan Clendening, 1932, Fasbender, 1897 and 1906).

In the year 1619 the word eclampsia first appeared in a treatise on gynaecology by Varandaeus, and in 1694 Peu mentioned generalized clonic spasms in pregnancy. One of the earliest uses of the word in obstetrics occurs in two papers by J.C. Gehler of Leipzig in 1776 and 1777 (Weiss 1941).

De-la-Motte (1722) recognised that delivery in pregnant patients with convulsions favoured their recovery, and in 1763 De Sauvage made a differential diagnosis between epilepsy and eclampsia. Mauriceau (1740) wrote about eclampsia and suspected toxins of the dead foetus as the cause. From about this time

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the condition was treated by bloodletting, blistering (Smellie 1747) purgation and enemas to induce labour (Puzos 1759). The use of opium was stressed by Manning in 1771. Speedy delivery with forceps was advocated by Hamilton in 1775, at first by manual dilatation of the cervix and later by the use of the Bossi dilator (Bossi 1896).

Convulsions in pregnant women therefore have undoubtedly always occurred, but no figures are available until the 19th century as to their frequency, when Collins noted in the Dublin Lying-in Hospital thirty cases of convulsions in 16,154 deliveries, with an incidence of 0.18 percent for the years 1826-1833 inclusive. (Collins 1841). Jardine in 1839 reported the mortality from eclampsia in the Glasgow Maternity Hospital to be 47%. Simpson (1847) introduced Chloroform and Schroeder (1873), Das and others emphasized its use in eclampsia.

It was only since 1840, when albumen was first found in the urine of normal pregnant women by Rayer, and by Lever in the urine of 9 out of 10 eclamptics in 1843, that medical interest started to grow about pre-eclampsia and eclampsia, and laid the foundation for the theory that kidney lesions were always associated with eclampsia. Since this time too, Sir James Young Simpson (Kellar 1939) taught his students that albuminuria was a precursor of eclamptic fits, and Johns of Dublin (1843) stated that oedema and headaches were a warning sign of fits. Oliguria has been recognised in pre-eclampsia since 1850, and Zangemeister (1912) stressed a positive water balance.

Veratrum viride was introduced in 1860 by Baker and chloral hydrate in 1869 by Lierbruch, as therapeutic measures in eclampsia. Veit (1887) emphasized the repeated use of Morphine in eclampsia. Halberema (1878) first suggested the use of Caesarean section in the treatment of eclampsia, and Saenger (1882) emphasized antisepsis with this procedure. In 1896, Dührssen introduced his modification of vaginal hysterotomy, first used by Lauverjat in

1788. In 1897 Von Vaquer reported that the blood pressure was increased in eclampsia. Krönig (1904) employed lumbar puncture, with improvement after withdrawing 10cc. of fluid. Stroganoff (1900) and Tweedy (1910) laid the foundation of more modern methods of treatment. Titus (1919-1927) introduced hypertonic intravenous glucose injections to protect the liver and induce diuresis.

The use of Magnesium Sulphate by injection came into general use after 1925, following emphasis of its use by Lazard, Allen and Lincoln (1925 and 1926), and barbiturates were introduced by Robbins and his Co-workers in 1929.

Deham 1768, Boër 1791, Löhlein and Virchow wrote about the morbid anatomy, but the pathology of eclampsia was studied accurately only from 1890 onwards by Pilliet, Lubarsch, Schmorl, Volhard, Fahr, Williams, Opie, Bell and others.

There is no doubt then that the toxaemias of pregnancy of all types must have been a very important cause of maternal and foetal deaths throughout the ages.

CHAPTER 2.

THE HISTORY OF THE TOXAEMIAS OF LATE PREGNANCY WITH SPECIAL REFERENCE TO SOUTH AFRICA.

Specific medical writing in South Africa dates back to the year 1847, and the information of earlier times must be treated with reservation.

In spite of the fact that Johan van Riebeeck, the founder and first governor of the Cape, was a ship's surgeon and his wife gave birth to a child a year after his arrival in 1653, nothing was written about pregnancy and its complications, primarily because he was occupied with administrative duties, scurvy and dysentery epidemics (Dagverhaal van Jan van Riebeeck, Archives, Cape Town), and secondly because it was not until 1663 that medical men started to do midwifery in earnest. This was the year when Louis XIV of France called Dr. Clement, the Court Physician to attend Madame De la Valliere in confinement, and only subsequently midwifery books were published by Mauriceau and Jane Sharpe, who emphasised that eclampsia improved with delivery (Gericke 1923).

After an extensive search in the Archives, Cape Town, I came across specific mention in a list of death notices of a case of "stuiptrekkings" which was then the name of eclampsia as opposed to "vallende ziekte" (epilepsy), which is mentioned as a separate cause of death in another instance. However, the causes of death are inaccurate, as can be seen from the following list obtained from Archives Documents Ref. 16/143 and 16/144 dated 1794:-

"Ambye" (Haemorrhoids).
"Koorsziekte" (Fever Illness).
"Stuiptrekkings" (Eclampsia).
"Beroerte" (Stroke).
"Engelse Ziekte" (English Disease).

"Tering"./....

"Tering" (Tuberculosis).

"Ouderdom" (Old Age) etc.

The report of the gravedigger at the Castle was of no help, neither was a treatise on the public health service of the Netherlands East India Company 1600 - 1900 (D. Schoute 1937) about the incidence or occurrence of eclampsia. Here it is mentioned that the native populations at the Cape and Batavia looked upon childbirth as a natural phenomenon which did not require treatment, and in complicated cases the priest only was consulted. If his assistance failed, they were quite content to acquiesce in the will of Allah. This naturally refers to the slaves, the ancestors of the Cape Malays.

Neither Thiel's 37 volumes nor Leibbrandt's Precis give any information with regard to eclampsia. However, the Cape Town Medical Gazette 1847, the first medical journal ever published in South Africa, does mention eclampsia as occurring in South Africa.

In this regard the editor, Dr. Ebden, discussing indigenous plants and remedies used by the colonists, mentions the Klipdas "Hyraceum", and states that its dried urine resembling bitumen, found on the rocks near caves as an evaporated, tenacious, sticky residue, hardened and mixed with earth and dirt, is made use of therapeutically as an extract by mouth in cases of hysteria "opwerkinge", epilepsy "vallende ziekte", eclampsia "stuiptrekkinge", St. Vitus Dance "spelde ziekte" or "toverziekte", and in short spasmodic affections of many kinds. The editor seriously mentions this as a possible article of export (Dasjespis), as the "dassie" apparently urinates on the same spot always, and so the article can be collected readily.

A letter in this journal discussing midwives, reflects that they did all the midwifery at this time, and were all untrained, and there were no hospital facilities for the lying-in period.

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Of interest is the fact that in 1870 the whole of the Cape Colony had only 60 doctors, and in 1886 an average country doctor dealt with as few as 20 midwifery cases a year, the rest being done by midwives. In 1894 the births per annum in Cape Town were 2,000. There could therefore not have been very many cases of eclampsia as the incidence of eclampsia in Europe was 1 in 500 at this time. However, (Beck 1894) mentions in his B.M.A. presidential address that an active medical society existed at the Cape between the years 1827 - 1847, and at their meetings eclampsia was discussed on two occasions, one case being fatal, the other recovering after severe purgation and stimulation with alcoholic beverages. The medical society was dormant between 1847 - 1890.

The first case of puerperal eclampsia was recorded in the South African Medical Journal in March 1895 by Dr. Strachan of Germiston. A single primipara not in labour was delivered by accouchement forcé and pilocarpine injections, and took 16 days to regain her memory. In 1896 Dr. Mc Gowan-Kitching writing in the South African Medical Journal, discusses cases of albuminuria without fits. This is the first time that the non-convulsive toxaemias of pregnancy are mentioned.

In Knysna there were five cases of eclampsia and three cases of severe albuminuria in the five year period 1901 - 1905 amongst 1,500 inhabitants (Marr 1905). From this time onwards case reports of fulminating eclampsia, post-partum eclampsia, etc., appeared from time to time in the South African Medical Record, Transvaal Medical Journal and South African Medical Journal. In 1907 at the Medical Congress in Bloemfontein, Caesarean Section and renal decapsulation in eclampsia were discussed (Klots 1907, quoting Ediballs - 1903).

The first case of placenta praevia complicated by eclampsia was reported in 1911 and a case of pyelonephritis and pregnancy, as well as the use of Veratrone in puerperal eclampsia were dis-

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cussed by Beck and Bruce Bays in 1913. An extensive discussion of eclampsia occurred at the Kimberley Medical Congress in 1914 (Thwaits 1914), and it was pointed out that up to this time, whereas interest had been centred around the kidney, the placenta and ductless glands were becoming more suspect, because the kidneys were often normal, and eclampsia occurred in women with no previous renal disease. Cases of Brights disease were recalled who, without active treatment, did not develop eclampsia. Eclampsia was more common in twin pregnancies, fits were rare before the fifth month, and expulsion of the foetus was noticed to have a favourable effect on the eclamptic attack. The general impression was that about 5% of pregnant women developed albuminuria, probably due to pressure on the ureters, that being the reason why termination had a favourable effect. A statement was made that the kidney of pregnancy is a transitory condition, and what damage such kidneys may suffer, is subsequently rectified after termination. The maternal mortality was 26%, and the infant mortality 50% according to German figures quoted at the time of the Congress. With regard to treatment, sedation, promoting excretion and removing the fountain source of poison, (the child and placenta) was stressed. In addition the use of Pituitrin to induce labour, Magnesium Sulphate by injection as a sedative, and Nitro Glycerine and Veratrium Viride to lower the blood pressure were advocated (Congress Notes 1914).

Malan (1928) mentions the immense volume of literature since 1843 on albuminuria and eclampsia, the diseases of theories, and puts forward his personal theory that whatever the real origin of the toxaemias, miscegenation plays an important role in bringing about the tendency to toxaemia in pregnant women, as with the mixing of the races, the foetus is a foreign element with different bloodgroups from the mother.

Crichton (1929) found the maternal mortality from eclampsia to be 20% at the Peninsula Maternity Hospital, in Cape Town and

stressed the importance of antenatal care and clinics, which had already been inaugurated in 1920 by the Cape Town Municipality.

Crichton (1932) collected 125 cases of eclampsia amongst the Peninsula Maternity Hospital admissions in the years 1927-1931, and states that eclampsia is an extremely common condition in Cape Town, with a 22% mortality. He pointed out that rapid changes of temperature, by preventing efficient action of the skin, led to an additional burden on the kidneys, and was responsible for the seasonal incidence of eclampsia in Cape Town in August, September and October.

Goldberg (1935) gave a statistical survey of local cases in Cape Town at the Peninsula Maternity Hospital - 216 eclamptics amongst 8,537 admissions between 1925 and 1934, with an incidence of 2.6%, that is 1 out of 39.4 deliveries, and pointed out that at the time the Peninsula Maternity Hospital was the clearing-house of the bulk of abnormal cases occurring in and around the Peninsula amongst a total population of 250,000. He again stressed the seasonal incidence of eclampsia locally with a peak in August, and gave the same explanation as Crichton for this seasonal incidence.

Crichton (1935) states that he doubts if there is another city in the world where the incidence of eclampsia is as high as it is in Cape Town, and if eclampsia is prevalent, he considers that cases of pre-eclamptic toxaemias should also be prevalent.

Simpson Wells (1935) quoting figures from the St. Monica Home, Cape Town, from 1917 - 1935, found 40 cases of eclampsia amongst 5,404 deliveries, that is 1 in 135 with a 15% mortality. This illustrates the marked variation in the incidence of eclampsia in two maternity hospitals in the same city during the same period.

More./.....

More recently Black (1938), te Groen (1941), Helman (1940), Sapieka (1945), Ordman (1950) and Crichton (1947 and 1952) have written about some aspects of the toxaemias of late pregnancy in South Africa. Ordman (1950) stressed the role of water and electrolyte balance and observed that the behaviour of the patient with regard to elimination of ingested fluid is the best criterion for the diagnosis of pre-eclampsia. He puts forward the suggestion that pre-eclamptic toxaemia is a disease of adaptation and advocates the use of Cortisone-like substances in treatment. (A preliminary report).

Crichton (1949) at the "Transactions of the Rotunda Hospital Bicentenary International Congress" restated that eclampsia and other toxaemias of pregnancy are prevalent in Cape Town. He found the incidence of eclampsia to be 2.1% from 1925 - 1934 and from 1937 - 1947 to be 1.8% at the Peninsula Maternity Hospital. He quoted figures indicating that the incidence of eclampsia in the coastal towns is high, and that the only common factor was a deficiency of calcium in the soil and water. On the other hand in the inland cities the incidence is low where there is no such calcium deficit. He found that with better antenatal care and treatment the mortality of eclampsia had declined from 20.7% over the period 1925 - 1934 to 8% over the period 1937 - 1947, in Cape Town at the Peninsula Maternity Hospital. In addition Crichton stated that 94 - 95% of women who have had eclampsia with their first pregnancy either recover completely or the evidence of vascular or renal damage is not sufficient to contra-indicate further issue. On the other hand the outlook for multiparae is not so bright, particularly those over 30 years who have had several pregnancies. All cases should be assessed at least 6 months or longer after the attack before further pregnancy is allowed. He thinks that an interval of two to three years should be allowed to elapse before the next pregnancy. In addition he emphasized the use of conservative treatment and Caesarean section only under special circumstances in the treatment of eclampsia.

CHAPTER 3.

A CRITICAL HISTORY AND REVIEW OF THE THEORIES OF THE ETIOLOGY AND PATHOGENESIS OF ECLAMPSIA AND THE TOXAEMIAS OF LATE PREGNANCY.

(A Brief Summary).

Sweifel (1904) called the toxaemias the diseases of theories and this is still true today. Eclampsia is a diseased condition limited to the human race and not found in animals except under experimental conditions.

In the 17th and 18th centuries eclampsia was regarded as a disorder of the nervous system. Merriman (1820) regarded eclampsia as an overloaded state, while Wilson (1833) thought it to be a form of Uraemia, which was strengthened by the finding of albuminuria by Rayer (1840), Lever (1843) and Simpson (1843). This was re-emphasised by Frerichs (1851). C. Schroder (1876) stated that eclampsia was due to Cerebral Anaemia, the result of arterial spasm.

Theories seem to be evolved pari-passu with the discoveries in other fields of medical science, and emphasis on pathological changes has shifted from the kidneys to the liver, placenta and endocrines. Thus around 1850 it was thought to be a type of Bright's disease. Then with the advent of bacteriology it became looked upon as an infectious disease, later allergic, then biochemical, nutritional and finally hormonal. The infective theory of Delore (1884) was based on the presence of pyrexia with eclampsia, and the occurrence of epidemics of cases. Talbot (1923) and Toombs (1932) found a high incidence of dental sepsis which they considered might cause placental infarction. In addition the toxins of the bacteria cause convulsions by acting on the sympathetic nervous system, thus lending support to the theory of Delore.

Next came the auto-intoxication theory of Bouchaard (1887),

later./...

later denied by the experiments of Lash and Walker (1909). The allergic theory of Veit (1902) supported by Weichardt (1903) and substantiated by the experimental work of Rosenau and Anderson (1908), was disproved by Johnston (1911), who thought that anaphylaxis played no part in the toxaemias of pregnancy.

Other observers also regarded the foetal elements to be causative as did Veit, but not through an allergic mechanism, but possibly by being toxic through autolysis on the maternal liver and kidneys (Hull and Rohdenberg 1914). Still others blamed foetal metabolic products, for example Fehling and Dienst (1902), as death of the foetus in utero or delivery cured the eclampsia. However, eclampsia can be cured with the foetus still alive in utero and sometimes although the foetus is dead for some time, toxaemia does not clear up until delivery. Also toxaemia and eclampsia occur in the absence of a foetus in cases of hydatidiform mole. (Powilewicz 1924).

The intestinal toxin theory of Tweedy or the Dublin theory (1913), subsequently supported by experimental work on dogs done by Dieckmann, states that protein poisoning may result during pregnancy due to changes in the mucosa and absorption of unsplit proteins. This theory has led to the use of the low protein diet in the treatment of the toxaemias.

The placental toxin theories come next. According to Browne (1951) there is much to be said for the assumption that if a toxin of some kind is the cause of eclampsia, its source is primarily in the placenta. More than 8 cases of eclampsia with hydatidiform mole without a foetus have been reported (Stander 1929). Usually there is a rapid subsidence of toxaemia after foetal death in utero, again pointing to the placenta. Young (1914) put forward the view that the toxaemias of pregnancy, albuminuria and eclampsia are due to placental infarction with autolysis, the result of interference with the blood supply.

Probably./...

probably due to toxins, and the toxic products of autolysis affect the liver and other organs. In the cases where the placenta is without obvious infarcts, minute areas of necrosis are present and give rise to sufficient toxin to produce the disease. Young has more recently (1927, 1937 and 1942), in a search for the factor that might lead to placental damage, studied the reproductive histories of 220 patients with pregnancy toxaemia, and concluded that "women with an eclamptic history commonly have resident in their bodies some morbid influence which is not inconsistent with good health between their pregnancies, but which is inconsistent with the normal continuance of pregnancy to term". Many such damaged pregnancies end in abortion, some end in premature birth or stillbirth, but only in comparatively few does this constant and imminent X-factor or abortion factor end in a toxaemic attack. The factor is not, he believes, a low reserve kidney or a chronic nephritis., Evidence is adduced for the view that it is an endocrine disturbance, or possible Vitamin E, which causes an upset in the prolan-progesterone mechanism, and that it acts by interfering with the maternal circulation in the placenta, leading either to placental infarction or to retroplacental haemorrhage or both. Against this is the fact that toxaemia does not occur in threatened abortion or in experimental placental separation in dogs (Theobald 1930). Furthermore many observers have failed to confirm Young's observations and views. Bartholomew et al (1932, 1934 and 1936) claimed that hypercholesterolaemia of pregnancy due to hypopituitary or hypothyroid activity and enhanced by a rich cholesterol diet is the cause of toxaemia by excessive cholesterol storage in the placental villi and resulting endarteritis and infarction. This is precipitated by foetal movements which leads to trauma, thrombosis or rupture of the foetal arteries. However, this theory is unlikely as the epithelium covering the villi is nourished by the maternal blood.

The placental infarction theory has possibly more recently gained support from the crush syndrome with renal tubular necrosis (Bywater and Dible 1942), but the clinical picture differs

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from eclampsia.

Ninian Falkiner (1950) in the Ciba Foundation Symposium again stressed the high incidence of placental infarcts in toxaemias of pregnancy and supports Young's contention that these are due to changes in the maternal circulation rather than the foetal circulation, but infarction need not be associated with eclampsia and the type responsible is an acute infarction, the result of spasm of the "utero-placental" arteries. In the nephritic toxaemia on the other hand the infarcts are chronic. He feels that the predisposing cause to infarction is a failure of the development of the "utero-placental" arteries in undernourished, overworked multiparae. Steigrad (1952) is also a protagonist of this theory while Montgomery (1953) feels that there is no relationship between the toxaemias and placental infarcts.

According to Dieckmann (1952) the occurrence of toxaemia in patients with hydatidiform mole where there are no foetal vessels to thrombose and where infarcts such as are found in the placenta do not occur, offers the best evidence against placental infarcts as the cause of toxaemia.

Placental ischaemia with the production of pressor substances like the Goldblatt Kidney was put forward by Page and Ogden (1939) as a possible cause, and he believes that ischaemia leads to premature senility and degeneration of the placenta, and so produces toxaemia; for instance in Hydatidiform mole with rapid growth it outstrips its blood supply. Possibly this mechanism also applies in multiple pregnancies. Beker (1948) and van Bouwdijk Bastiaanse and Maatboom (1949) have done work suggesting that ischaemia of the uterus and placenta can cause hypertension and confirm the views of Page.

The next theory, the water poisoning theory of Zangemeister (1915) states that a toxin produces water retention by increasing capillary permeability with oedema of the brain, anaemia and

convulsions./....

convulsions, and a secondary rise in the blood pressure from increased intracranial pressure, and ischaemic albuminuria. This theory was supported by the work of Rowntree (1923). However, it has been shown that (a) oedema does not always precede hypertension in pre-eclamptic toxaemia and (b) that oedema by itself does not cause hypertension.

Paramore (1929 and 1932), promulgated the theory of increased intra-abdominal pressure during pregnancy, leading to an alteration in the circulation of the liver and kidneys, with degenerative changes as a result. Hence the greater incidence in primiparae, multiple pregnancies and hydramnios. However, this is disproved by normal renal bloodflow in the toxaemias, and often with death of the foetus in utero without an appreciable change in girth, the toxaemia abates.

Peters (1936 - 1938) claimed pyelitis and pyelonephritis as important factors in the causation of pre-eclampsia and eclampsia. This has not been substantiated by other observers.

Theobald (1930) advanced the hypothesis based on experimental work with dogs that all major and minor toxaemias of pregnancy are expressions of dietetic deficiency, and may be regarded as relative deficiency diseases. A diet apparently adequate for the mother is no longer adequate for the mother and foetus, especially regarding vitamins, minerals and, most important, calcium. Against this theory is the fact that in the first World War, the incidence of eclampsia fell in Germany, in spite of an underfed population (Baader, 1939). A decreased meat, fat and cholesterol consumption and hard work by the women in the open air and sunshine were said to be the factors. In Holland and Belgium (1939 - 1945) a marked drop in the incidence of toxaemias occurred with an average intake of 800 calories per day (Smith 1947). In Denmark a similar fall in the recent war was attributed to a decreased incidence of primaparae (Hubinant, Holmer and ten Berge, 1947).

Theobald./....

Theobald, Mendenhall and Drake (1934) have shown by experiments on pregnant women, that a lack of calcium and vitamin B and D may be a factor, yet women with osteomalacia have not been found to show a higher incidence of toxaemia. Minot and Cutler (1928) found dogs, and Theobald found cats, highly susceptible to carbontetrachloride poisoning on a calcium deficient diet.

Gordon King (1940) showed that eclampsia is common in regions of the world where the incidence of Beri-Beri is high, e.g. China, Japan and Phillipine Islands, thus relating toxaemias to a vitamin B deficiency.

Nixon, Wright and Feiller (1942) found that in eclampsia the amount of vitamin B_1 excreted in the urine on admission to hospital is significantly lower than in normal pregnancy, and that the concentration of vitamin B_1 in the placenta is also significantly below that of the placenta of normal patients.

Browne (1943) found no diminution of the incidence of toxaemias by giving vitamin B Complex to pregnant women, confirming the findings of Ross and others (1938).

A more recent view held is that protein tends to protect against the advent of toxaemia, and Strauss (1935, 1937 and 1939) believes that inadequate protein intake, especially with the increased demands of pregnancy, leads to oedema and pre-eclampsia. He found that toxaemia cases improved on a high protein diet. The work of Bibb (1941), Davis and Whipple (1918) Goldschmidt, Vars and Ravdin (1939), Himpsworth and Glynn(1944) tend to support Strauss' views, but does not explain the hypertension in toxaemia.

De Snoo (1938) emphasized the importance of a salt free diet in the treatment of pre-eclamptic toxaemia, and the prevention of eclampsia by disallowing patients foods with a high salt quality and content.

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In the People's League of Health experiment, (London 1938-1939), it was claimed that women receiving special supplementary diet are protected against the risk of toxaemia (Lancet 1942).

The Toronto experiment in 1941 by Ebbs, Tisdall and Scott on women with varied diets showed (a) that during the course of pregnancy the mothers on a good or supplemented diet enjoyed better health, had fewer complications and proved to be better obstetrical risks than those left on a poor prenatal diet.

(b) The incidence of miscarriages, stillbirths and premature births in the women on poor diets were much higher. The experiment was done on a small group of women and all authorities feel that many more large scale, carefully planned and statistically controlled experiments are necessary, before final decisions can be made on the effect of diet, and its relations to the disorders of pregnancy.

The possible role of the endocrine glands has received more and more attention in the last twenty years. Erdheim and Stumme (1908) found the pituitary enlarged in normal pregnancy, and Hofbauer (1918) suggested that the secretion of the posterior lobe might be the cause of the toxaemias of pregnancy. In 1932 Anselmino, Hoffman and Kennedey claimed that hyperfunction of the posterior pituitary gland was the cause of water retention, oedema, capillary spasm, a rise of blood pressure and toxic albuminuria. Their conclusions were based on experiments on rabbits and pregnant females, and they demonstrated anti-diuretic and pressor substances in the sera of toxaemic patients. This work was not confirmed by Hurwitz, Bullock or Levitt (1936). Cushing (1932) also noted basophilic infiltration in the pituitary in eclampsia, but Biggart (1934) and Rasmussen (1936) found this in all pregnant women. Byrom (1938) produced lesions in Albino rats closely resembling those of eclampsia by injecting vasopressin and believed the lesions were due to arteriolar spasm. The sensitivity of the rat to vasopressin could be increased tenfold by preliminary oestrogen therapy and inhibited by simultaneous progesterone./.....

progesterone therapy. If the hypothesis of vascular spasm is accepted, then either some unknown pressor agent is concerned or the vessels must become hypersensitive in some way. That the vascular system is sensitized in women with pre-eclamptic toxaemia was shown by Shockaert and Lambillon (1937) and Dieckmann et al (1938). If a pressor substance e.g. pituitrin or tonephin is injected intravenously into normal pregnant, non-pregnant and women with pre-eclamptic toxaemia, the mean rise of systolic blood pressure is much greater in the latter group. This abnormal sensitivity has been shown to be acquired between the seventeenth week and the usual time of occurrence of pre-eclamptic toxaemia (Browne 1946). Its cause is unknown and efforts to reproduce it have not been consistently successful. Addis (1937) regards angiospasm as the common pathogenic factor underlying all the various expressions of eclampsia, causing in the brain hypertensive encephalopathy, in the kidney albuminuria and oliguria, in the liver peri-portal necrosis, and oedema in the subcutaneous tissues. He states that the cause of the angiospasm is unknown, but in his opinion it is not due to obstruction in the renal circulation. More recently Brill et al (1952) have used the Krasno-Ivy nitroglycerin flicker fusion threshold test to demonstrate retinal vasospasm in the toxaemias of late pregnancy and claim that they can distinguish such cases before other signs are evident, by means of this photometer.

However, Marty and Hardy (1952) and Rugart (1953) do not think this is such a useful instrument because of many normal variants and pitfalls in its use.

Chesley et al (1939-1940), by producing sudden vascular constriction by immersing the hand in ice water invariably produced albuminuria when the systolic blood pressure rose 16 mm. or more, and Dill and Erikson (1938) by artificially constricting the renal artery in pregnant dogs and rabbits produced a rapidly fatal eclampsia-like syndrome, with pathological lesions in the liver and kidneys, resembling human eclampsia, and not readily

reproducable./....

reproducable in non-pregnant animals. Subsequently, Goldblatt et al (1934), Page and Ogden (1939) and Corcoran and Page (1941) experimented on the lines of renal ischaemia with a pressor substance production affecting arterioles and arteries. However, this is unlikely to be causative, as it has been shown that in normal pregnancy and in pre-eclampsia, the renal blood-flow is normal (Chesley, Connel et al, 1940).

Kellar and Sutherland (1941) proved that the pressor mechanism in pre-eclamptic toxaemia is humoral and not nervous. The suprarenal gland has more recently gained prominence amongst the possible etiological factors with the discovery of Cortisone and A.C.T.H. and extensive research work in this direction, since 1944. The suprarenal gland plays an important part in the regulation of water balance, mineral, carbohydrate and protein metabolism, and normally hypertrophies during pregnancy, and may play a role in the pigmentation, chloasma uterinum.

Perebee et al (1939), treating cases of Addison's disease with D.O.C.A. found striking salt and water retention and a rise in blood pressure within two to four weeks, with clinical oedema. Tobian (1949) found that pregnant women with toxaemia and excessive oedema excreted about 46% more corticosteroid than pregnant women with little or no oedema. Selye and Hall (1943) found that following the administration of sodium chloride to rats treated beforehand by the administration of D.O.C.A. there is a more significant rise in the concentration of chlorides in the brain and blood than in the animals not thus treated. Thus at least part of the salt is retained in the brain, but we do not know if this could be a cause of motor disturbances in human beings. ten Berge (1947) thinks this may be a factor in eclamptic cases.

Rodbard and Freed (1942) showed that daily injections of D.O.C.A. into normal spontaneous hypertensive and "Goldblatt" hypertensive dogs led to a rise of bloodpressure in nine out of

twelve./.....

twelve cases. In some the hypertension remained for a considerable period, in others it fell rapidly or slowly to normal. However, as Swingle pointed out in 1944, one should be cautious in the application of physiological data obtained from the use of synthetic D.O.C.A., which is not elaborated in significant amounts by the adrenal cortex. On the other hand Perera (1952) has shown that Cortisone and Hydrocortisone have many similar affects to D.O.C.A.

Fauvet and Münzer (1937) reported that the adrenals were small in fatal eclampsia and 50% of pregnant women had an increase of corticotrophic hormone using Jore's biologic hormone test. They concluded from their studies that the hypertension of pre-eclamptic toxaemia is not caused by an excess secretion of the adrenal gland. Smith and Smith (1941) confirmed that the adrenal glands are small in eclampsia, but postulated cortical exhaustion in this condition. Macchiarulo (1952) found eclamptic women had a definite hyperadrenalaemia and he thought this was partly responsible for the symptoms of eclampsia. Hofbauer (1952) regards nor-adrenaline as the powerful over-all constrictor in toxaemia of pregnancy, and feels that it is produced by the Frankenhauser plexus adjacent to the enlarged uterus and acts as an accessory adrenal medullary formation.

Devis et al (1950) found a very high excretion of corticosteroids in pre-eclampsia and eclampsia, especially during the convulsions, and refers to Selye's adaptation syndrome, and suggests a similarity between the symptoms of eclampsia and D.O.C.A. intoxication. Selye (1946) carried out numerous experiments which showed that sudden or chronic exposure to stress such as cold, injuries, infection, chemicals and nervous strain etc., elicited a reaction of alarm followed by an adaptation syndrome with enlargement of the adrenal cortex and an increase in its hormonal output. This may be a defence mechanism to raise resistance to stress, but detrimental side effects may occur due to the inherent toxicity of the corticoids. It was

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It was a defence reaction which partly defeated its own purpose. Selye showed too that overdosage with salt active corticoids cause sodium retention, hyperchloraemia, hypopotassaemia and hypertension especially if the salt intake is not restricted. Was it then possible that pre-eclampsia was the result of a derailed or excessive adaptive reaction on the part of the adrenal cortex in producing disproportionate amounts of salt active corticoids? Selye in 1949 found the glucocorticoid compound E and indirectly A.C.T.H. to have an inhibitary action on the salt active corticoids. Reichstein's compound S, the naturally occurring corticoid corresponding to D.O.C.A. has been shown by Selye (1950) to be highly active in the production of a raised blood pressure and other changes like the toxic affects of D.O.C.A. Selye and others (1950) have suggested that pre-eclampsia and eclampsia may be diseases of adaptation. Thus, although it seems possible that the adrenals are possibly involved in the toxaemias, the exact mechanism is at present unknown.

More recently the theory of a placental production of hormones with an adreno-cortico-steroid structure in toxaemic cases, has been shown to be extremely likely, especially if the blood supply of the placenta becomes insufficient (Westboom 1952).

The thyroid gland has been blamed (Kustner 1933), as hypothyroid states may be associated with oedema and haemo-concentration somewhat resembling the toxaemias. Thus thyroid medication has come into use in the therapeutic regimen of the toxaemias.

Removal of the parathyroid glands (Davis 1950) in pregnant animals, with forced protein feeding, caused lesions of the liver resembling those of eclampsia, and Brougher (1942) used parathyroid extract with success in reducing oedema and relieving the symptoms of pre-eclamptic toxaemia.

Smith and Smith (1933, 1934, 1935, 1937, 1939, 1940 and 1948) reported abnormally high levels of anterior pituitary-like

hormone./.....

hormone in fact chorionic gonadotrophins in the serum and urine of patients with pre-eclampsia and eclampsia, and a diminished blood oestrogen and progesterone leading to hormonal imbalance. This has been confirmed by Govan (1952). Other observers have not had the same results and therapy with these substances have not changed the course of the toxaemias. (Taylor 1942). Greenhill (1953) states increased serum gonadotrophins is merely an indication of pituitary hyperactivity and not conferred to toxaemic pregnant women. Smith and Smith state that the explanation of excess A.P.L. in toxaemia is due to failure of utilization of the hormone in the production of progesterone and oestrogen due to syncytial degeneration and its accumulation in the blood. The resulting decidual regression leads to toxic absorbtion and to toxaemia. Also gonadatrophic hormone is able to sensitize rats to vasopressin, and in this way act as a factor. G. Smith (1950) still concludes that products of decidual regression are the final etiology of the toxaemias of pregnancy due to the above mechanism, and advises stilboestrol therapy as a preventative measure in the toxaemias. In more recent years the Smiths have observed a toxic englobulin occurring in the menstrual discharges and in the blood of menstruating and toxaemic women, with a marked fibrinolytic activity. They postulate that the toxaemias of late pregnancy might therefore be due to a withdrawal of hormonal support resulting in the elaboration of the toxin, possibly the result of placental ischaemia. This toxin causes the generalized vascular damage found in the toxaemias (Smith et al 1945). This is called the menotoxin theory, but as Stander (1949) stated it is still based on speculation.

Many workers have from time to time put forward the view on theoretical grounds that organic poisonous substances cause eclampsia. Guanidine and methylguanidine, physiological calcium antagonists, are found in increased amounts in the blood in renal insufficiency and are said to be toxic to the liver, with pressor effects. (Major 1926 and Major and Weber 1927). They lead to

hypoglycaemia, and in dogs to convulsions. They were therefore thought to be etiological factors. It was shown that the blood-guanidine level is raised in the toxaemias of pregnancy and even higher in eclampsia. Minot and Cutler (1928) found the increase in guanidine always followed the rise in blood pressure and so could not be its cause. This formed the basis of calcium therapy in the toxaemias (Malmèjac 1931), but Stander (1933) felt there was no justification for its use. This was further supported by the experimental work of Krieger in 1934, who failed to confirm the previous work on guanidine. On the contrary he showed that calorimetric methods of bloodguanidine estimation used were inaccurate, and that the blood level was normal in toxaemia cases.

As an etiological factor acute histamine or histidine poisoning was put forward by Hofbauer (1926) but denied by Best and MacHenry (1931) and thought unlikely by Kapeller-Adler (1941) and Potter (1929). Johnson (1940) attributes to tyramine a leading role in eclampsia and showed that injections into the portal vein produces liver necrosis. However, Goldring, Chassis, Ranges and Smith (1941) feel that it is an unlikely cause as it produces spasm of the efferent glomerular arteries which is not found in pre-eclamptic toxaemia.

A constitutional predisposition to eclampsia was first mentioned by Boër in 1791 (Weiss 1943), who lost one of the Grand Duchesses in eclampsia when physician to Emperor Joseph II of Austria. She had thick bones and a robust musculature. Ayman (1933) found indications that hypertensive subjects tend to have increased psychomotor activity with a large and steady output of energy. Vorzimer et al (1937) found a high incidence of short, thick, stocky habitus in toxaemia cases, acromegalic features, abnormal hair distribution, android or anthrapoid pelvis and a low B.M.R. Maltby and Rosenbaum (1942) claimed that 77% of eclamptic women had electro-encephalographs indicative of cerebral dysrythmia and 58% gave a family history of convulsive seizures.

Icenhour et al (1942) found that toxaemia of pregnancy occurs mainly in women whose vascular systems are endowed with a tendency towards hypertensive disease, and the cold pressor tests was introduced by Hines and Brown (1935) to pick out these cases. However, the results of the use of this test are inconclusive (Dieckmann (1952), Reid and Teel (1938).

The Rh. factor has been put forward as a cause by Javert (1942), Schwartz and Levine (1943) but how does this explain toxaemia and eclampsia in hydatidiform mole without a foetus. Furthermore iso-immunization can probably be ruled out as an etiological factor since Hurst, Taylor and Wiener (1946) found no significant difference in the incompatible blood groups in infants of mothers with toxaemia, from those of mothers without toxaemia, and no correlation between toxaemia and Rh. incompatibility.

The Fibrin Embolism theory (Schneider 1947) making the placenta and its extracts a mediator of the pregnancy toxaemias is still under investigation but cannot yet explain all the signs, symptoms and effects of the toxaemias (Schneider 1950).

A number of workers have attributed eclampsia and pre-eclamptic toxaemia to abnormalities in the haemodynamic balance (Becker, Page and others already referred to). Kellogg (1945), Newell and Smithwick (1947), Peet and Isberg (1949) have recorded successful pregnancies following lumbar-sympathectomy in hypertensive cases. Theobald (1953) introduced denervation of the internal iliac vessels to improve the blood supply of the uterus and to cut off afferent and efferent nervous impulses to and from the uterus via the sympathetic nerves, thus preventing toxaemic symptoms in succeeding pregnancies. Part of his reasons for this was based on the hypothesis of Franklin and Sophian (1949) Franklin (1951, Sophian (1953). This hypothesis, based on the Trueta mechanism of renal shunt, states that toxaemia of pregnancy is or includes a progressively increasing tendency for the renal

shunt./.....

shunt to be brought into operation and that fatal bilateral cortical necrosis is the maximal irreversible result of this tendency. This is the most recent theory, and like all other preceding theories is to my mind not watertight, being unable to explain many biochemical changes and features, such as the occurrence of postpartum eclampsia and eclampsia in multipara, etc.

Mc Kay et al (1953) feel that the basic pathologic physiologic process that is at fault , is the same in eclampsia, bilateral cortical necrosis, pituitary necrosis and other fatal complications of pregnancy. This is thought to be due to a sudden intravascular deposition of fibrin, caused by a mechanism similar to the generalised Schwartzman phenomenon in experimental animals, with resulting fibrinogenopenia and fibrinolysins in these cases. The toxin which causes this is similar to the menstrual toxin described by Smith et al (1945). This theory has still to be tested.

After a brief consideration of all the theories it seems that there are many possible etiological factors, some predisposing and others causing the toxaemias, and that any one hypothesis fails to explain all the facts. It seems that the toxaemias are diseases of multiple etiology. The exact way in which the puzzle fits together is far from solved and will entail a great deal more of research work by teams of obstetricians, physicians, biochemists, endocrinologists and others. The final history of the etiology of the pregnancy toxaemias has still to be written and the most important purpose all the theories serve is as working hypothesis to be tested by experimental work.

In conclusion I think a quotation by the famous neurologist Hughlings Jackson can be aptly applied:-

> "We have multitudes of facts, but we require organization of them into higher knowledge".

CHAPTER 4.

A REVIEW OF THE LITERATURE WITH REGARD TO FOLLOW-UP STUDIES TO ELUCIDATE THE RENAL AND VASCULAR EFFECTS OF PRE-ECLAMPSIA, ECLAMPSIA AND OTHER TOXAEMIAS OF LATE PREGNANCY.

The question of the remote sequelae of the toxaemias of late pregnancy has long attracted attention. Schroeder (1878) first called attention to the frequency of renal lesions after eclampsia, and since then many workers have emphasized renal damage in the toxaemias of pregnancy. Meyer and Weiz (1904) stated that in 35 autopsies on eclamptic patients chronic nephritis was found in 8%. Le Page (1912), Slemons (1913), Gibson (1921) emphasized the frequency of chronic nephritis following eclampsia, and stated that at that time many believed eclampsia and pre-eclampsia conferred an immunity on the kidney in subsequent pregnancies. Slemons and Gibson first recognized the fact of recurrence of toxaemia. Slemons found one in six patients had recurrence of albuminuria. Gibson found chronic nephritis in 5 out of 14 eclamptics and 2 out of 12 pre-eclamptics. Both these authors noticed that even if the blood pressure were normal, and the urine albumin free, it was no criterion of the non-occurrence of toxaemia in a subsequent pregnancy.

Harris (1924) reported a series of 177 women with 218 pregnancies followed up for periods up to 4 years. He found that of 55 cases of pre-eclamptic toxaemia returning for re-examination after one year, 33 or 60% had chronic nephritis and of 27 eclamptics only 3 had chronic nephritis, that is 11%. He pointed out that this was an unexpected finding, as the "hitherto regarded less serious condition is more important in producing renal lesions". He thought the reason for this might be that probably at least two entities were grouped with pre-eclampsia because of faulty methods in diagnosis. The one he

thought./.....

thought to be a forerunner of eclampsia, and if no eclampsia occurs, the prognosis is good; the other being a larval form of chronic nephritis. He distinguished nephritic toxaemia, and mentions that in this condition the complications make themselves manifest in increasing severity and at an earlier period in each succeeding pregnancy. He also stated that with regard to pre-eclampsia and eclampsia the absence of signs of nephritis three weeks after delivery in no way precludes the possibility of permanent renal damage. He deduced that if the symptoms of pre-eclampsia and eclampsia had lasted for more than 4 weeks before delivery, the incidence of chronic nephritis was much higher and so the chance of chronic renal damage was probably increased by allowing the pregnancy to continue too long. Since then a number of papers by various authors have amplified and confirmed Harris's findings viz., Caldwell and Lyle (1921), Dewesselow (1922), Kellogg (1924 and 1931), Peckham (1929), Sym (1929), Young (1929), Gibberd (1928, 1929 and 1931), Berman (1930), Peckham and Stout (1931), Acosta-Sison (1931) and others.

Subsequently other views have been evolved regarding the sequelae of the toxaemias. First was the emergence of the concept of recurrent toxaemia by Kellogg (1925), defined as the recurrence in more than one pregnancy of some of the symptoms of toxaemia of pregnancy in patients not definitely having chronic nephritis. Kellogg suggested that it might be an indication of faulty renal balance which allowed the patient to live without renal manifestations when not pregnant, but under the load of pregnancy caused her to develop renal insufficiency. He considered that each toxaemia should be looked upon as likely to recur until it is found that the given woman does not belong to the group of recurrent toxaemias by the test of complete pregnancy. He stated that he was not sure whether the condition was a concealed chronic nephritis or that if the patient lived long enough she might not develop a manifest degree of that disease. Gibberd (1928) found that in a series of 37 toxaemic patients who were

believed to be healthy before pregnancy began, in 5 (or 14 %) undoubted chronic nephritis developed as a result, while in 21 patients in whom there was no history suggesting pre-existing chronic nephritis, "albuminuria" recurred in 12 (or 57%) of the cases.

Gibberd adopted the view of Kellogg that in those patients in whom toxaemia recurred, and yet in whom there was no clinical evidence of chronic nephritis, a chronic nephritis of a very low grade existed, which manifested itself when the load of a further pregnancy was added. He expressed the view that pregnancy was one of the most delicate tests of renal function we possess, since an amount of structural damage, insufficient to give rise to signs or symptoms, might yet make itself felt during pregnancy. In 1929 he introduced the term "Occult Nephritis". In the same year Stander and Peckham introduced the term "low reserve kidney" for similar cases, and stressed that, if properly treated, they were not followed by renal damage.

In 1929 Young wrote that the recognition of recurring toxaemia was the most significant addition to our knowledge of the subject in recent years. He could find no evidence that the tendency to recurrence was due to any persistent renal defect. On the contrary, he believed that recurrence was caused by some factor which during pregnancy involved the life of the placenta, tending to give rise to abortion, accidental haemorrhage or toxaemia. The last would occur if the area of placenta damaged was large enough and the placenta retained for a sufficiently long time. He estimated that the recurrence of toxaemia takes place in over 50% of eclamptics and albuminuria patients combined.

Thus amongst the earlier authors the incidence of chronic nephritis following eclampsia was given as anything from 0 to 42 %, and in the nonconvulsive toxaemias from 0 to 74%. As Dieckmann (1938, 1939 and 1952) and Dexter and Weiss (1941 and 1943) pointed out, the term chronic nephritis was used by the obstetricians for many years to designate those patients who

have hypertension and/or evidence of albuminuria on a vascular basis, and was not restricted to what is today called chronic glomerular nephritis. In some instances cases of chronic nephritis prior to pregnancy were included, and in others the follow-up study was not long enough. In still others hypertension with or without nephrosclerosis aggravated by pregnancy was included. Young's theory about recurrent toxaemia, as well as Gibberd's "Occult Nephritis" was not substantiated by definite pathological proof. Gibberd (1928) states that he used the term Chronic Nephritis in the sense of permanent renal damage from any cause.

With regard to Gibberd's statement that pregnancy is the most sensitive test for renal function, the validity of this assumption is in doubt because it is known that even cases of chronic glomerulo-nephritis may sometimes improve while pregnant, albuminuria may diminish, and even temporarily disappear. Also, in cases of essential hypertension the hypertension may remain unaltered, or occasionally diminish and even disappear temporarily during pregnancy in spite of the presence of renal damage (Dieckmann 1953). However, in both conditions pregnancy may possibly lead to an aggravation of the underlying condition, especially in those with renal changes. Such cases end up with cerebrovascular accidents, cardiac accidents or uraemia during or after the pregnancy, or may develop progressive hypertensive vascular disease and even malignant hypertension, as Dexter and Weiss (1943) pointed out. However, it is only those that develop super-added toxaemia or eclampsia that suffer a permanent aggravation of their hypertension and/or renal changes according to Chesley, Annito and Jarvis (1947).

These clinicians were supported by pathologists for instance Meyer and Weiz (1904), who found an 8% incidence of chronic nephritis after eclampsia, and Acosta-Sison (1931), who in 38 autopsies on cases of eclampsia, found chronic nephritis in 38%. They do not list the criteria used for making the diagnosis, and

one can readily doubt the validity of their conclusions.

Peters (1937) and Addis (1937) state that eclampsia is identical with acute glomerular nephritis, but all other authors disagree with them. Fahr (1924), Bell (1932), Baird and Dunn (1933), Herrick and Tillman (1935), Sheehan (1950) and others are convinced that the kidney lesions found both in the acute stage of eclampsia and in cases who die some time later are of a degenerative rather than an inflammatory nature. In the acute stage of eclampsiathe changes are reversible in a few days, but in cases with subsequent hypertensive vascular and renal damage the lesion is that of nephrosclerosis rather than of acute/chronic glomerular nephritis.

Another great change has become manifest more recently. That is that the emphasis is now placed on the cardiovascular sequelae rather than upon chronic renal damage of a nephritic nature, as the sequel to pre-eclamptic toxaemia and eclampsia. This was pointed out first by German and American authors. Hussy (1921) doubted the occurrence of chronic nephritis as a sequel to eclampsia and stated that he had never seen such a case. Doderlein and Nevermann (1925) also doubted the occurrence of chronic nephritis and found the kidneys of eclamptic cases to be normal after 15 months. Corwin and Herrick (1927) made the same observations. Kobes (1930) in a follow-up of 32 eclamptics and 19 pre-eclamptics found only one case in which there appeared to be residual chronic nephritis.

Schultz (1933) found one case of malignant hypertension eight years after eclampsia, seen at autopsy, but found no post-mortem support for nephritis as a sequel in the cases studied. Heynemann (1934) from his follow-up study of 254 women found that it took some time for albuminuria to disappear after pre-eclampsia and eclampsia. He called this delayed healing. This, he felt, had wrongly been called chronic nephritis in the past. The most important subsequent changes being in the cardiovascular

system, and occurring more frequently after pre-eclampsia than after eclampsia. He thought that existing nephrosclerosis is made worse by pregnancy, and found no clinical case of chronic glomerulonephritis in his series. He also mentioned the importance of a hereditary predisposition in the causation of vascular injury, and stated that vascular changes appeared earlier in pre-eclampsia than in eclampsia.

Herrick and Tillman (1935) studied the largest series of cases up to that time and stressed vascular rather than renal injury, as well as the part played by pregnancy in unmasking a latent hypertension and aggravating hypertension already established. They felt that it is possible that pregnancy reveals rather than causes the disease.

Schultz doubted if chronic nephritis ever occurred as a sequel. The follow-up studies of Browne and Dodds (1939), Teel and Reid (1937 and 1939) bear this out. Dieckmann (1952), Dexter and Weiss (1941) conclude that the preponderance of evidence leaves no doubt that eclampsia is not a nephritis nor does it cause chronic glomerulonephritis.

No one doubts that cases of chronic glomerulonephritis can have an exacerbation during pregnancy, convulsions like eclampsia, and be left subsequently with their chronic nephritis. Browne and Dodds (1939) followed up 17 cases of chronic glomerulonephritis in 19 pregnancies and concluded that chronic glomerulonephritis was a rare entity in association with pregnancy, with a bad ultimate prognosis, pregnancy being always a very serious risk. In 50% of the cases studied however, the patients did not seem to be any worse as a result of their pregnancy. In following up pre-eclampsia and eclampsia cases as well they found no instance of chronic nephritis. The subsequent incidence of hypertension they found to be 60% and 50.9% in eclampsia and pre-eclampsia respectively.

Chronic pyelonephritis may do the same as chronic glomerulo-

nephritis./.....

nephritis and Peters (1937) puts forward the view that it was often associated with eclampsia. His contentions have not however, been substantiated by other authorities.

With regard to recurrent toxaemia, Browne and Dodds (1939) in a series of 114 patients in 278 pregnancies found that 60% of cases with recurrent toxaemia had a blood pressure of over 130/70 mm. Hg. between toxaemic pregnancies but seemed well in the interim. With each subsequent pregnancy they had an exacerbation of hypertension, often with the reappearance of albuminuria and oedema, and not infrequently ending in abortion. In the remaining 40% of cases the blood pressure, though normal, was borderline, with an instability that in succeeding pregnancy probably predisposed to the recurrence of hypertensive toxaemia. They believe that in these cases there is a familial hypertensive tendency, and that pregnancy does nothing more than unmask a latent hypertension, that would have developed even if pregnancy never occurred, though possibly at a somewhat later period. Furthermore, they see no reason to believe that this borderline hypertension and instability of blood pressure, which in their opinion is an important cause of recurrent toxaemia, is entirely the result of previous pre-eclamptic toxaemia. They think that it probably existed before the first pre-eclamptic toxaemia as a familial hypertensive tendency and predisposed to it. This theory of Browne was thus put forward instead of Gibberd's occult nephritis theory as the explanation for recurrent toxaemia. Browne (1952), in opposing Gibberd's theory, states that if it is accepted that manifest chronic glomerulonephritis does not occur as a sequel of pre-eclamptic toxaemia or eclampsia, this occult or concealed nephritis does not occur either.

The next question and problem that arises is whether eclampsia and pre-eclampsia leave behind residual vascular damage, and whether they result in subsequent hypertensive cardiovascular disease.

Dexter and Weiss (1941, 1943) are convinced that toxaemia

often caused./.....

causes irreparable damage. Peckham (1929 and 1941), Peckham and Stout (1931), Gibberd (1931), Young et al (1932), Herrick and Tillman (1935), Peters (1937), Stander (1945), De Lee and Greenhill (1947), as well as many other authors are proponents of the theory that there is sometimes (or always) residual damage, and most of these authors find a higher incidence of residual vascular damage amongst the non-convulsive toxaemias than amongst the cases of eclampsia. Teel and Reid (1937 and 1939) conclude that eclampsia causes little damage, but that non-convulsive toxaemia perhaps causes more. One reason for the high incidence of subsequent hypertension found in many follow-up studies of non-convulsive toxaemia is as Teel and Redi (1937 and 1939), Dexter and Weiss (1943) and Dieckmann (1952) have indicated, namely that many cases diagnosed as pre-eclampsia, are in reality cases of essential hypertension. Furthermore, as Browne (1939 and 1951) points out, the patients with residual hypertension, after pre-eclamptic toxaemia and eclampsia have a familial hypertensive tendency which pregnancy has merely revealed or hastened, so that it manifests itself earlier.

Browne (1952), De Lee and Greenhill (1947) and others do not support the view first held by Harris in 1924 and since by many authors, namely that as regards residual damage, eclampsia is less serious than pre-eclamptic toxaemia. Browne in his follow-up study (1939) found a higher incidence of subsequent hypertension in the eclamptic cases than in the pre-eclamptic cases. On the other hand Dieckmann (1933, 1935, 1941), Dieckmann (1938-1939), Dieckmann, Smitter and Rynkiewicz (1952), are equally convinced that pre-eclamptic toxaemia and eclampsia cause no permanent damage, or if so, very rarely, and only in those cases who would have had hypertension eventually, even if they never were pregnant. Chesley, Somers and Vann (1948). Bryans and Torpin (1949), Light (1948), Mc Clellan, Strayhorn and Densen (1942), Browne and Dodds (1939) and others have all presented follow-up studies which they interpret as confirming this point

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of view. Bryans and Torpin (1949), Barnes and Browne (1945) and others feel that eclampsia and pre-eclamptic toxaemia does not cause hypertensive cardiovascular disease, though it may aggravate a pre-existing hypertension or hypertensive tendency causing it to be clinically evident, and at an earlier age.

Dieckmann (1952) states that pre-eclampsia and eclampsia rarely cause vascular and renal damage, and that there are two types of pre-eclampsia and eclampsia which are indistinguishable clinically, but with different subsequent histories. The one type has no vascular renal damage, the other has. In this latter group the original diagnosis was incorrect, at the time of the pregnancy and they are not "true" toxaemias of pregnancy. Dieckmann et al (1952) found that of 1,600 patients with toxaemic pregnancies 51% with non-convulsive toxaemia, 85% with pre-eclampsia and 75% with convulsive toxaemia, had subsequent normal pregnancies. This supports their contention that vascular-renal damage is rare from pre-eclampsia.

Icenhour, Kuder and Dill (1942) examined 900 nulliparous women and 900 parous women and found no demonstrable difference in the incidence of hypertension and average blood pressure levels in the two groups. Williams and Weiss stated that this study is not satisfactory because of the small number of cases. Barnes and Browne (1945) made a similar study of 915 nulliparous and 1,044 parous women with similar results. However, they do not mention what percentage of their parous women had pre-eclamptic toxaemia, eclampsia, or manifest hypertension and if these were small percentages, one would be able to criticise their findings and doubt the validity of their conclusions.

Theobald, in a remarkable paper, published in 1933, produced figures from the Registrar-General's decennial report for England and Wales for the 10 year period 1911 to 1920, which in his opinion, places considerable doubt on the view that pregnancy toxaemia could cause chronic nephritis or even disease of the circulatory system. The figures in the report showed that

"during./....

"during these years the mortality curves from Bright's disease, including hypertensive vascular disease, followed the same upward and downward trends as those in men, and that there was no significant difference between the mortality rates from these disease for married and single women up to the age of 55 years". According to Browne (1951), Theobald's contentions have never been adequately answered, and must be taken as correct. Golden, Dexter and Weiss (1943) cast some doubt on the statistical significance of these figures.

From the above consideration of a very extensive literature, it is obvious that there is still a marked controversy and difference of opinion amongst various authors as to the effects of toxaemias in general and the permanent cardiovascular renal damage, if any, that may result. Statistical and other studies from all over the world can be quoted to confirm or disprove almost any view held. Further follow-up studies taking into consideration all the features mentioned, and a critical analysis of all the material one collects, will, I feel, help to elucidate this rather confused and perplexing problem. It is only from exhaustive studies that data will be obtained to aid in determining the incidence, nature and type of post-toxaemic vascular and renal complications.

S E C T I O N III.

THE INCIDENCE OF THE VARIOUS TOXAEMIAS OF LATE PREGNANCY WITHIN THE MUNICIPAL BOUNDARIES OF CAPE TOWN AND THE LANGA NATIVE TOWNSHIP; AND THEIR RACIAL GROUPING.

CHAPTER 1.

I N T R O D U C T I O N:

There are neither accurate published figures nor statistical studies available, of the incidence of the toxaemias of pregnancy in Cape Town or South Africa. This is because the toxaemias of pregnancy are not notifiable diseases. In addition hospital statistics are notoriously inaccurate because of the general tendency to admit abnormal cases more readily than normal cases. In the third place a large percentage of toxaemia and eclamptic cases encountered in public and private maternity institutions are not Cape Town residents. Many of these are abnormal and toxaemia cases referred from the outlying districts and from centres many miles away from Cape Town. These cases tend to produce a false impression and false figures suggesting a high incidence of the toxaemias of late pregnancy and eclampsia in Cape Town.

To indicate how an error can arise the medical officer of health's report in Cape Town can be quoted. It gives a figure of 17,740 deliveries in Cape Town during the year 1950-1951, and of these only 13,905 were amongst residents within the Cape Town municipal area and Langa. Another reason why hospital statistics are not accurate in Cape Town is that only 55% of the deliveries of Cape Town residents occur in private and public institutions. The remainder are delivered by private midwives certificated and uncertificated, student midwives, student doctors and qualified private doctors. Consequently hospital figures will not truly reflect the incidence of toxaemias in the city in which they are situated. It is fortunate, however, that of the group delivered outside institutions, a very large percentage attend some or other municipal or hospital clinic before their confinement at home. Consequently records are available for study of their state of health during pregnancy, if one is prepared to scrutinise all the records and cards at the various clinics.

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In this study of the toxaemias of late pregnancy the area chosen is the whole municipal area of the city of Cape Town and the Langa township adjoining it. This area is illustrated by aerial photographs (see photographs 1 and 2 page 40 and 41), on which the boundaries are mapped out by dotted red and white lines. The Cape Peninsula, situated at latitude 33 degrees 36 seconds, S., and longtitude 18 degrees 30 seconds, E., lies off the west coast of the mainland of South Africa and, as will be seen, only part of it falls within the municipal boundaries and Langa native township. The northern half of its eastern side borders on the Cape Flats, a wide low-lying sandy isthmus. The backbone of the peninsula is a mountain range extending from Table Mountain at its north end to Cape Point at the south.

The municipal area of the city of Cape Town extends over 81.7 sq. miles and onto two seaboards and is divided into the following 15 wards :-

1. The area from Bakoven to Sea Point.
2. The area from Greenpoint to the harbour.
3. Signal Hill, Kloofnek and part of Camps Bay.
4. The Gardens.
5. The area known as the old District Six.
6. The area surrounding the Castle and Woodstock.
7. Salt River area.
8. Brooklyn, Maitland, Kensington, Windermere, and Rugby, but excluding Milnerton and Goodwood and the other northern suburbs.
9. Observatory, Mowbray and Rosebank, excluding Pinelands.
10. Athlone, Lansdowne, including Rylands and Crawford but excluding Phillipi, Epping and Matroosfontein.
11. Rondebosch area as far as the Cape Flats line.
12. Newlands and Claremont districts.
13. Kenilworth.
14. Wynberg, Plumstead, Southfield and Zeekoe Vlei but excluding Grassy Park.

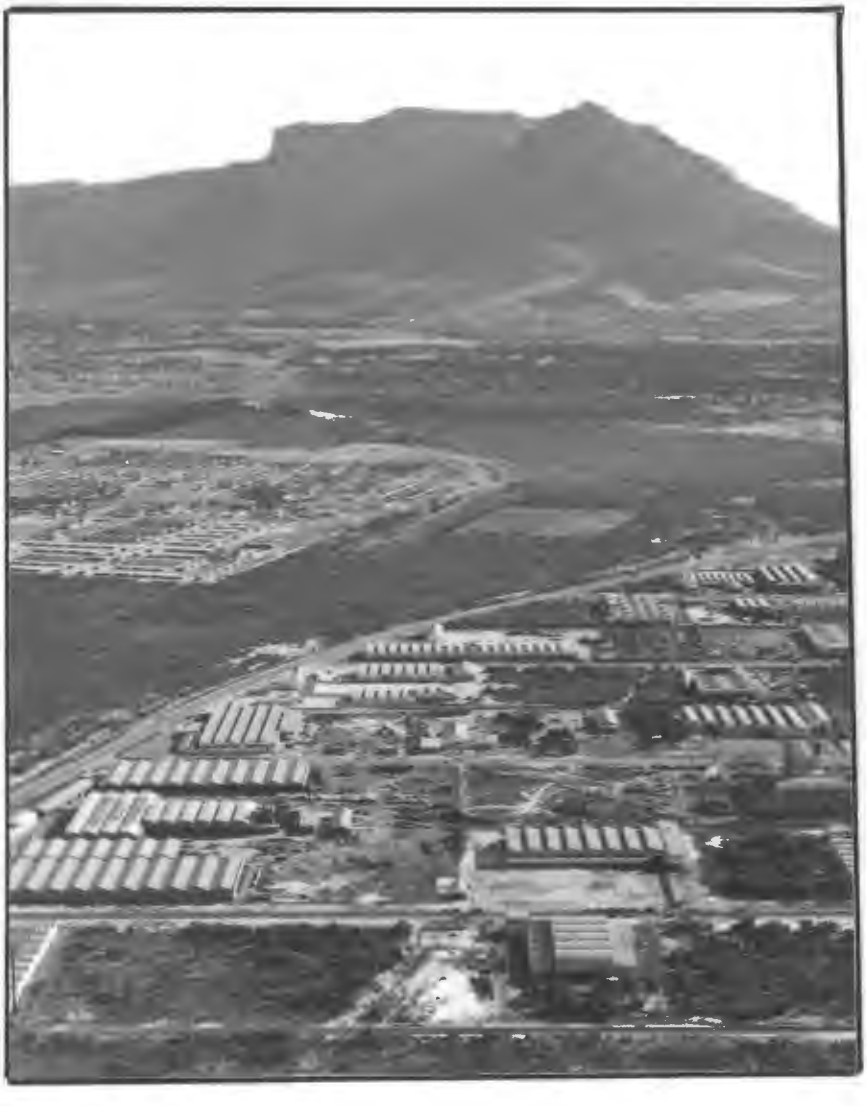
The./....

PHOTOGRAPH I.

AERIAL PHOTOGRAPH OF THE CAPE PENINSULA SHOWING PRACTICALLY THE WHOLE OF THE MUNICIPAL AREA OF CAPE TOWN, WHERE THE STUDY WAS UNDERTAKEN. THE AREA IS MAPPED OUT BY RED AND WHITE DOTTED LINES, AND DESCRIBED IN DETAIL IN THE TEXT.

PHOTOGRAPH II.

PHOTOGRAPH SHOWING THE LANGA NATIVE TOWNSHIP WITH THE EPPING INDUSTRIAL TOWNSHIP IN THE FOREGROUND.



15. The area from Diep River to Clovelly, excluding Constantia, Pollsmoor and Bergvliet, but including Retreat, Lakeside, Muizenberg and Kalk Bay.

The Langa native township is an additional area included in this study for the purpose of comparing the incidence of the toxaemias of late pregnancy amongst the urbanized Natives (or Bantu people) with that of the other races.

The population of the area included in this study is multiracial (see photograph 3) and this gives a unique opportunity for comparing the incidence of the toxaemias amongst the various racial groups. The European part of the population descended mainly from the peoples of European countries e.g. Holland, the British Isles, France and Germany, constitutes 44% of the population and their state of health and mortality statistics is much the same as in a healthy European town.

The non-European or coloured population constituting 56% of the total population is made up of the Cape coloured people, including the Malays, the Bantu tribes called the natives, and Asiatics more recently imported from India and China etc. (Medical officer of Health report 1950 - 1951).

The Cape coloureds are largely the descendants of the slaves of earlier days, whose emancipation was completed in 1835. Their ancestors of the 18th century and earlier were mainly Europeans, Hottentots, Natives from Mozambique, St. Helena, Madagascar and other parts of Africa, and East Indians from the Dutch East Indies. In more recent years they have received additions from Europeans, Bantu and other stocks. There is one section of the Cape coloured people, Moslem in religion, known as the Malays, who are more immediately descended from the Dutch East Indians. They constitute 20% of the so-called Cape coloured population (Batson 1952) and are distinguished by the fact that they attend the mosque and the men wear a fez, while the women are veiled. They tend to live a

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more segregated life with domestic and personal and possibly dietary differences from the other non-Europeans. These differences in customs and their names and surnames were used to distinguish them in the hospital and clinic records studied, as a separate group.

The social and economic conditions of the non-European population is on the whole unsatisfactory, but a percentage of them are well to do, especially a section of the Malays, Indian shopkeepers and some coloured skilled workers. Excluding these, there is much malnutrition and a lack of good housing conditions as well as a low social and cultural level amongst the remainder of the coloured community. In contrast only a minority of Europeans belong to the depressed classes as opposed to the non-European majority living under slum conditions. The natives constitute 16% of the non-European population and live in a modern township at Langa and in other non-European slum areas. Many of them are detribalized and permanently resident in Cape Town, but others retain a link with the native territories and return there eventually. They include Xosas, Fingos, Zulus, Basutos, etc., and live under poorer conditions than the Cape coloureds generally, and are distinguished by their features, customs and names from the Cape Coloured, Malays and Indians.

The Asiatics, mainly Indians and a few Chinese, number less than 7,000 and are nearly all traders and are well-to-do. These various non-European races show striking contrasts if a study of their vital statistics is made. (Medical officer of health's report 1950 - 1951).

RELATIVE DATA OF THE POPULATION OF CAPE TOWN AND THE LANGA NATIVE TOWNSHIP 1950 - 1951:

The following data are reproduced to indicate the population and its racial distribution in the area considered in this study.

Total Population:	448,740
Total European Population:	187,452

Total./...

Total Coloured Population: (excluding Malays)	170,936.	
Total Malay Population:	42,734.	(Taken as 20% of the coloured population).
Total Native Population:	40,738.	
Total Asiatic Population:	6,880.	

The following indicates the number of births in the above population groups during the period 1950-1951, chosen for this study.

Coloured Births:	6,892	Alive and	217	Stillbirths = 7,109.
European Births:	3,346	Alive and	41	Stillbirths = 3,387.
Malay Births:	1,724	Alive and	54	Stillbirths = 1,778.
Native Births:	1,230	Alive and	78	Stillbirths = 1,308.
Asiatic Births:	314	Alive and	9	Stillbirths = 323.
TOTAL BIRTHS:	13,506	Alive and	399	Stillbirths =13,905.

The following indicates the number of births in the population groups whose records were traced during the period 1950-1951.

Total Births: 11,383
European Births: 2,859 of whom 360 were associated with toxaemia.
Coloured Births: 6,075 of whom 775 were associated with toxaemia.
Malay births: 1,235 of whom 209 were associated with toxaemia.
Native births: 1,198 of whom 94 were associated with toxaemia.
Asiatic births: 16 of whom 2 were associated with toxaemia.

These data are graphically reproduced in photographs 3, 4 and 5, on pages 45, 46 and 47.

PHOTOGRAPH III.

PHOTOGRAPH OF A GRAPH SHOWING

THE RACIAL DISTRIBUTION OF THE

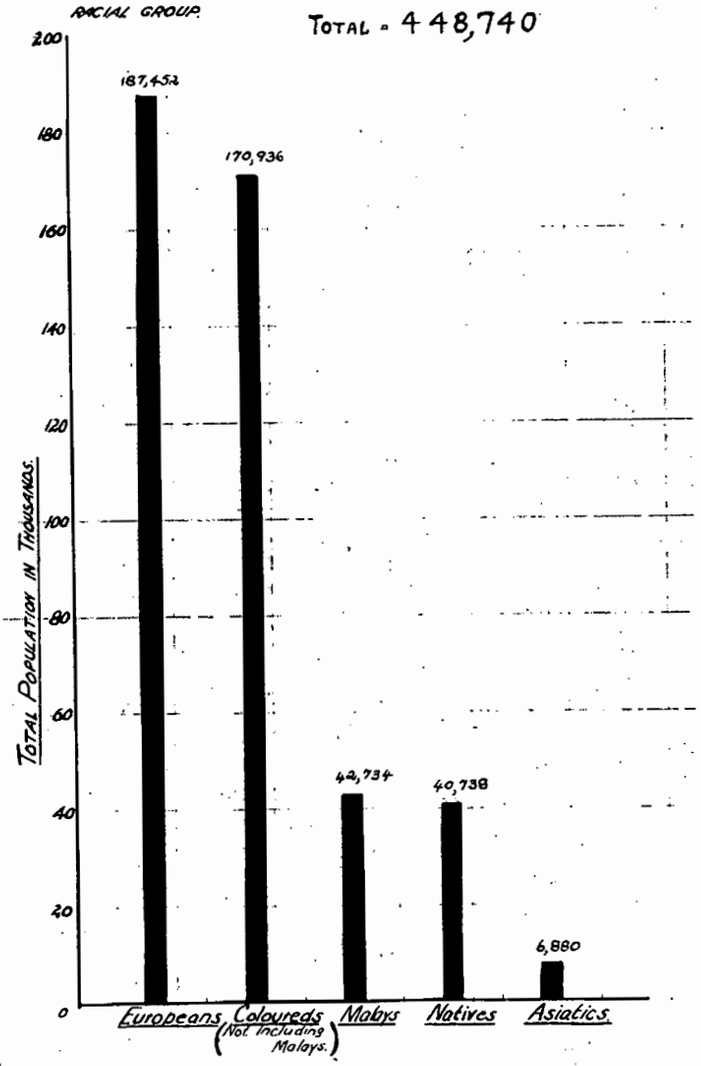
POPULATION OF CAPE TOWN

AND LANGA USED IN THIS STUDY

(1950 - 1951).

FIGURE INDICATING THE POPULATION IN THE CAPE TOWN MUNICIPAL AREA INCLUDING THE L.ANGA NATIVE TOWNSHIP (1850 – 1951) SHOWING THE DISTRIBUTION AND NUMBER OF PEOPLE IN EACH RACIAL GROUP.

TOTAL = 448,740



PHOTOGRAPH IV.

A PHOTOGRAPH OF A GRAPH SHOWING

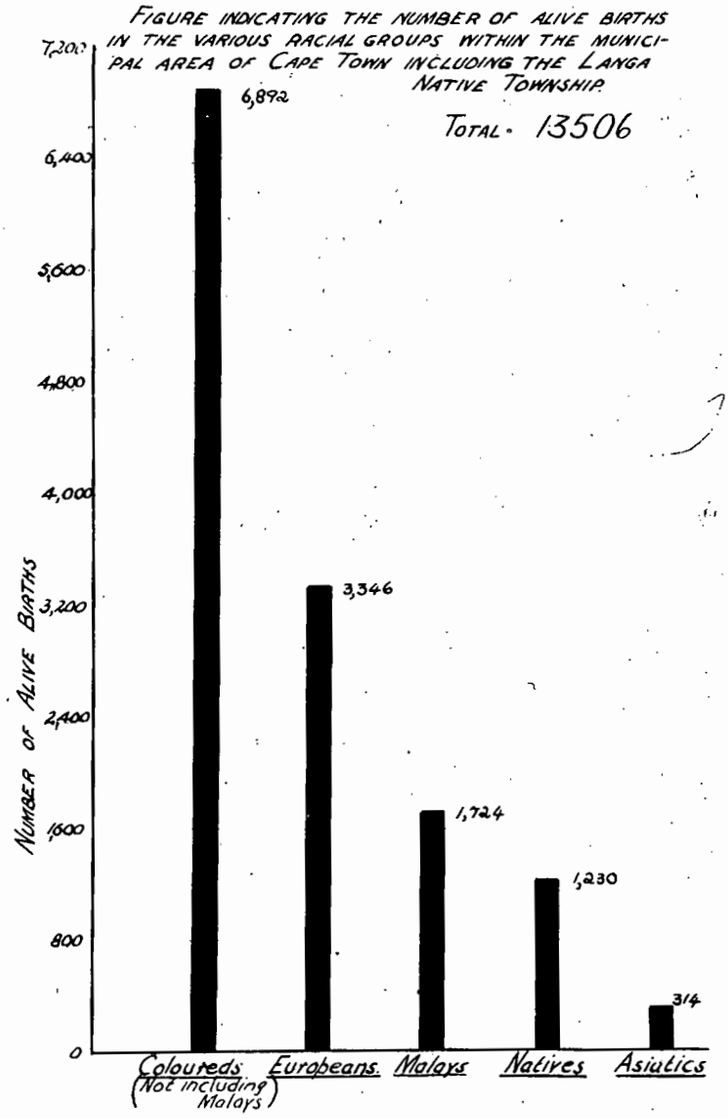
THE ALIVE BIRTHS AND THEIR

RACIAL DISTRIBUTION.

(1950 - 1951).

FIGURE INDICATING THE NUMBER OF ALIVE BIRTHS IN THE VARIOUS RACIAL GROUPS WITHIN THE MUNICIPAL AREA OF CAPE TOWN INCLUDING THE LANGA NATIVE TOWNSHIP.

TOTAL. 13506



PHOTOGRAPH V.

A PHOTOGRAPH OF A GRAPH SHOWING

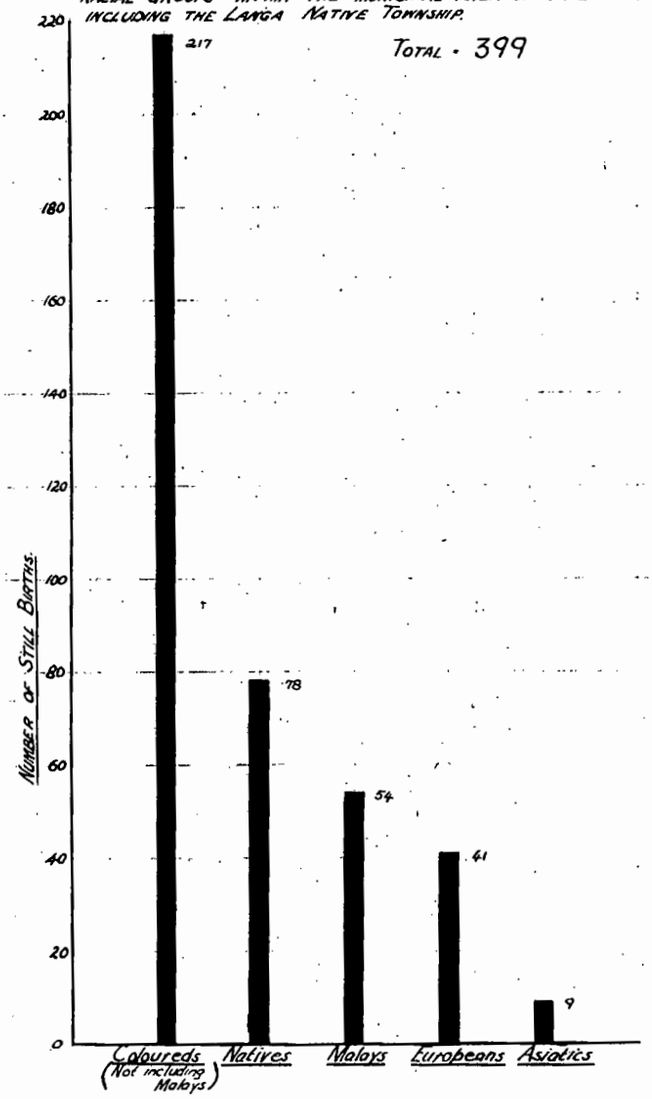
THE STILLBIRTHS AND THEIR

RACIAL DISTRIBUTION

(1950 - 1951)

FIGURE INDICATING THE NUMBER OF STILL BIRTHS IN THE VARIOUS RACIAL GROUPS WITHIN THE MUNICIPAL AREA OF CAPE TOWN INCLUDING THE LANGA NATIVE TOWNSHIP.

TOTAL - 399



CHAPTER II.

THE PROBLEMS INVESTIGATED

The aim of this section of the thesis is to prove or disprove the longstanding impression that the incidence of the pregnancy toxaemias and eclampsia is significantly higher in Cape Town amongst the non-white or non-European population, or a particular section of the non-European population than amongst the European section.

The second objective is to verify or reject the validity of the statement that the incidence of the toxaemias of late pregnancy and eclampsia in the population of Cape Town as a whole is amongst the highest in the world.

These two objectives I shall attempt to attain by statistical analysis of the research data collected.

A preliminary pilot survey of the municipal clinics that I made, proved statistically that the Malays show a significantly higher incidence of pregnancy toxaemias than the other racial groups. To verify this a survey of the entire female population in the area chosen was therefore undertaken.

Pari-passu Brock and Batson (1952) undertook a dietary budget survey to determine whether there are essential and important dietary differences between the Malays and other sections of the population, thereby attempting to explain the difference in the incidence of the pregnancy toxaemias. On my part I attempted to discover any differences in personal and domestic habits and customs which might explain the varied incidence. This was done by interrogation of the "follow-up study cases" I personally examined.

Finally, I attempted a classification of the toxaemia cases encountered, in order to ascertain what percentage were really cases of hypertensive vascular disease with superadded symptoms of toxaemia. In addition I correlated the race, age and parity

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with each subgroup.

CHAPTER III.

STANDARDS EMPLOYED IN THIS INVESTIGATION.

In this investigation pregnancy toxaemia is defined as the appearance in any patient during pregnancy of:-

1. A blood pressure of 130/85 mm. Hg. or above and 120/80 mm. Hg. or above in respect of cases under the age of 20 years on two or more separate occasions.

2. Recognisable oedema.

3. Albuminuria.

4. Coma with or without fits before, during or soon after labour in cases of eclampsia, in addition to the first three criteria.

A Malay is defined as one who adheres to Malay customs notably the following:-

1. The men wear fezzes.

2. The women wear veils over their faces.

3. They attend the mosque and adhere to other Malay traditions such as fasts, feasts and ceremonial burials.

4. In addition they are readily recognised by their unusual names and surnames. They tend to live in certain areas "the Malay quarters", whence their addresses also serve as a guide to their classification of race.

The natives, or Bantu people, are easily distinguished by their features, language, habits, names, surnames and addresses. Their division into specific tribes e.g. Zulus, Xosas, etc. was

not./.....

not attempted, because then the numbers would have been too small and of no statistical value.

All Asiatics encountered were Indians, who are easily recognised by their features and names. There were only 16 cases classified into this group, because their numbers are small in this part of South Africa.

The remainder of the cases, besides the Europeans or Whites, were classed as the Cape Coloureds or "Coloureds" for the sake of brevity.

CHAPTER IV.

METHODS AND MATERIAL.

To determine the incidence of the toxaemias of late pregnancy on a reliable statistical basis, the period 1st of April, 1950, to the 31st of March, 1951, was chosen. No stone was left unturned to collect all available records of women, of all races, who attended the antenatal clinics, public and private maternity hospitals and nursing homes, and were delivered during this period. However, only those cases who were residents of the City of Cape Town and the Langa Native Township were included in this study.

All such cases were classified according to the previously defined standards into normal or toxaemia cases, and into their respective racial groups, namely Native, Coloured, Malay, European and Asiatic, as well as into their respective age and parity groups.

The study was initiated by scrutinizing all the case history records at the municipal clinics, which are attended by the vast majority of non-Europeans and some Europeans.

All the following municipal clinics were visited:-

1. Langa Clinic.
2. Aspeling Street.
3. Lansdowne Clinic.
4. Maitland Clinic.
5. Salt River Clinic.
6. Bokmakierie Clinic.
7. Shortmarket Street Clinic.
8. Bloemhof Flats.
9. Station Road, Claremont and Wynberg Clinic.
10. Windermere Clinic.
11. Lawrence Road, Athlone, Clinic.
12. Retreat Clinic.

This entailed the personal scrutiny of 6,200 case records of which 1,185 were discarded, because they were either non-resident in the area chosen or were not confined in the period under consideration.

Some of the municipal clinic cases were referred to hospital clinics for consultation, or for the remainder of their antenatal supervision, for various reasons, but especially if they were abnormal or complicated. All such cases, toxaemic and non-toxaemic, were retained amongst the municipal clinic records which I compiled, for the sake of convenience and in order to prevent duplication at a later stage when the hospital clinic records were to be studied.

A complete record of identification number, name, address and all the facts concerning the pregnancy in question and past pregnancies was kept for each case. At a later stage, when the hospital records were examined, further changes in their signs and symptoms later in pregnancy were noted, and added to the municipal records already made. Such cases were then deleted from the hospital records, which naturally decreased the nett number of cases reproduced in the tables from the various hospitals. It was deemed necessary to do this to avoid duplication errors, and at the same time to ensure that any later developments in

the clinical condition of a case could be traced up to the time of her delivery. This precaution therefore prevented the omission of cases who developed toxaemia at or near term.

On the other hand the majority of municipal clinic cases had home confinements by licensed midwives. Many toxaemia cases similarly had their confinements at home, often against medical advice and their better judgment, but fortunately, with few exceptions, they attended the municipal clinics right up to or near term.

The individual records at the clinics state where the baby was born, and contain postnatal information, in addition to the patient's general and obstetric history, blood pressure and urine records, etc., and results of other examinations and investigations done. These facts made the research investigations possible.

The nett number of case histories at the municipal clinics that fulfilled the criteria and other considerations enumerated previously were 5,015, and included 508 cases of toxaemia, with an incidence of 10.1%. (See Table I pages 56,57 & 58 for detailed classification of these cases).

The reason why the municipal clinic records were studied, was to obtain the thousands of additional records of cases, normally not considered when figures and statistics of hospital inpatients and district cases are analysed and quoted, thus avoiding one of the main factors leading to false impressions of the incidence of the toxaemias in a city like Cape Town, where practically half the deliveries are conducted in private home surroundings.

Not until the day when all confinements are conducted in institutions or under institutional care will hospital statistics be an accurate reflection of the incidence of the toxaemias of pregnancy in South Africa. Alternatively the toxaemias would have to be made legally notifiable diseases.

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The next step in the investigation was the study of the records of all the hospitals, including records of district cases under hospital supervision delivered within the period chosen in this study.

The case records and charts of all the following hospitals and institutions were scrutinized:-

1. The Peninsula Maternity Hospital and District Service.
2. The New Somerset Hospital and District Service.
3. The Booth Memorial Hospital and District Service.
4. St. Monica Maternity Hospital and District Service.
5. "Vrede-Oord" Salvation Army Hospital and District Service.
6. Mowbray Maternity Hospital.
7. Groote Schuur Hospital Maternity Section.
8. Delherbe Maternity Hospital.
9. Leighwood Maternity Hospital.
10. Gilmour Nursing Home.

The above institutions cater for about 98% of Cape Town and Langa residents who have their deliveries done in institutions.

Unfortunately, in a small number of these institutions, particularly those frequented by the upper social class of European patients, the records are not accurately kept, and permanent records of only the severer toxaemia cases were available for scrutiny. I reproduced their figures as I found them. They show an incidence of toxaemia varying from 7.1 to 8.6 per cent. However, I am quite convinced that if complete records were kept of all cases and the criteria used in this thesis applied, the incidence would be between 10 to 12 % in these three institutions (Gilmour, Delherbe and Leighwood Maternity Homes). The Booth Memorial Hospital, a home similar to these and catering for the more well-to-do European, have adequate and accurate records like the remainder of the institutions whose records were investigated. By applying the criteria used in this study to their figures and records, an incidence of toxaemia of 11.8% was found amongst Cape Town residents delivered there. This supports very strongly

the./.....

the contention I have previously mentioned concerning the incidence of the toxaemias of pregnancy amongst the well-to-do.

There appears to be a greater incidence of Caesarean section for terminating severe toxaemia cases in the institutions catering for the well-to-do, and this may be a factor tending to lower the incidence of eclampsia in such institutions. Eclampsia is thus prevented by timely interference and termination of pregnancy.

To sum up, I should like to emphasise the methods used to avoid errors while investigating the hospital records. Firstly, the records of all cases not resident within the municipal area of the City of Cape Town and the Langa Native Township were excluded and discarded. Secondly, the records of cases not delivered within the period chosen for this study were excluded. Thirdly, cases already recorded and compiled from the case records of the municipal clinics, who in addition attended one or other of the hospitals, whether normal or toxaemic, were avoided or excluded. At the same time, any additional information on the latter cases was entered into their already existing records compiled from the municipal clinic records, e.g. whether they had developed further signs of toxaemia or eclampsia or, of previously normal cases, whether they had developed toxaemia of pregnancy in the interim. The third precaution involved a great deal of tedious labour, but was essential if accurate figures were to be produced.

To indicate how the inclusion of non-resident cases, and cases already documented at the municipal clinics can produce a false reflection of the incidence of the toxaemias, I quote the following figures obtained:-

The gross number of records scrutinised at the hospitals and Nursing Homes was 9,857. This included 1,697 cases of toxaemia, giving an incidence of pregnancy toxaemia of 17.2%.

However, if the nett hospital and Nursing Home figures are quoted after discarding those cases not pertinent to the study, then 6,368 records were obtained, including 932 cases of toxaemia

with an incidence of 14.4%.

Further, if the nett number of pertinent cases from the municipal clinics are added to the preceding nett hospital figures, then the nett number of pertinent records studied is 11,383 including 1,440 cases of toxaemia. This gives an incidence of 12.6% of the pregnancy toxaemias amongst the population of the Cape Town municipal area and the Langa Native Township. It is therefore obvious that the gross hospital figures first quoted give an unduly high, and false reflection of the incidence of the toxaemias of pregnancy in the area studied, and differs considerably, and more than could be explained by chance, from the real incidence as indicated by my figure of 12.6%.

The foregoing explanation elucidates the basic reason for the impression that the pregnancy toxaemias have a high incidence in the City of Cape Town. There is another possible reason for this belief. That is that the incidence of pregnancy toxaemias might have been relatively high prior to the inauguration of the antenatal clinics in 1920. The progressive expansion of the antenatal clinics to cope with the needs of the pregnant female population has probably led to a steady decline in the incidence of eclampsia and probably of the toxaemias in Cape Town. This has been the experience throughout the world (Dieckmann 1952) and is probably due firstly to antenatal care, and secondly to timely intervention and treatment. There is yet another possible factor namely, that there has been an improvement in the general standard of living of the population as a whole during the last quarter of a century. However, the assessment of hygienic, dietetic, social-economic and similar factors in the etiology and pathogenesis of the toxaemias is very difficult as was indicated under the discussion of the importance of these factors in a previous section.

On the succeeding pages the detailed figures of all clinics and hospitals and the incidence of toxaemia in each respective clinic or hospital are tabulated. (Table I). A total of 16,057 case history cards were scrutinised to obtain the nett figures.

TABLE I.

FIGURES INCLUDING ONLY CAPE TOWN RESIDENTS AND THOSE WITHIN THE LANGA NATIVE TOWNSHIP WHO HAD CONFINEMENTS WITH OR WITHOUT TOXAEMIA DURING PREGNANCY DURING THE PERIOD 1ST APRIL, 1950 TO 31ST MARCH, 1951.

	Nursing Homes, Hospitals and Clinics.	Total No. of cases.	Race of the total no. of cases.					No. of Normal Cases.	No. of Toxaemic cases	%	Race of Toxaemic Cases.				
			Europ.	Col.	Malay.	Native.	Asiatic				Eur.	Col.	Malay.	Native.	Asiatic
1.	Aspeling Street Clinic.	754	1	392	310	48	3	633	121	16.0	No. 0 % 0	61 15.5	55 17.7	5 10.4	0 0
2.	Lansdowne Clinic.	247	26	156	28	37	0	214	33	13.4	No. 4 % 15.3	20 12.8	7 25	2 5.4	0 0
3.	Maitland Clinic.	395	22	327	1	45	0	377	18	4.6	No. 0 % 0	15 4.5	0 0	3 6.6	0 0
4.	Langa Clinic.	257	0	0	0	257	0	239	18	7.0	No. 0 % 0	0 0	0 0	18 7	0 0
5.	Salt River Clinic.	561	155	345	55	5	1	479	82	14.6	No. 6 % 3.8	65 18.8	10 18.1	1 20	0 0
6.	Bokmakierie Clinic.	378	0	341	37	0	0	323	55	14.6	No. 0 % 0	49 14.3	6 16.2	0 0	0 0
7.	Shortmarket Street Clinic.	176	0	96	58	22	0	162	14	7.9	No. 0 % 0	10 9.6	4 6.8	0 0	0 0
8.	Bloemhof Flats Clinic.	66	0	44	20	2	0	56	10	15.1	No. 0 % 0	5 11.3	4 20	1 50	0 0

Continued page 57./.

TABLE I CONTINUED.

FIGURES INCLUDING ONLY CAPE TOWN RESIDENTS AND THOSE WITHIN THE LANGA NATIVE TOWNSHIP WHO HAD CONFINEMENTS WITH OR WITHOUT TOXAEMIA DURING PREGNANCY DURING THE PERIOD 1ST APRIL, 1950 TO 31ST MARCH, 1951.

	Nursing Homes, Hospitals and Clinics.	Total No. of cases.	Race of the total no. of cases. Europ.	Col.	Malay.	Native.	Asiatic	No. of Normal Cases.	No. of Toxaemic cases	%		Race of Toxaemic Cases. Eur.	Col.	Malay.	Native.	Asiatic
9.	Station Road Clinic, Claremont.	311	74	154	43	40	0	273	38	12.2	No.	15	15	7	1	0
											%	19.6	9.6	15.9	2.5	0
10.	Windermere Clinic.	658	0	340	10	308	0	645	13	2.0	No.	0	8	0	5	0
											%	0	2.3	0	2	0
11.	Lawrence Road Clinic, Athlone.	573	2	484	35	50	2	507	66	11.5	No.	1	57	5	3	0
											%	50	11.7	14.2	6	0
12.	Retreat Clinic.	639	24	445	7	162	1	599	40	6.3	No.	1	34	0	5	0
											%	3.7	7.4	0	3.2	0
13.	St. Monica's Maternity Hospital and District.	520	0	390	110	20	0	453	67	12.8	No.	0	45	12	10	0
											%	0	11.4	11.8	50	0
14.	Booth Memorial Hospital and District.	841	841	0	0	0	0	741	100	11.8	No.	100	0	0	0	0
											%	11.8	0	0	0	0
15.	New Somerset Maternity Hospital and District.	979	0	830	118	28	3	808	171	17.4	No.	0	139	21	10	1
											%	0	16.8	17.9	37.3	33.3
16.	Mowbray Maternity Hospital.	774	774	0	0	0	0	644	130	16.8	No.	130	0	0	0	0
											%	16.8	0	0	0	0

Continued. Page 58./.....

TABLE I CONTINUED.

FIGURES INCLUDING ONLY CAPE TOWN RESIDENTS AND THOSE WITHIN THE LANGA NATIVE TOWNSHIP WHO HAD CONFINEMENTS WITH OR WITHOUT TOXAEMIA DURING PREGNANCY DURING THE PERIOD 1ST APRIL, 1950 TO 31ST MARCH, 1951.

	Nursing Homes, Hospitals and Clinics.	Total No. of cases.	Race of the total no. of cases. Europ.	Col.	Malay.	Native.	Asiatic	No. of Normal Cases.	No. of Toxaemic cases	%		Race of Toxaemic Cases. Eur.	Col.	Malay.	Native.	Asiatic
17.	Vrede Oordt, Salvation Army Home & Dist.	252	0	198	30	20	4	225	27	10.8	No.	0	17	3	6	1
											%	0	8.9	10	30	25
18.	Peninsula Maternity Hospital & District.	1,614	234	950	300	128	2	1,350	264	16.3	No.	48	150	54	12	0
											%	20.5	15.7	18	9.7	0
19.	Groote Schuur Hospital	682	0	583	73	26	0	564	118	17.3	No.	0	85	21	12	0
											%	0	14.6	28.7	46.3	0
20.	Delherbe Maternity Home.	282	282	0	0	0	0	262	20	7.1	No.	20	0	0	0	0
											%	7.1	0	0	0	0
21.	Gilmour Nursing Home.	150	150	0	0	0	0	137	13	8.6	No.	13	0	0	0	0
											%	8.6	0	0	0	0
22.	Leighwood Maternity Hospital.	274	274	0	0	0	0	252	22	8.1	No.	22	0	0	0	0
											%	8.1	0	0	0	0
23.	T O T A L S:	11,383	2,859	6,075	1,235	1,198	16	9,943	1,440	12.6	No.	360	775	209	94	2
											%	126	12.8	16.9	7.8	12.5

CHAPTER V.

THE RESULTS OF THE INVESTIGATION OF THE INCIDENCE OF TOXAEMIA OF LATE PREGNANCY WITHIN THE BOUNDARIES OF THE MUNICIPALITY OF CAPE TOWN & THE LANGA NATIVE TOWNSHIP, DURING THE PERIOD 1ST APRIL, 1950 TO 31ST MARCH, 1951, AND THEIR RACIAL GROUPING.

(Only cases resident in this area were considered in this investigation).

1. EUROPEANS: 2,859 European women delivered in this period were traced at the various clinics and hospitals.

   360 Of these had toxaemia of pregnancy i.e., 12.6 %.

2. CAPE COLOUREDS: 6,075 Coloured women delivered in this period were traced at the various clinics and hospitals.

   775 Had toxaemia of pregnancy i.e. 12.8 %.

3. MALAYS: 1,235 Malay women delivered in this period were traced at the various clinics and hospitals.

   209 Of these had toxaemia of pregnancy i.e., 16.9 %.

4. NATIVES: (Including Xosa, Zulu etc.)
   1,198 Native women delivered in this period were traced at the various clinics and hospitals.

   94 Had toxaemia of pregnancy i.e., 7.8 %.

5. ASIATICS: (Indians, Chinese etc.)
   16 Asiatic women delivered in this period were traced at the various clinics and hospitals.

   2 Of these had toxaemia of pregnancy but as the numbers are too small the incidence calculated at 12.5% is probably inaccurate and will not be statistically analysed further.

6. Of all non-Europeans i.e., Cape Coloureds, Malays, Natives and Asiatics, a total of 8,524 women delivered in this period, 1,080 had toxaemia of pregnancy i.e., 12.6%.

The./.....

7. The records of a total of 11,383 cases were traced, who delivered in this period, at the various hospitals and clinics. This constitutes 82% of the pregnant female population who had confinements during the period chosen for this thesis.

1,440 Of these developed toxaemia of pregnancy i.e., 12.6%.

8. According to the Medical Officer of Health's report 1950-1951, there were 13,905 deliveries amongst residents within the municipal boundaries of Cape Town and the Langa native township. There were thus 2,522 women who had confinements during this time, about whom no information was obtained, as they did not attend any of the Municipal Clinics, nor were they confined in any of the public or private maternity hospitals within the municipal boundaries. This constitutes 18% of the pregnant female population who had confinements in the period chosen for this study.

9. If only cases with a blood pressure of 140/90 mm. Hg. or higher, irrespective of their age, with or without the other criteria are regarded as toxaemic, then only 1,003 out of 11,383 cases are toxaemic i.e., an incidence of 8.7%.

THE INCIDENCE OF ECLAMPSIA:

24 Out of 11,383 cases who were resident within the municipal boundaries of Cape Town and Langa native township, developed eclampsia before, during or after delivery. This is an incidence of 0.211% i.e., 1 in every 474 pregnancies ended in eclampsia.

It is unlikely that many, or even any cases of eclampsia occurred besides the 24 already mentioned amongst the cases whom we have no record of, because all cases of eclampsia are referred to institutions as soon as the diagnosis is made.

The assumption is justified that no further cases of eclampsia occurred amongst the residents of Cape Town and Langa than the 24 already mentioned. This would given an incidence of 24

out./.....

of 13,905 pregnancies over the period 1st April, 1950 to the 31st March, 1951, i.e., 0.172%, in other words 1 out of every 579 pregnancies resulted in eclampsia, if this assumption is correct.

If it is assumed that eclampsia occurred at the same rate of incidence in the remaining cases not seen or studied, as amongst the 11,383 cases whose records we have information of, then 29 cases of eclampsia should have occurred amongst the total of 13,905 deliveries in Cape Town. However, this is unlikely for reasons stipulated above.

THE INCIDENCE OF ECLAMPSIA RELATIVE TO THE INCIDENCE OF TOXAEMIA.

Twenty-four of the 1,440 toxaemia cases found amongst 11,383 Cape Town and Langa residents developed eclampsia. That is, 1 out of every 60 toxaemic pregnancies resulted in eclampsia. The incidence of eclampsia was 1.7% amongst toxaemic pregnancies. (See photograph 6 on page 62 portraying these results).

PHOTOGRAPH VI.

SHOWS THE RACIAL GROUPING AND

RESULTS OF THE INVESTIGATION

IN GRAPHIC FORM.

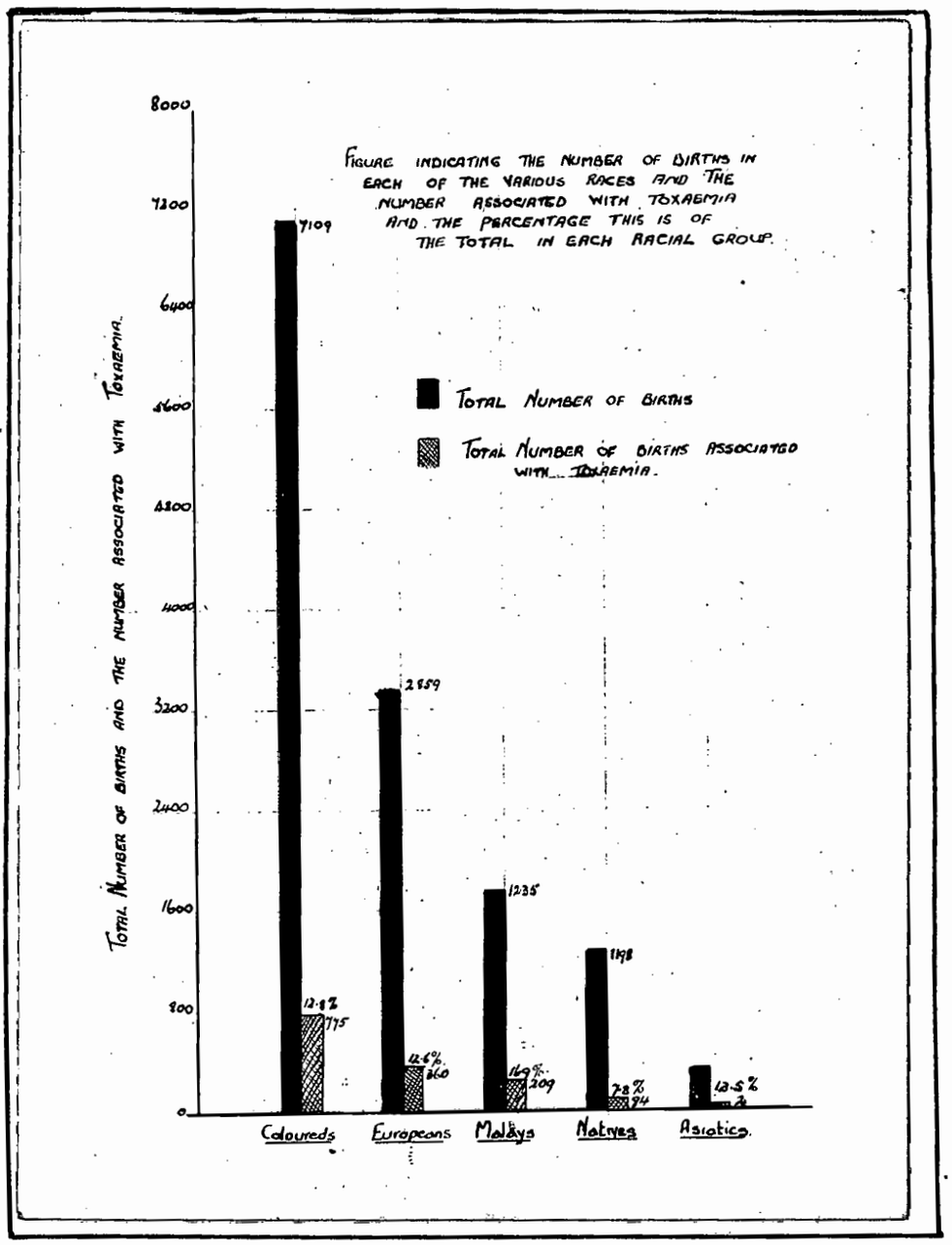


FIGURE INDICATING THE NUMBER OF BIRTHS IN EACH OF THE VARIOUS RACES AND THE NUMBER ASSOCIATED WITH TOXAEMIA AND THE PERCENTAGE THIS IS OF THE TOTAL IN EACH RACIAL GROUP.
TOTAL NUMBER OF BIRTHS AND THE NUMBER ASSOCIATED WITH TOXAEMIA.
TOTAL NUMBER OF BIRTHS
TOTAL NUMBER OF BIRTHS ASSOCIATED WITH TOXAEMIA.
8000
7200
6400
5600
4800
4000
3200
2400
1600
800
0
7109
12·8%
775
2859
12·6%
360
1235
16·9%
209
198
7·8%
14
12·5%
Coloureds
Europeans
Malays
Natives
Asiatics.

CHAPTER VI.

STATISTICAL ANALYSIS OF THE RESULTS OF THE INVESTIGATION OF THE INCIDENCE OF PREGNANCY TOXAEMIAS, WITHIN THE MUNICIPAL BOUNDARIES OF THE CITY OF CAPE TOWN AND THE LANGA NATIVE TOWNSHIP.

DEFINITIONS:

1. The standard error of any statistical value is a measure of the variability that that value would show in taking repeated samples from the same universe of observations.

2. "Significance": If two values differ by more than twice the value of the standard error (S.E.) of the difference, the difference is said to be "significant", i.e., more than is easily likely to have arisen by chance. In fact such a difference would arise by chance about once in 20 times. If the difference is 3 times its standard error it would arise by chance less than once in 370 times.

RACE:	NO. OF CASES:	NO. THAT WERE TOXAEMIC :	PERCENTAGE:
Malay:	1,235	209	16.9% (A)
Coloured:	6,075	775	12.8% (B)
European:	2,859	360	12.6% (C)
Native:	1,198	94	7.8% (D)
Asiatic:	16	2	12.5% (E)

---

1. The test of significance of difference between Malay and Coloured percentages (A. and B.).

Let n_1 = the size of the Malay sample which is the number of cases whose records were studied over a period of 1 year. Let p_1 = the percentage of Malay pregnancy toxaemias. Let q_1 = 100 minus p_1.

$n_1 = 1,235$ $p_1 = 16.9$ $q_1 = 83.1$

$n_2 = 6,075$ $p_2 = 12.8$ $q_2 = 87.2$

Difference in percentages = 16.9 - 12.8 = 4.1

Estimate./.....

Estimate of the standard error of difference $= \sqrt{\frac{p_1 q_1}{n_1} + \frac{p_2 q_2}{n_2}}$

Here S.E. of difference $= \sqrt{\frac{16.9 \times 83.1}{1235} + \frac{12.8 \times 87.1}{6075}}$

$= 1.15\ \%$

Now $\frac{\text{difference}}{\text{S.E. of difference}} = \frac{4.1}{1.15} = 3.6$

This is significant.

It may be concluded that, as far as the Cape Town municipal area and Langa is concerned Malays are considerably more susceptible to pregnancy toxaemias than Coloureds.

In fact the difference of 4.1% is only likely to arise by chance less than once in 370 times.

2. The test of significance of difference between Coloureds and Europeans percentages (B. and C).

Here: $n_1 = 6075.$ $p_1 = 12.8$ $q_1 = 87.2$

$n_2 = 2859.$ $p_2 = 12.6$ $q_2 = 87.4$

Difference in percentages $= p_1 - p_2 = 0.2\%$

Estimate of standard error of difference. $= \sqrt{\frac{12.8 \times 87.2}{6075} + \frac{12.6 \times 87.4}{2859}}$

$= 0.75\ \%$

$\frac{\text{Difference}}{\text{S.E. of Difference}} = \frac{0.2}{0.75} = 0.27$

Here the difference is not even as much as its standard error and this is not significant.

It may be concluded that the difference between the Coloured and European percentages may be due to chance alone, being almost negligible.

3. The difference between European and Native percentages (C. & D)

Continued./.....

$n_1 = 2859 \quad p_1 = 12.6 \quad q_1 = 87.4$

$n_2 = 1198 \quad p_2 = 7.8 \quad q_2 = 92.2$

Difference in percentages = $p_1 - p_2 = 4.8$

Estimate of standard error of difference. $= \sqrt{\frac{12.6 \times 87.4}{2859} + \frac{7.8 \times 92.2}{1199}}$

$= 0.99$

$\frac{\text{Difference}}{\text{S.E. of difference.}} = \frac{4.8}{0.99} = 4.8$

This is highly significant.

It can be concluded that as far as the Cape Town Municipal area and Langa are concerned Europeans are considerably more susceptible to pregnancy toxaemias than Natives.

4. Difference between Coloured and Native percentages (B. & D.).

Here: $n_1 = 6075 \quad p_1 = 12.8 \quad q_1 = 87.2$

$n_2 = 1198 \quad p_2 = 7.8 \quad q_2 = 92.2$

Difference in percentages = 5.0%.

S.E. of difference $= \sqrt{\frac{12.8 \times 87.2}{6075} + \frac{7.8 \times 92.2}{1198}}$

$= 0.885$

$\frac{\text{Difference}}{\text{S.E. of difference}} = \frac{5.0}{0.885} = 5.6$

This is highly significant.

It can be concluded that as far as the municipal area of Cape Town and Langa are concerned, Coloureds are more susceptible to pregnancy toxaemias than natives.

The probability that the difference in percentages would occur by chance is infinitesimal.

5. Difference between Malay and European percentages (A. & C.).

$n_1 = 1235 \quad p_1 = 16.9 \quad q_1 = 83.1$

$n_2 = 2859 \quad p_2 = 12.6 \quad q_2 = 87.4$

Difference in percentages = 4.3%

Continued./...

$$\text{S.E. of difference} = \sqrt{\frac{16.9 \times 83.1}{1235} + \frac{12.6 \times 87.4}{2859}}$$

$$= 1.23$$

$$\frac{\text{Difference}}{\text{S.E. of Difference}} = \frac{4.3}{1.23} = 3.5$$

This is significant.

It can be concluded that as far as the Cape Town municipal area and Langa are concerned, Malays are more susceptible to pregnancy toxaemias than Europeans.

The difference of 4.3% between Malays and Europeans is only likely to occur by chance once in 370 times.

6. The difference between Malays and Native percentages (A & D).

$n_1 = 1235$ $p_1 = 16.9$ $q_1 = 83.1$

$n_2 = 1198$ $p_2 = 7.8$ $q_2 = 92.2$

Difference in percentages: 9.1 %

$$\text{S.E. of difference} = \sqrt{\frac{16.9 \times 83.1}{1235} + \frac{7.8 \times 92.2}{1198}}$$

$$= 1.32$$

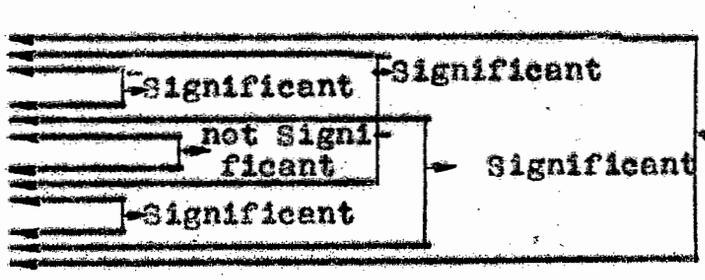
$$\frac{\text{Difference}}{\text{S.E. of difference}} = \frac{9.1}{1.32} = 6.9$$

This is highly significant.

It can be concluded that in the Cape Town municipal area and Langa the Malays are far more susceptible to pregnancy toxaemias than the Natives.

CONCLUSIONS:

1. Malay : 16.9
   Coloured : 12.8
   European : 12.6
   Native : 7.8



2. It can be concluded that as far as the Cape Town municipal area./.....

and Langa Native Township are concerned the incidence of pregnancy toxaemias in Malays is significantly high compared with any other race.

3. It can be concluded that as far as the Cape Town Municipal area and Langa Native Township are concerned the incidence of pregnancy toxaemias in Natives is significantly low compared with that of any other race.

4. The Asiatic figures obtained were not statistically analysed as the number involved are too small.

CONFIDENCE LIMITS:

This is the estimation of the possible upper and lower limits of a proportion or percentage obtained by statistical investigation.

Let P = population proportion and $\frac{t}{n}$ = sample proportion in a random sample of size n.

$$\text{Lower Limit} = P_L = \frac{\left(\frac{t}{n} + \frac{2}{n}\right) - 2\sqrt{\frac{1}{n} + \frac{1}{n}\left(\frac{t}{n}\right)\left(1 - \frac{t}{n}\right)}}{1 + \frac{4}{n}}$$

$$= \frac{(t + 2) - 2\sqrt{1 + \frac{t(n - t)}{n}}}{n + 4}$$

$$\text{Upper Limit} = P_U = \frac{(t + 2) + 2\sqrt{1 + \frac{t(n - t)}{n}}}{n + 4}$$

In this case the "population" would be the number of pregnancy cases in the area chosen over a period of years, amongst the individual racial groups. The "sample" is the great majority of pregnancy cases in this area, amongst the individual racial groups over a period of one year (1950 - 1951). The possible lower or upper limits of the percentages to be calculated should be valid over any period of years provided there is no radical change in the mode of living of the population, considerable

migration./....

migration, or the addition there-to of new elements, and provided of course that toxaemia is not an epidemic disease, of which it is not suspect.

If these formulae are applied:-

A. <u>To Malays:</u>

$n = 1235 \quad t = 209 \quad n-t = 1026$

$$P_{U,L} = \frac{211 \pm 2\sqrt{1 + \frac{209 \times 1026}{1235}}}{1239} \quad \text{(given in fractions)}$$

Upper Limit = 19.2%

Lower Limit = 14.9%

It can be concluded that from year to year the percentage of Malay pregnancy toxaemias in Cape Town and Langa areas will be between 19.2% to 14.9%.

B. <u>To Coloureds:</u>

$n = 6075 \quad t = 775 \quad n-t = 5300$

$$P_{U,L} = \frac{777 \pm 2\sqrt{1 + \frac{775 \times 5300}{6075}}}{6079}$$

Upper Limit = 13.6%

Lower Limit = 11.9%

It can be concluded that from year to year the percentage of Coloured pregnancy toxaemias in Cape Town and Langa areas will be between 13.6% and 11.9%.

C. <u>TO Europeans:</u>

$n = 2859 \quad t = 360 \quad n-t = 2499$

$$P_L = \frac{362 - 2\sqrt{1 + \frac{360 \times 2499}{2859}}}{2859 + 4}$$

$$= \frac{362 - 36}{2063}$$

Continued./...

$$= \frac{326}{2863} = 11.4\%$$

$$p_U = \frac{362 + 36}{2863} = 13.9\%$$

It can be concluded that from year to year the percentage of European pregnancy toxaemias in Cape Town and Langa areas will be between 13.9% and 11.4% with a risk of 1 in 20 of the range of percentages being greater.

D. To Natives:

$n = 1198 \quad t = 94 \quad n-t = 1104$

$$p_{U,L} = \frac{96 \pm 2\sqrt{1 + \frac{94 \times 1104}{1198}}}{1202}$$

Upper Limit: = 9.5 %

Lower Limit: = 6.4 %

It can be concluded that the number of native pregnancy toxaemias in Cape Town and Langa areas will be between 9.5% and 6.4% from year to year, with a chance of 1 in 20 of the range of percentages being greater.

E. The number of Asiatics in Cape Town and Langa areas, are too small and accordingly the statistical analysis was not considered.

CHAPTER VII.

CLASSIFICATION OF TOXAEMIA CASES.

The nett figures of the toxaemia cases encountered in the study of the incidence of the toxaemias of pregnancy will be further analysed into the following subgroups:-

1. CASES OF ECLAMPSIA:

There were 24 cases of eclampsia, and the detailed features of the individual cases are portrayed in Table II on the following page. From a study of their records the diagnosis appears to be justified in each case, because of the typical symptoms and signs. No case was encountered in this series with coma only without fits. Oedema was clinically absent in one case and minimal in another, but varying amounts of proteinuria were invariably present in all cases. A study of the features of these cases suggests that the older hypertensive cases with superadded toxaemia are the ones tending to show minimal oedema. They may, in fact, be cases of hypertensive encephalopathy as opposed to the classical eclampsia cases, a feature emphasised by Dieckmann (1952). It is noteworthy that three of the 24 cases were associated with twin pregnancies, a known predisposing factor as emphasised by Eden (1922) and Guttmacher (1939).

2. CASES WITH OEDEMA ONLY:

The question of cases with oedema only was difficult to assess from the case records. In many cases where oedema was remarked on the other causes of oedema were not satisfactorily ruled out by the medical officers who conducted the antenatal examinations of cases. Further the question of oedema occurring in normal as well as in toxaemic pregnancies is in its own right a subject for further study, and I have therefore not enlarged on this aspect of the problem at all. However, 3 native antenatal cases encountered are worth recording because they apparently had gross oedema, but no other signs of toxaemia. All 3 of them originated from the Langa Municipal Antenatal Clinic.

Case./.....

TABLE II.

The following table shows the total number of cases of eclampsia encountered amongst Cape Town and Langa residents at all the hospitals, nursing homes and clinics during the period 1st April 1950 - 31st March 1951, with details of individual cases.

	Hospital:	Locality:	Name:	Race:	Age:	Parity:	Emergency or Antenatal;	Type of Eclampsia:	Height of B.P.:	Albumen:	Oedema:	Child:
1.	Groote Schuur.	Claremont	H.D.	C	46	5	E.	I.P.	188/105	+++	-	S.B.
2.	Groote Schuur.	Athlone.	N.S.	C	26	6	E.	I.P.	165/100	++	+	A.B.
3.	Groote Schuur.	Kensington	H.M.	C	20	2	E.	A.P. & I.P.	150/130	+	++	Twins AB
4.	Groote Schuur.	Langa	R.S.	N	15	1	E.	A.P.	135/110	+++	+++	A.B.
5.	Groote Schuur.	Brooklyn	A.M.	C	31	6	A.N.C.	P.P.	195/120	+	+	A.B.Twins
6.	Groote Schuur.	Cape Town.	S.K.	M.	36	6	E.	A.P. & I.P.	140/100	+++	+	Neo.D.
7.	Groote Schuur.	Cape Town.	S.W.	C.	18	1	E.	I.P. (Died)	186/120	++++	+++	S.B.
8.	Groote Schuur.	Cape Town.	G.D.	C	26	1	A.N.C.	I.P.	144/100	+++	++	Neo.D.
9.	Groote Schuur.	Langa	V.T.	N.	24	1	A.N.C.	I.P.	138/72	+++	++	A.B.
10.	Gilmour.	Cape Town.	E.C.	E.	32	1	A.N.C.	I.P.	165/100	++	+	S.B.
11.	Peninsula Maternity	Cape Town.	M.W.	C	18	1	E.	P.P.	165/110	+++	+	A.B.Twin
12.	Peninsula Maternity	Cape Town.	S.F.	M	18	1	E.	I.P.	135/110	+++	+++	Neo.D.
13.	Peninsula Maternity	Crawford.	M.A.	C	23	1	E.	A.P.	200/120	++	++	A.B.
14.	Peninsula Maternity	Woodstock.	G.W.	M	16	1	A.N.C.	I.P.	190/110	++	++	A.B.
15.	Peninsula Maternity	Cape Town.	M.M.	C	16	1	E.	A.P. & I.P.	180/144	++	++	S.B.
16.	S.A. Home.	Cape Town.	S.J.	M	18	1	E.	I.P.	180/110	++	++	A.B.
17.	S.A. Home.	Cape Town.	C.P.	C	26	1	E.	I.P.	195/110	+++	+++	S.B.
18.	Mowbray Maternity	Rondebosch.	S.G.	E	36	1	E.	I.P.	230/130	+++	+	A.B.
19.	Mowbray Maternity	Cape Town.	L.B.	E	25	1	E.	I.P.	260/130	++	++	A.B.
20.	New Somerset	Windermere.	M.W.	C	30	6	E.	I.P.(Died)	170/130	+++	+	S.B.

Continued./...

TABLE II CONTINUED.

The following table shows the total number of cases of eclampsia encountered amongst Cape Town and Langa residents at all the hospitals, nursing homes and clinics during the period 1st April 1950 - 31st March 1951, with details of individual cases.

	Hospital:	Locality:	Name:	Race:	Age:	Parity:	Emergency or Antenatal:	Type of Eclampsia:	Height of B.P. :	Albumen:	Oedema:	Child:
21.	New Somerset	Heathfield	E.duT.	C	42	2	E.	I.P.	240/116	+	±	S.B.
22.	New Somerset	Cape Town	A.B.	M	19	1	A.N.C.	P.P.	160/100	+++	+++	A.B.
23.	New Somerset	Maitland	L.T.	C	17	1	E.	I.P. (Died)	210/125	++	++	S.B.
24.	New Somerset	Cape Town	J.M.	M	20	1	E.	I.P.	170/105	++	++	A.B.

The abbreviations used indicate the following:-

A.P. - Antepartum.
I.P. Intrapartum.
P.P. Postpartum.
A.B. - Alive Birth.
S.B. - Still Birth.
Neo.D. - Neonatal death.
A.N.C. - Antenatal Care.

(Case No. 122, 179 and 251 respectively). It is possible that these were cases of oedema of nutritional origin, but no special investigations were done and any opinion I express can only be speculative. Although this may not be the most suitable place in the thesis to remark on the blood pressure readings of the native cases, I should like to record the fact that at all the clinics where natives were seen I was impressed by the very low blood pressure levels they demonstrate throughout pregnancy. Readings of 80/40 to 60/30 mm. Hg. were often encountered, and on discussing this phenomenon with medical practitioners experienced in this type of clinic work, they concurred that they often see such low blood pressure readings amongst native cases.

3. CASES WITH ALBUMINURIA ONLY:

Three cases were encountered that can be classified in this subsection.

Case 1: J.E., a Malay attended the St. Monica Hospital, aged 30, a fourth para, presented with albuminuria ++ and general lassitude. Her blood pressure varied from 110/65 to 100/60 mm. Hg. and on further examination pus and micro organisms were found in her urine. Special investigation showed a calculus in the left kidney and a hydronephrosis. She had a premature alive delivery and subsequently a nephrectomy. In this case therefore the albuminuria is adequately explained.

Case 2: An European aged 34. A fourth para from the Booth Hospital presented with albuminuria. This was proven to be due to a vaginal discharge, the result of a carcinoma of the cervix in association with a 34 weeks pregnancy. She had the appropriate treatment.

Case 3: A Native aged 19 from the Retreat Municipal Clinic. A primipara 20 weeks pregnant with blood pressure readings varying from 110/60 to 120/75 mm. Hg. with gross albuminuria and microscopic casts and a past history suggestive of nephritis was encountered. However, it appears from the record that she returned to Pondoland before further investigation was done. In her case the albuminuria is probably

explicable./...

explicable on the basis of chronic glomerulonephritis complicated by pregnancy.

4. The Total of 1,440 toxaemia cases were analysed into the following subgroups:-

(a) Cases with hypertension only:

i) Mild.

This includes cases with a blood pressure of 130/85 to 169/99 mm. Hg. and 120/80 to 159/99 mm. Hg. in respect of cases under the age of 20 years.

ii) Severe:

This includes all cases with a blood pressure of 170/100 mm. Hg. or higher.

(b) Cases with hypertension and albuminuria and/or oedema:

i) Mild:

This includes cases with a blood pressure of 130/85 to 169/99 mm. Hg. and 120/80 to 159/99 mm. Hg. in respect of cases under the age of 20 years.

ii) Severe:

This includes all cases with a blood pressure of 170/100 mm. Hg. or higher.

The cases in each of these subgroups were correlated with their age and parity.

On pages 75 and 76 a Table illustrating this classification and correlation is reproduced.

TABLE 111.

SHOWING THE CLASSIFICATION OF THE TOXAEMIA CASES ENCOUNTERED AND THE CORRELATION OF RACE, AGE & PARITY IN THE SUBGROUPS.

(a) 1. CASES WITH MILD HYPERTENSION ONLY. B.P. 135/85 TO 169/99 OR 120/80 TO 169/99 MM. HG.

PARITY:

Race:	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Total:
E.	71	33	21	10	10	5	2	2	1	1	1	-	1	-	-	-	158
C.	103	54	35	24	19	19	19	10	7	7	14	4	5	1	1	3	325
N.	8	2	4	3	3	2	1	-	1	1	1	1	-	-	-	-	27
M.	27	12	5	7	2	6	7	-	5	3	2	2	1	3	1	1	84
Total:	209	101	65	44	34	32	29	12	14	12	18	7	7	4	2	4	594

AGE GROUPS IN YEARS:

Race:	15-18	19-21	22-25	26-29	30-32	33-35	36-39	40-44	45-49	Total
E.	6	24	32	31	13	19	19	12	2	158
C.	40	59	53	44	26	26	42	29	6	325
N.	3	3	3	4	2	5	4	2	1	27
M.	9	9	15	8	10	6	18	8	1	84
Total:	58	95	103	87	51	56	83	51	10	594

(a) 11. CASES WITH SEVERE HYPERTENSION ONLY I.E., B.P. OF 170/100 MM. HG. OR HIGHER.

PARITY:

Race:	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Total:
E.	-	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	4
C.	2	-	-	1	-	-	3	1	-	1	2	-	-	1	-	-	11
N.	-	-	-	-	-	-	1	-	-	-	-	-	-	-	-	-	1
M.	-	1	-	-	-	-	-	-	-	-	-	-	-	-	1	-	2
Total:	2	2	1	2	1	-	4	1	-	1	2	-	-	1	1	-	18

AGE GROUPS IN YEARS:

Race:	15-18	19-21	22-25	26-29	30-32	33-35	36-39	40-44	45-49	Total
E.	-	-	-	-	-	-	2	2	-	4
C.	1	1	-	-	1	-	3	5	-	11
N.	-	-	-	-	-	-	-	1	-	1
M.	-	-	-	-	-	-	-	1	1	2
Total:	1	1	-	-	1	-	5	9	1	18

TABLE III CONTINUED.

SHOWING THE CLASSIFICATION OF THE TOXAEMIA CASES ENCOUNTERED AND THE CORRELATION OF RACE, AGE & PARITY IN THE SUBGROUPS.

(b) i. CASES WITH MILD HYPERTENSION, ALBUMINURIA AND/OR OEDEMA.

PARITY:

Race:	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Total:
E.	103	23	14	8	1	5	1	3	1	1	-	-	-	-	-	-	160
C.	144	48	23	26	21	12	13	7	4	7	5	1	3	2	1	-	317
N.	24	9	5	6	2	3	4	-	1	-	-	1	-	-	-	-	55
M.	43	12	8	9	5	4	3	2	3	1	4	3	1	-	1	-	99
A.	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2
Total:	315	93	50	49	29	24	21	12	9	9	9	5	4	2	2	-	633

AGE GROUPS IN YEARS:

Race:	15-18	19-21	22-25	26-29	30-32	33-35	36-39	40-44	45-49	Total
E.	10	28	50	28	14	11	15	4	-	160
C.	44	75	68	39	23	25	26	16	1	317
N.	6	13	9	7	4	9	4	2	-	54
M.	20	17	21	9	11	6	11	4	1	100
Total:	81	134	148	83	52	51	56	26	2	633

(b) ii. CASES WITH SEVERE HYPERTENSION I.E., B.P. OF 170/100 & WITH ALBUMINURIA AND/OR OEDEMA.

PARITY:

Race:	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Total:
E.	18	7	3	4	1	3	-	-	-	-	-	1	-	1	-	-	38
C.	40	8	7	5	6	10	8	7	10	8	4	4	1	2	1	1	122
N.	3	2	1	1	1	-	3	-	-	-	-	-	-	-	-	-	11
M.	8	2	2	1	2	-	1	3	-	1	-	3	1	-	-	-	24
A.	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0
Total:	69	19	13	11	10	13	12	10	10	9	4	8	2	3	1	1	195

AGE GROUPS IN YEARS:

Race:	15-18	19-21	22-25	26-29	30-32	33-35	36-39	40-44	45-49	Total
E.	2	3	6	5	4	4	4	8	2	38
C.	15	13	14	8	10	12	26	20	4	122
N.	2	3	1	-	-	3	1	1	-	11
M.	3	3	3	1	-	5	4	4	1	24
Total:	22	22	24	14	14	24	35	33	7	195

CHAPTER VIII.

A DISCUSSION OF THE TOXAEMIA CASES STUDIED.

1. THE INCIDENCE OF ESSENTIAL HYPERTENSION AMONGST THE TOXAEMIA CASES COLLECTED.

One of the greatest difficulties in any study of this nature of the toxaemias of late pregnancy is the inability to differentiate at the time between the various toxaemias encountered. This is especially the case with the differentiation of "true" pre-eclamptic toxaemia from those cases where toxaemia is superimposed upon nephritis, latent or manifest, or hypertensive vascular disease, especially if latent.

A knowledge of the pre- pregnancy state of the renal and vascular system is of immense value if available. In addition the patient should be examined regularly from the beginning of pregnancy. However, many cases are seen only for the first time from the 18th to the 24th week, and if they are hypertensive at this stage it is probable that they have underlying hypertensive vascular disease, which pregnancy has revealed. On the other hand if they develop signs of hypertension after the 28th week with or without albuminuria and oedema they are usually regarded as cases of true pre-eclamptic toxaemia. I believe this latter type of case never develops permanent vascular or renal sequelae. The snag is that latent hypertensive cases with superadded toxaemia may faithfully mimic these latter cases for some years. Therefore, follow-up study is the best available method at present to aid in the differentiation of the various types of toxaemia. Nevertheless, the latent hypertensive group may or may not be hypertensive after the first pregnancy, when followed-up and, are wrongly labelled true pre-eclamptic toxaemia cases. If they are hypertensive at follow-up examination they are usually interpreted as being cases of true pre-eclamptic toxaemia with a chronic legacy of the preceding toxaemia. This view is incorrect in my opinion. I do not believe that true pre-eclamptic toxaemia leaves the patient with residual lesions. If a series of latent hypertensive cases with superadded

toxaemia./....

toxaemia are studied, some of them only become permanently manifestly hypertensive after the second or third pregnancy, yet they behave like true pre-eclamptic toxaemias on each occasion prior to this. Before the stage is reached when they become clinically hypertensive they have a normal blood pressure in the interim period between the first two or three pregnancies. Such cases then have in reality escaped their correct diagnosis of essential hypertensive vascular disease because of a lack of our present day diagnostic methods. This aspect is discussed in a latter section of the thesis.

These difficulties make the precise distinction of the toxaemias encountered here almost insurmountable because they have been studied from their case histories which were often incomplete, and they have not been followed-up. Many were seen for the first time after the 28th week of pregnancy.

To form an approximate idea of the percentage of these cases who really have underlying hypertension, latent or manifest, I included all the mild and severe cases manifesting hypertension as the sole sign during pregnancy, if it occurred before the 30th week, with the cases over 35 years of age in the group manifesting hypertension and albuminuria with or without oedema. These latter cases are to my mind almost certainly cases of essential hypertension and the former are very likely so. They comprised a sum total of 771 of the 1,440 toxaemia cases encountered i.e., 53% (see Table III).

This figure corresponds exactly with the incidence of hypertensive vascular disease found amongst a mixed group of 100 eclamptics and a 100 non-convulsive toxaemia cases followed-up and investigated.

The stated incidence of hypertensive vascular disease with superadded toxaemia amongst any group of toxaemia cases of late pregnancy vary from author to author because of these difficulties in differentiation. Figures reported by various authors vary from 40 to 70% Torpin (1952). Dieckmann (1952) states that 50% of toxaemia patients have essential hypertension as the basis of their

toxaemia./....

toxaemia, a figure which closely corresponds to the findings in the present series.

2. THE DIFFERENCE IN INCIDENCE OF THE TOXAEMIAS AMONGST THE VARIOUS RACIAL GROUPS:

The first question to be discussed is why the incidence of pregnancy toxaemias are higher in the Malay section of the population than in any other racial groups.

The first possible reason that springs to mind is that a dietary deficiency may be a contributing factor. However, Brock and Batson (1953), from a dietary budget survey investigation, comparing the Malay and Christian Cape Coloured diets, found no significant difference between the diets of these two groups of the population. There were minor dietary differences e.g. the Malays per head consumed more fish, more condensed milk, cooking oil and bread, but less fresh milk, margarine and eggs than the Christian coloured people.

While doing the follow-up studies, I enquired into the habits and diets of all cases examined, but could not find a common factor. A few of the Malays developed eclampsia during the Ramazan fast, but this is not invariably the case. Others thought excessive meat and salt fish in their diets may have been responsible for their toxaemic manifestations, while further cases brought forward psychological reasons e.g. marital unhappiness, financial difficulties etc., as possible etiological factors.

De Lee and Greenhill (1947) state that pregnancy toxaemias are less frequent amongst members of races whose diet is composed chiefly of vegetables. This may be applicable to the Natives, especially in the rural areas, but the urbanised Bantu in South Africa has modified his diet considerably and it is doubtful whether this alone explains the low incidence found locally amongst the Natives.

The next possibility to consider is whether there is a hereditary predisposition amongst the Malays to develop pregnancy toxaemia and/or eclampsia. In section 4 of the present thesis heredity and

hypertension is discussed. Hypertension is a common known predisposing factor to toxaemia, but as indicated under that section, we do not know sufficient about the genetics and inheritance of hypertension to reach any final conclusions. We do not know the incidence of hypertensive vascular disease amongst the Malay section of the population, which will appear to be a fruitful future investigation and may help to elucidate this as a possible factor leading to the higher incidence of toxaemia amongst the Malays.

In a later section a Malay family is quoted in which eclampsia occurred in seven different members of the same family. (A world record because I could find nothing to squal this number of cases occurring in one family in the literature). Anders (1952) states that there may be hereditary tendency in eclampsia, but I feel that this possible etiological factor is still far from proved.

Another possible reason is that the Malays may have a higher incidence of toxaemia because of a tendency to marry young. It is known that in India where marriage occurs early, 75% of the eclampsia is found in patients who are between the ages of 15-19 years. 75% of all eclampsias occur before the age of 30 years. Dieckmann (1952).

If all the patients in the age group 15 to 18 years are considered in the preceding table, then the following data are obtained in this regard.

The percentage of pregnant cases with toxaemia in the age group was as follows:-

European:	5.0%
Native :	11.9%
Coloured:	12.9%
Malays :	15.4%

The fact that the percentage of Malay toxaemias in this young age group exceeds those in the other races, may indicate that early marriage is a factor tending to lead to a higher incidence of toxaemia cases amongst the Malays.

A further factor in this regard may be that Malays tend to have more children than the other races, or tend to have more children after the age of forty years than the other sections of the local population. To see what influence this might have, all the patients grouped in the age groups 40-49 years amongst the various races in the tables were collected and calculated as a percentage of the total in each respective racial group. The results were as follows:-

The percentage of pregnant cases with toxaemia in these age groups were:-

Natives	:	7.5 %
Europeans	:	8.3%
Coloureds	:	10.1%
Malays	:	10.1%

These data indicate that in the older age groups the incidence of pregnancy toxaemias amongst coloureds and Malays is of the same order and therefore one can assume that age and underlying hypertension plays the same role in both groups. Moreover there does not appear to be an appreciable difference between the size of coloured and malay families.

3. A COMPARISON OF THE LOCAL FIGURES WITH THE INCIDENCE OF THE TOXAEMIAS IN OTHER CENTRES:

This is a very difficult matter to discuss because different standards and classifications are used by various authors who have written on the subject. In many instances the standards used are not mentioned, the cases considered do not fall within the same time period, or only institutional figures are quoted. To give an illustrative example: the incidence of the pregnancy toxaemias, found to be 12.6% in the population of the area considered by me with the standards used, can be reduced to 8.7%. This can be done, if only cases of all ages with a blood pressure of 140/90 mm. Hg. or above, and satisfying the other criteria mentioned, are included, instead of utilising the blood pressure levels mentioned. This agrees with a figure of 6 - 9% incidence of pregnancy toxaemias which is quoted

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by Dexter and Weiss (1943), using similar standards.

All over the world toxaemias are not notifiable diseases. This also applies to eclampsia, except in the case of 3 states in Germany, namely Saxony, Hamburg and Baden, where only eclampsia is legally notifiable. However, I reproduce Table IV on pages 83 and 84, compiled from data by Theobald (1930), Küstner (1931), De Snoo (1938), Baader (1939), Crichton (1947), Falkiner (1949), Browne (1951) Dieckmann (1952), Decio and Centaro (1952) and others that indicates approximately the incidence of eclampsia and the non-convulsive toxaemias in all the continents of the world. Unfortunately the figures are derived from hospital statistics which rarely give a true picture, as I have indicated previously. If one examines these tables, it is obvious that there are 40 centres mentioned having a higher incidence of eclampsia than our local figure of 0.21%. There are 14 centres with a lower incidence than this figure. The fact remains, however, that the figures are not strictly comparable, and the only conclusion I can draw with some justification is that it does not appear that the incidence of eclampsia in Cape Town is amongst the highest in the world.

With regard to the incidence of the toxaemias quoted for the various centres, there seem to be so many obvious discrepancies in the figures, which must indicate that they are inaccurate. Some centres have a high incidence for eclampsia and yet an extremely low incidence for toxaemia. This unusual state of affairs is found in at least 13 centres mentioned in the Table. This is quite contrary to the usual sequence found when accurate statistics are kept. In such centres the incidence of the toxaemias are much greater than that of eclampsia. In the present study one out of sixty toxaemic pregnancies resulted in eclampsia. If the incidence of the non-convulsive toxaemias in the centres with apparently more acceptable figures are compared to those in the present study, then the incidence of the non-convulsive toxaemias appears to be higher in at least 7 of these centres mentioned in the Table. As previously mentioned, if the blood pressure criterion of 140/90 mm. Hg. of higher is applied to my figures, the incidence of the toxaemias is 8.7%. This

TABLE IV:

SHOWING THE INCIDENCE OF ECLAMPSIA & THE NON-CONVULSIVE TOXAEMIAS OF LATE PREGNANCY IN VARIOUS HOSPITALS & AREAS OF THE WORLD.
(Modified after Dieckmann and De Snoo and others approximately 1930 - 1940).

COUNTRY	CITY	Incidence of Eclampsia %	Incidence of Non-convulsive Toxaemias %	No. of Deliveries
China	Hong Kong	0.92	0.42	19,800
	Shanghai	1.27	3.31	9,239
	Canton	0.98	-	4,823
	Peiping	1.04	12.1	2,355
	Tsinan	1,50	0	1,574
India	Bombay	2.18	2.34	144,343
	Calcutta	3.10	-	17,116
Ceylon	Colombo	2.76	2.93	16,385
Malay States	Singapore	0.55	-	8,224
Japan	Tokio	0.88	-	242,404
Java	Suriname	0.33	-	4,698
Dutch East Indies	Batavia	0.21	-	13,924
	Serarang & Soerabaya	0.15	-	23,673
Fiji Islands		0.63	-	782
Virgin Islands		1.25	0.26	1,525
Phillipine Islands		1.03	0.16	66,630
Australia	New South Wales	0.53	-	222,635
Hawaii	Honolulu	0.15	-	2,000
West Indies	Curacao	0.43	-	6,248
Puerto Rico		2.54	27.33	2,477
Trinidad	Port of Spain	4.28	18.0	2,847
Persia		0.19	0.47	1,513
Africa	Kenya	0.14	0.8	2,070
	Tanganyika		0.13	5,774
	Ngonda	0.1	0.05	2,017
	Algiers	2.85	-	2,000
My Figures 1950-51	Cape Town	0.211	12.6	11,383
Peninsula Maternity Home (Crichton 1937-1947).	Cape Town	1.8	-	15,529
Sweden	Goteborg	0.31	-	85,036
	Stockholm	0.60	2.85	48,053
Finland	Helsingfors	0.31	-	68,543
Denmark	Copenhagen	0.17	-	737,701
Holland	Utrecht	0.11	24.6	19,000
Germany	Berlin	0.39	-	2,688,304
Russia	Leningrad	1.14	-	12,708
Austria	Vienna	0.68	-	385,226
Hungary	Budapest	0.29	-	186,496
British Isles	Rotunda 1938-39	0.317	6.0	5,985
	Queen Charlotte 1936 - 1938.	0.504	6.4	4,951
	Liverpool 1939-40	0.479	4.5	3,963
	St. Mary Manchester 1936-37	1.28	15.3	3,359

TABLE IV CONTINUED.

COUNTRY	CITY	Incidence of Eclampsia %	Incidence of Non-convulsive Toxaemias %	No. of Deliveries
British Isles	Glasgow 1933-34	2.0	9.2	7,513
	Edinburgh 1937-1938.	1.091	14.8	4,399
Australia	Brisbane 1939-1941.	0.709	8.90	6,351
	Sydney 1946-49	0.363	13.2	15,433
	Melbourne 1949-1950	0.667	7.5	5,850
New Zealand	Otago 1947-1949	0.560	7.0	3,000
U.S.A.	Illinois 1943-1947.	0.206	2.35	528,526
	Boston 1937-38	0.25	11.5	5,177
	New York 1938-1939.	0.17	7.6	6,341
	Brooklyn 1937-1939	0.12	2.6	3,449
	Chicago 1937-1940.	0.24	11.9	8,224
	John Hopkins 1945-1949.	0.138	15.8	11,607
	Cincinnati 1940-1945.	0.290	9.2	13,748
	San Diego 1949	0.17	3.2	4,680
Italy	Florence 1929-1951.	0.7	-	39,751
South Africa	Port Elizabeth 1942-1945.	1.08	-	4,332
	Durban	0.7	-	22,000
	Johannesburg 1935 - 1945.	0.34	-	41,755
	Kimberley	0.14	-	8,439

figure is in the same range as the figures quoted from Edinburgh, Dublin and Glasgow, New Zealand and Australian cities, but higher than most other British and American figures from their hospital centres.

Dieckmann (1947) found the mean incidence of eclampsia in the world to be 1%, and for the United States of America, 0.66%. Stander (1929) states that about 10% of pregnant patients suffer from one or another of a group of disorders termed the toxaemias of pregnancy.

I agree with the view held by Gibberd (1951) that if the same standards, criteria and methods are utilised, the incidence of toxaemia will be nearly the same in all parts of the civilised world. This opinion is supported by the following fact. The incidence of eclampsia in Saxony, quoting Küstner (1931) and Browne (1951), is one in 430 deliveries, and in Cape Town 1 in 474 deliveries. One cannot help thinking that if elsewhere accurate figures are produced the vast differences in the incidence of eclampsia would not be found.

CHAPTER IX.

SUMMARY AND CONCLUSIONS :

1. The time-honoured impression that the incidence of the toxaemias of late pregnancy is higher amongst the non-European population than amongst the European section of the population, is not substantiated by the present investigation. In fact the incidence in both these population groups is the same, namely 12.6%.

However, the incidence amongst the Malay section of the population (16.9%) has been found to be higher than amongst the Cape Coloured section of the population (12.8%) and the European section of the population (12.6%). The Native population shows the lowest incidence (7.8%). These figures have been subjected to statistical analysis.

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2. A comparison of the incidence of the toxaemias of late pregnancy in the population within the municipal boundaries of the city of Cape Town and the Langa Native Township, with that of the incidence in other centres in the world, although difficult because of different criteria used, indicates that the time-honoured impression of the high incidence locally is misleading and incorrect. There are many centres showing a much higher incidence.

3. The incidence of eclampsia in the Cape Town Municipal area and the adjoining Langa Native Township is of the order of 1 in 474 deliveries, i.e., 0.211%. This figure is strictly speaking, comparable only with the reported incidence of eclampsia in Saxony, which is of the order of 1 in 430 deliveries.

4. It is my opinion that if the same methods and criteria were applied in all the civilised areas of the world, different centres will tend to show a closely related incidence of eclampsia. There will however, be variations in the incidence depending on the adequacy of preventative, therapeutic and other measures adopted in the treatment of pre-eclamptic toxaemia. I believe that in the great majority, if not in all cases, eclampsia is a preventable disease, though pre-eclamptic and other toxaemias may not be.

5. In this investigation it was found that 1 out of every 60 cases of toxaemia developed eclampsia, i.e., an incidence of 1.7% amongst toxaemic pregnancies.

6. Those cases of eclampsia with minimal oedema were the older hypertensive cases with superadded toxaemia, the cases regarded as examples of hypertensive encephalopathy rather than "true eclampsia" by Dieckmann.

7. A preliminary observation made is that Native antenatal cases have extremely low blood pressures normally during pregnancy.

8. The incidence of underlying essential hypertensive vascular disease amongst the toxaemia cases traced in this investigation was found to be 53%.

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9. The higher incidence of the toxaemias of late pregnancy in the Malay population in comparison with the other racial groups, does not appear to be due to dietary difference.

It may be explicable on a hereditary basis, but this is not possible to prove or disprove with the available data, and in the present state of our knowledge.

One possible factor appears to be that a greater proportion of Malays tend to marry young, and therefore bear children while in the age group below 19 years. This is an age period known to be associated with a higher incidence of toxaemia during pregnancy, and may therefore be the factor explaining the high incidence of the toxaemias of late pregnancy in the Malays.

S E C T I O N IV.

THE FOLLOW-UP STUDY OF ECLAMPSIA AND THE NON-CONVULSIVE TOXAEMIAS OF LATE PREGNANCY.

CHAPTER I.

(A) MATERIAL :

(1) 100 Cases of Eclampsia who had eclampsia prior to 1948.

(2) 100 Cases of severe toxaemias of pregnancy without the occurrence of fits who had toxaemia prior to 1948.

A total of 200 cases of the various toxaemias were examined by me personally during the period 1 August 1952, until 31 August 1953. All the cases found to be abnormal were re-examined on at least two occasions.

SOURCE OF CASES:

The names of all the above patients were obtained from the registers at the Peninsula Maternity Hospital, New Somerset Hospital, St. Monica's Maternity Home, Groote Schuur Hospital and the Mowbray Maternity Hospital in Cape Town. Only definite cases of eclampsia were followed-up. With regard to the toxaemia cases, all cases were classified as severe toxaemias at the hospitals. However, because no finer diagnostic distinction was made at the time on their cards, they were automatically a mixed group.

At the beginning of the investigation I thought one would be able to collect a large series of cases. However, various difficulties which will be pointed out later, made it impossible to collect a greater number of cases than I have already indicated.

Armed with hundreds of names and addresses the first objective was to find the patients, and in this respect no stone was left unturned. On finding the patient, after taking the history, enquiring into her family history, and where possible, examining the members of the family from the point of view of a hypertensive tendency and arteriosclerosis, a complete physical examination was made and subsequently repeated in all borderline and abnormal cases.

A great deal of the field work was accomplished with the help of a specially trained social worker, who traced the patients, asked

preliminary questions and made appointments for them to be seen at the Groote Schuur Hospital, with special instructions to bring an early morning sample of urine with them on the day of examination in a specially supplied container. In addition they were instructed not to take any fluids as from the previous evening at 6 p.m. and to empty their bladders before retiring. This was done with the objective of doing a concentration and dilution test on all cases as outpatients, because there is a great scarcity of beds, and no research beds available for investigation of this kind. On the day of the examination the patient was given 2 pints of fluid, and several urine specimens taken within 2 - 3 hours where possible, for the purpose of the dilution test in all abnormal cases.

I found the patients very co-operative, especially those who were abnormal or had medical complaints. A fair number of the patients traced had to be seen at home, and if they were abnormal, they were persuaded to come to the hospital for a further examination, with the same instructions about the urine. This gave me an opportunity to examine some of their relatives at home as well, and in other cases the patients were asked to bring their mother or sisters with them for a check-up from the point of view of hypertensive cardiovascular disease. In this respect I was less successful.

In addition, all past records of previous pregnancies, clinic and hospital attendance, as well as records from private medical practitioners were obtained of each patient, so that eventually as much information as possible was collected of the past history and health of each patient in the series examined. With regard to this work which had taken me 18 months to complete, a great number of difficulties and obstacles were encountered. Firstly a great deal of time was spent going through case records of various hospitals and clinics to extract the necessary information, where inefficient filing systems, difficulty in reading handwritings and poor records of patient's addresses, led to a tremendous loss of time and labour. It also involved looking up old stored records in dark corners, in mortuaries and elsewhere.

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The biggest difficulty of all, actually, was to find all the past cases of toxaemia and eclampsia, because of inaccurate addresses, and with the immense expansion and development of Cape Town, and the lapse of time since the admission. (Up to 30 years). Many of the cases had thus moved from one abode to another and had further confinements at other hospitals, or at home, and after attending various clinics. A further difficulty was that a fair percentage of cases were single at the time, and some of these cases had subsequently married and changed their surnames and sometimes even their christian names.

A marked migration of the population in the last 20 years, especially amongst the Cape Coloured people, from amongst whom many of the cases came, was another obstacle. Industry has claimed many old dwelling sites. Natives live in many slum houses previously occupied by coloured people, and the latter have moved to new housing estates. There has also been a movement of coloured people into houses formerly occupied by Europeans whose present whereabouts are quite unknown. Some other cases have left Cape Town and are now living upcountry, and consequently could not be traced.

Native patients (fortunately few in the series) were rarely found because of language and other difficulties, e.g. the constant migration to and from the Native territories. The response to questionaires and postal letters was practically nil, and it meant that every case had to be traced by personal contact. After establishing one's innocency of motive, one had to use tact and patience to obtain the patient's co-operation. Only one patient of those traced refused to be examined. She, however, displayed definite paranoid traits.

It goes without saying that the patients most willing to be seen and most co-operative, were those who did not feel well. Some of these were brought to hospital by ambulance for re-examination and special investigation, after being seen at home. Some of the cases of eclampsia were flabbergasted by the fact that they were

traced so many years later for re-examination, because they were feeling fit and well. Those in employement had to be seen after hours and over the weekends. Considerable help came from maternity and welfare centres, housing estate officers, policemen, postmen and the patient's relatives and friends, displaying kindliness and co-operation. The interviews and fieldwork of this survey took more than a year to complete, and some cases had to be discarded because of insufficient available information for the purposes of this study.

The percentage of success in the follow-up of eclamptic cases was 43.1% (100 out of 232) and included 24 White or European and 76 non-European patients. The percentage of success in the follow-up of non-convulsive toxaemias was 25.5% (100 out of 391) including 38 European and 62 non-European patients. The time interval that had elapsed since the eclamptic attack, varied from 4 to 30 years, the average being 10.56 years. In the case of the non-convulsive toxaemias the time elapsed since the first attack of toxaemia varied from 4 to 30 years, the average being 13.5 years. The racial grouping of the cases followed-up is depicted on photographs 7 and 8 on pages 92 and 93.

It became apparent from this survey that those of us who do medical consulting work apart from obstetrics, must be more conscious of pregnancy toxaemias, and every female who presents herself at the medical outpatients department, especially those with hypertensive vascular and renal disease, should be specifically asked about past toxaemia of pregnancy and eclampsia, otherwise the patient will omit to mention such events. I make this statement because quite a few patients diagnosed as cases of hypertension, angina etc., by physicians, were in fact old eclamptics and toxaemia cases, who did not divulge their past toxaemic histories. It would be very interesting to do a survey at the medical outpatients in order to find out the exact percentage with hypertensive cardiovascular or renal disease, who have had toxaemia in the past. There is no figure of this nature available

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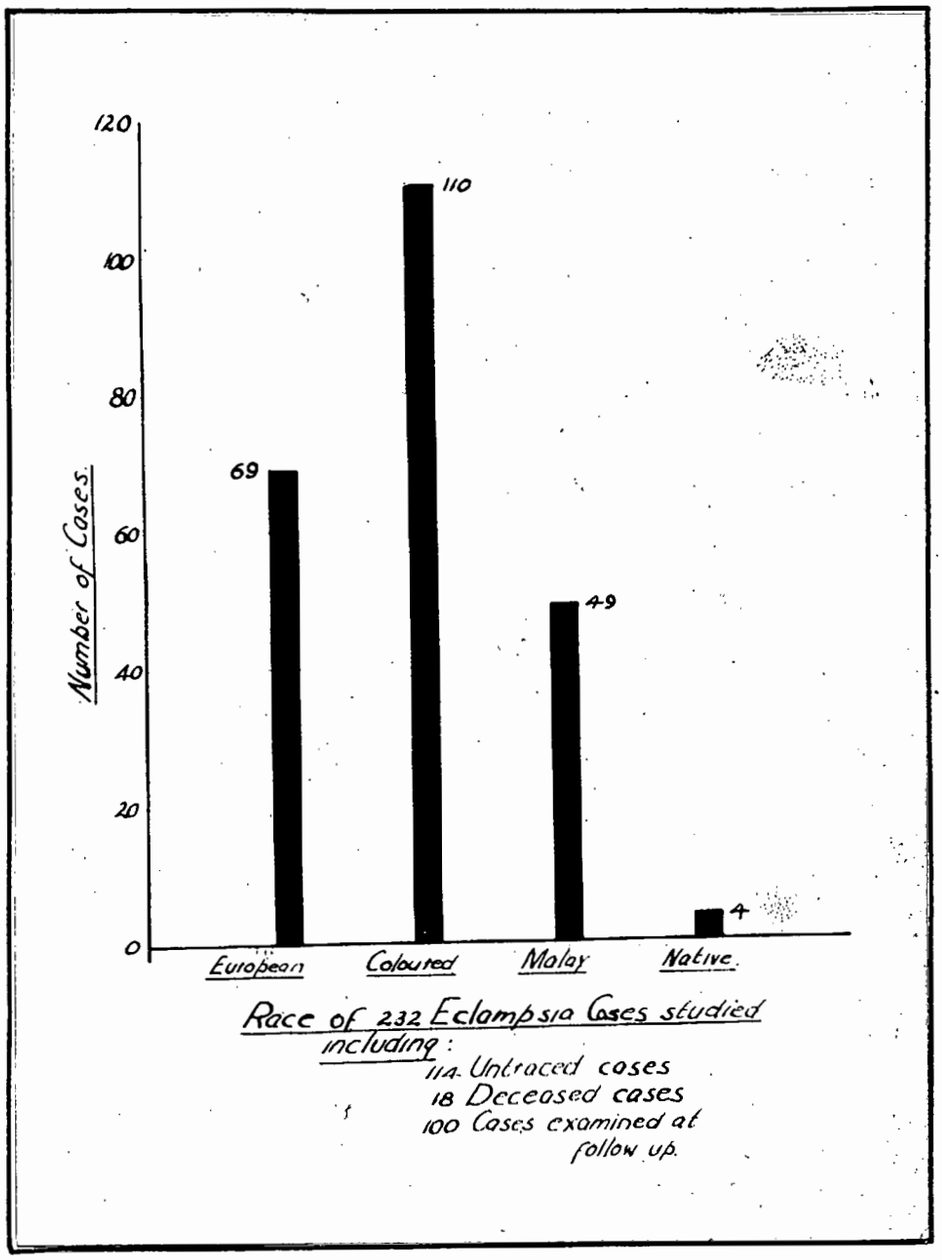
PHOTOGRAPH VII.

THIS PHOTOGRAPH PORTRAYS THE RACIAL DISTRIBUTION AMONGST ALL THE ECLAMPTICS ON WHOM A FOLLOW-UP WAS ATTEMPTED :

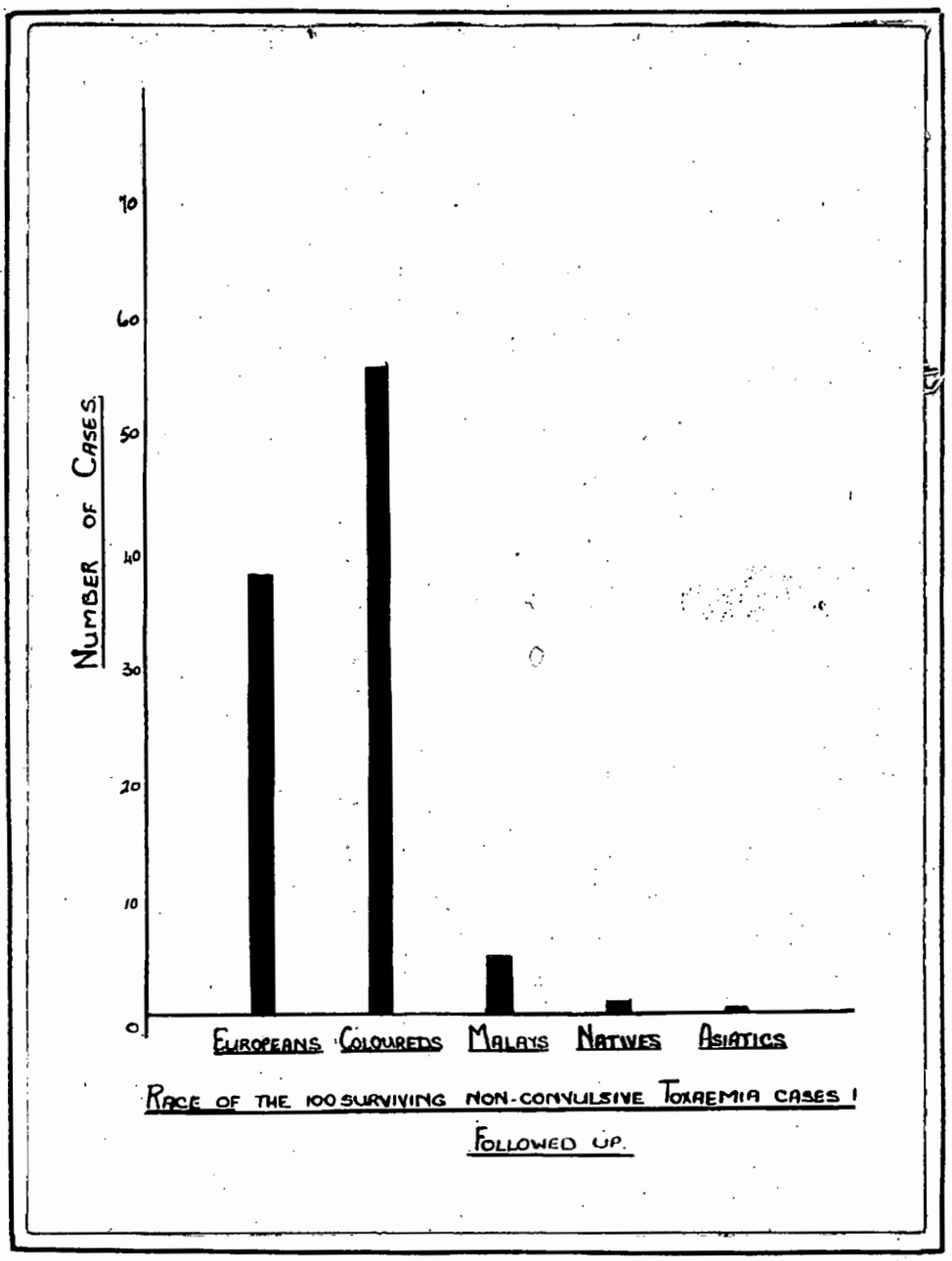


Race of 232 Eclampsia Cases studied including:

114 Untraced cases
18 Deceased cases
100 Cases examined at follow up.

PHOTOGRAPH VIII:

THIS PHOTOGRAPH SHOWS THE RACIAL DISTRIBUTION AMONGST THE 100 SURVIVING NON-CONVULSIVE TOXAEMIA CASES FOUND & FOLLOWED-UP.



Race of the 100 surviving non-convulsive Toxaemia cases followed up.

in the literature. This would serve as a double check with regard to the subsequent sequelae of the toxaemias.

(B) METHODS:

(1) GENERAL METHODS:

In all cases a complete medical history with emphasis on all past illnesses, pregnancies, personal habits and customs, as well as the obstetrical and gynaecological facts were taken and subsequently checked on the past records. This was followed by a full clinical examination, urine analysis and microscopy, and in selected cases a catheter specimen examination as well. In addition the height and weight were recorded in every case and a funduscopic examination made, and where necessary the pupils were dilated with Homatropine.

(2) METHODS OF BLOOD PRESSURE ESTIMATION USED:

Here possible fallacies were constantly born in mind. A standard mercurial sphygmomanometer with a 5" cuff was used and readings were taken with the patient lying relaxed, comfortable, and after a period of preliminary rest, varying from a quarter to half an hour or more, with the arm bare from the shoulder and at heartlevel, and the cuff applied so that its lower border was 1" from the bend of the elbow, with the middle of the rubber band lying over the brachial artery. Preliminary readings by palpation to avoid the auscultatory gap were taken. The accepted systolic blood pressure is the highest level at which successive sounds are heard, and as the pressure is lowered the dull thud is replaced by a murmur and then louder and sharper sounds. The point at which the clapping sounds suddenly become muffled was taken as the diastolic pressure except in cases of aortic valve regurgitation. (Two cases in the present series). In cases of auricular fibrillation (one in this series) only approximate

readings./.....

readings can be taken, and here the systolic blood pressure was taken at the point where the majority of beats come through, and the diastolic where the majority of beats become muffled, and, as the blood pressure varies with respiration, it was taken with quiet breathing. These are the methods recommended by the British Cardiac Society and the American Heart Association for the standardisation of methods of measuring the arterial blood pressure (1939).

For the purposes of this study normal systolic blood pressure was taken as 95 - 139 and normal diastolic blood pressure 60 - 89 mm. Hg. Thus an abnormal or raised blood pressure in this follow-up study was taken as 140/90 mm. Hg., or above (Wood 1950).

In any doubtful case after a period of rest on a couch, up to half an hour or more, repeated readings were taken at 5 minute intervals with the cuff left in situ until a steady reading was obtained. This was then taken as the patient's blood pressure. In 3 cases regarded as normal, preliminary readings were 140/90 mm. Hg., but the final reading was in the region of 120/80 mm. Hg.

Physiological vaso-constriction due to emotion, cold, or other causes, was excluded, and the examination done at room temperature.

Disparity between readings taken from each arm was common, especially in athero-sclerotic and hypertensive cases. However, the difference seldom exceeded 5 to 10 mm. in keeping with the findings of Amsterdam and Amsterdam (1943). The blood pressure in the legs was only taken to exclude co-arctation of the aorta where this possibility was suspected. In every case the femoral pulses were felt to exclude this possibility. The possibility of phaeochromocytoma was borne in mind in taking the history, but there was no justification to do special tests, such as the pipe-roxane test (only 6 cases have been reported in pregnancy, Bowen 1950).

According to Bechgaard (1946), the high blood pressure accompanying Thyrotoxicosis (none in this series) and the climateric

a/.....

(a fair number in this series) is coincidental and statistical analysis shows no significant correlation and the pressure does not fall when these disorders are corrected. Hypertension associated with mitralstenosis is a chance association (3 cases in the present series). Wood (1950) states the blood pressure in obese subjects may appear to be higher than it really is owing to the unreliability of the cuff method of measurement when applied to a fat limb, and lower pressures may be recorded by direct arterial puncture. This however, is not a procedure that is practicable in a study of this nature.

3. METHODS OF CARDIAC EXAMINATION USED:

For the purposes of estimating cardiac size clinically, the apex beat (that is the site of maximum cardiac impulse) was found, and its position recorded with reference to the intercostal spaces, the midline and the mid-clavicular line. If it was beyond 9 cm. to the left of the midline and/or outside the mid-clavicular line, it was concluded there was clinical cardiomegaly provided scoliosis, an elevated diaphragm or pulmonary adhesions were excluded. In all doubtful cases an X-ray examination was made to confirm the diagnosis.

4. SPECIAL INVESTIGATIONS:

Some of these were preformed in the vast majority of cases, but all the methods of special investigation were not always performed in each case. The following special investigations were carried out :-

a) The Blood Urea:

This was estimated in all cases with the help of the Pathology laboratory. The estimations were performed by Conway's urease method (1933).

b) Bloodsugar:

In all cases with glycosuria a fasting bloodsugar estimation was done with the co-operation of the Pathology laboratory. Folin' and Wu's method of determination was employed.

c) Bacteriological Examination of Urine:

A bacteriological examination of a catheter specimen of urine was made in all cases where there was a clinical history past or present suggestive of pyelitis and where pus cells were found microscopically in the urine.

d) Radiography of the Heart and Lungs:

As the clinical assessment of the cardiac size is often inaccurate, in all suspect cases, a radiological examination was resorted to.

It has been pointed out by Parkinson, Evans (1952) and others that for some time cardiomegaly need not be evident in hypertensive vascular disease and rounding of the left ventricle occurs first before the transverse diameter is increased, and is best seen in the left oblique view. Elongation, widening and unfolding with or without atheroma and calcification of the aorta is a common helpful sign in hypertension associated with prominence of the ascending aorta to the right, and bowing of the descending aorta to the left in the region of the pulmonary bay, these signs plus the measurement of the cardio-thoracic ratio were used as criteria to decide whether or not cardiomegaly existed.

A standard 6 ft. P.A. view was taken in all suspect cases as a routine. In some cases oblique views were done as well, and other cases were examined fluoroscopically in addition, applying the methods of Evans (1952).

e) Electrocardiography:

Electrocardiograms were recorded with a Sanborn Cardiette and a Sanborn Viso Cardiette in all abnormal cases in the Eclamptic series and in some abnormal cases in the non-convulsive

toxaemic./.....

toxaemic series. In each case the three standard limb leads, the Goldberger Unipolar limb leads and the unipolar chest leads V1 to V6 were used (Goldberger 1951).

f) Pyelography:

Intravenous pyelograms were done in all cases where the past or present history as well as the microscopic urine findings were suggestive of possible pyelitis or pyelonephritis.

g) Liver Function Tests:

They were not done as routine, but only in a few special cases, by the Pathology laboratory.

(i) a. Colloidal Gold Test.
b. Thymol Turbidity Test.
c. Thymol Floculation Test.

These three tests were performed according to the method of MacLagan (1944). The Colloidal Gold reading should normally be 0 and the Thymol Turbidity reading should not exceed 3. These tests were impaired in one case, presumed to have sub-acute disseminated Lupus Erythematosis.

(ii) Serum Proteins: Serum albumen and Globulin were estimated by a modification of Fine's Biuret Method (1935) in the above-mentioned case.

h) Blood Count:

A complete blood count by the standard methods in haematology (Whitby and Britton 1946) was done in a few cases who appeared anaemic, to exclude anaemia and its cardiovascular manifestations as the cause of abnormal clinical signs in the cases studied. In no case however, was the abnormal findings explicable on this basis.

CHAPTER 2.

ECLAMPSIA FOLLOW-UP STUDY.

The results of the follow-up study after an avenage interval of 10.5 years of the 100 surviving eclamptic cases found, who had a total of 512 pregnancies, and 18 eclamptic cases traced to have died in the interim, with pertinent discussions in the respective subsections. (See photograph 9 on page 100, depicting the results. See photographs 11 and 12 on pages 113 and 114, showing in summary form the pertinent obstetrical history and other data of the 100 eclamptic cases followed-up.)

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1. NORMAL CASES:

There were 70 cases with a normal blood pressure, without retinal changes or proteinuria, amongst the 100 surviving eclamptic cases studied.

2. HYPERTENSIVE CASES:

There were 30 cases out of the 100 surviving cases with a blood pressure of 140/90 mm. Hg. or higher, with varing degrees of fundal changes. Twenty-two of these cases had a blood pressure of 180/100 mm. Hg or higher and could be regarded as severely hypertensive. Detailed discussions of these hypertensive cases will follow in later subsections.

3. CASES WITH PROTEINURIA:

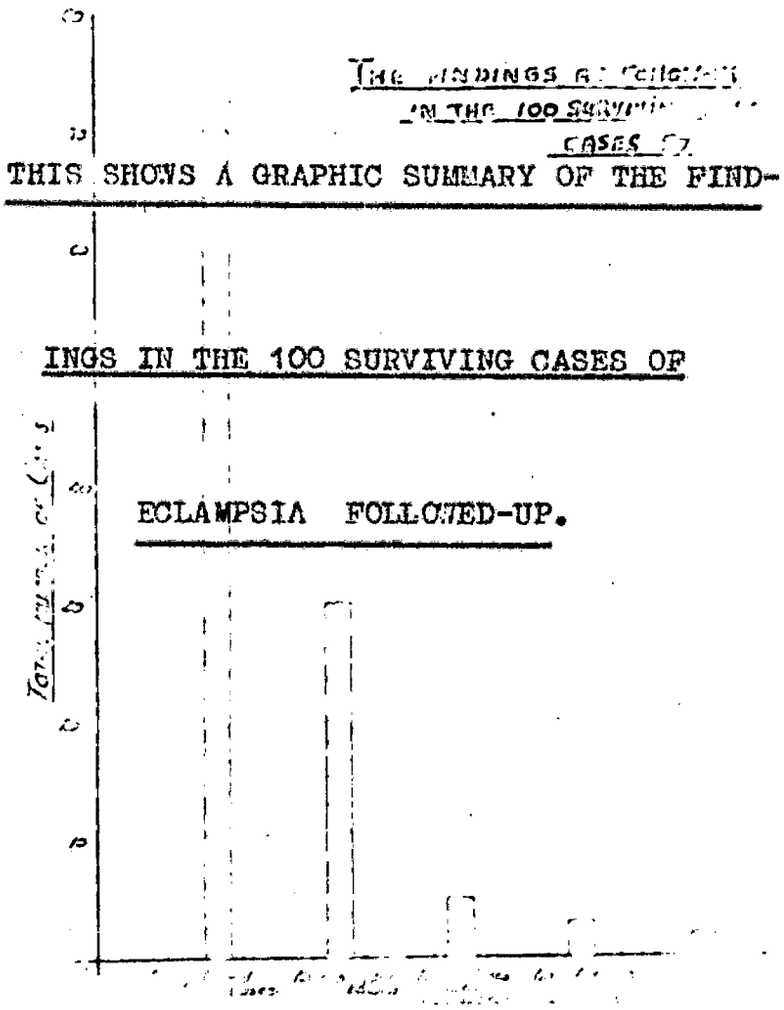
There were 5 cases of the total number with proteinuria. They all had hypertension as well, and are therefore included in the hypertensive group. In 4 out of the 5 cases there was only a trace of proteinuria.

4. CASES WITH DIABETES MELLITUS:

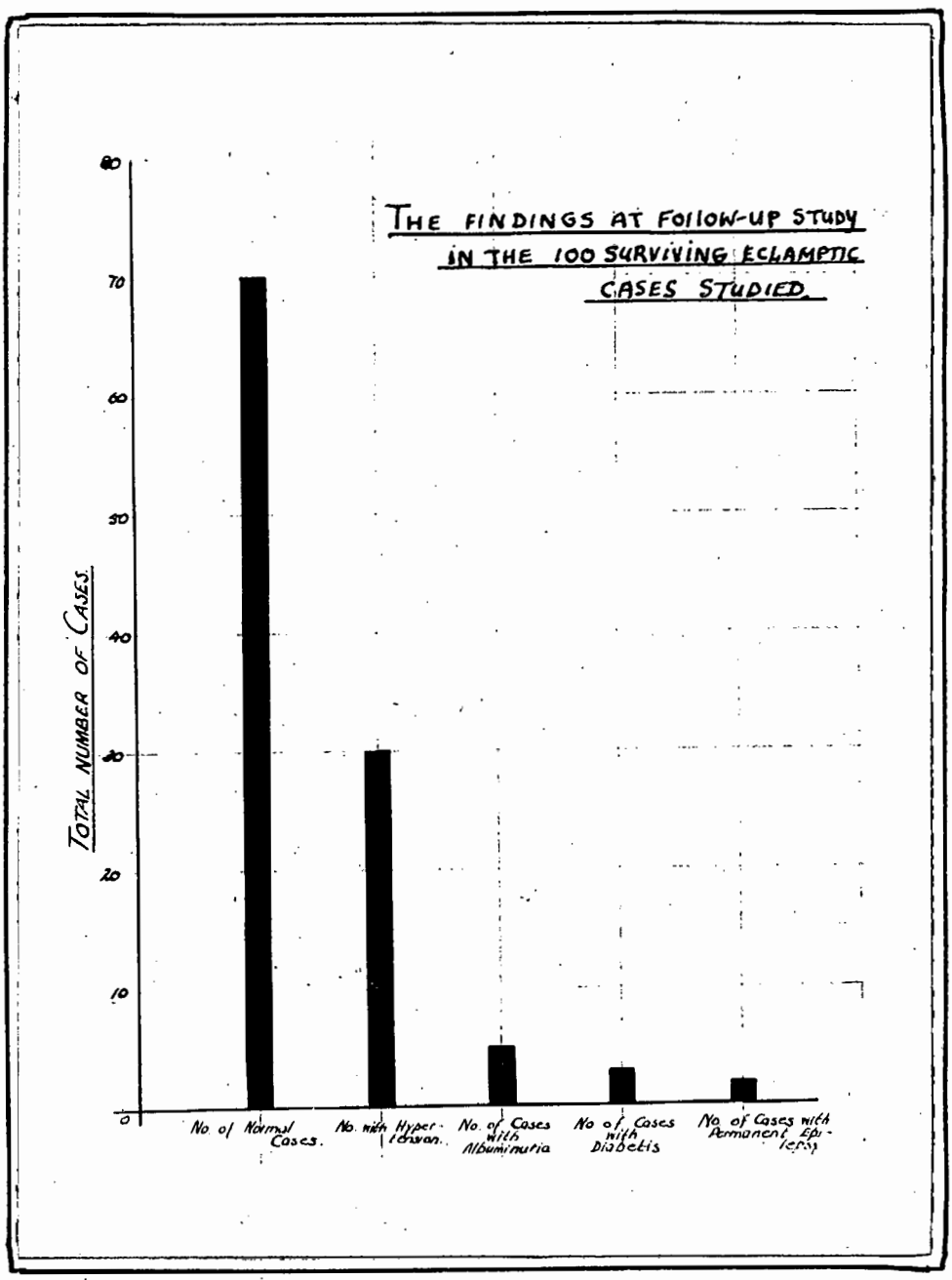
There were 3 cases of diabetes mellitus amongst the total number. In each case the diabetes mellitus developed some years after the eclamptic attack. One of these cases was found to be hypertensive at the time of the follow-up examination. There is no reason to believe that the diabetes was a cause of the convulsions. None of these cases had developed diabetic nephrosis or clinically detectable intracapillary glomerulosclerosis. According to Dieckmann (1952) 0.4% of toxaemia cases have diabetes

mellitus./.....

PHOTOGRAPH IX.



THIS SHOWS A GRAPHIC SUMMARY OF THE FINDINGS IN THE 100 SURVIVING CASES OF ECLAMPSIA FOLLOWED-UP.


THE FINDINGS AT FOLLOW-UP STUDY IN THE 100 SURVIVING ECLAMPTIC CASES STUDIED.
TOTAL NUMBER OF CASES.
80
70
60
50
40
30
20
10
0
No. of Normal Cases.
No. with Hypertension.
No. of Cases with Albuminuria
No of Cases with Diabetis
No. of Cases with Permanent Epilepsy

mellitus and although toxaemia is a major complication in diabetes, diabetes is a negligible factor in toxaemia cases. Chesley and Somers (1941) found that 3 out of 167 eclamptics followed up, had developed diabetes mellitus in the interim.

5. CASES WITH EPILEPSY FOLLOWING ECLAMPSIA:

Two of the cases followed-up had permanent epilepsy (grand-mal) following eclampsia. The one case was normotensive and had eclampsia once (Case 78). The other case had eclampsia 5 times in succession with epilepsy following the fifth attack, and is now hypertensive as well (Case 43). In both cases there was no past history of epilepsy and no family history of convulsive seizures. Maltby and Rosenbaum (1942) found 65% of eclamptic women (13 out of 20 cases) had electroencephalographs indicative of cerebral dysrythmia, and 60% gave a family history of a convulsive diathesis. Although Whitacre and Loeb (1947) have found electroencephalographic changes in 6 cases of eclampsia with the attack, this work has not been generally confirmed.

If the same method of estimation of convulsive diathesis used by Maltby and Rosenbaum is applied, and the two cases with post-eclamptic epilepsy in addition to the 14 other cases with a family history of eclampsia are included, as they do, there is a 16% incidence of a convulsive diathesis in the present series. However, there were no cases of epilepsy in this series or in their families apart from the two cases of post-eclamptic epilepsy already mentioned. The occurrence of epilepsy after eclampsia, although a rare entity, is recognised by neurologists as a complication, and such cases have been reported by Dexter and Weiss (1941) Maltby and Rosenbaum (1942) and others.

In contrast the incidence of a convulsive diathesis was 8% amongst the non-convulsive toxaemia cases followed-up. A consideration of the facts, and the incidence of a convulsive diathesis found in the present series, does not confirm that the

work of Maltby and Rosenbaum is correct, and it has been planned further, to do routine electroencephalographs in the toxaemia wards in the future, to prove or disprove, their suppositions.

6. THE PREMENSTRUAL TENSION SYNDROME & ITS ASSOCIATION WITH ECLAMPSIA:

Green and Dalton (1953) and others put forward the view that there may be an etiological association between this syndrome and the toxaemias of pregnancy, therefore a study of this aspect was included in the follow-up investigations even if only to disprove their contentions.

The fellowing symptoms occur in this syndrome, headaches, abnormal hunger, painful breasts, lumbar pain, emotional irritability etc. and epileptiform seizures in about 3% of cases. In addition palpable oedema and excessive water retention and a gain in weight are usually found, and is thought to be due to an endocrine imbalence, especially of the oestrogen, progestrone ratio (Morton 1946). The syndrome has been treated successfully with progestrone and a low salt diet. It is thought that these features become exaggerated in certain women and predispose to toxaemia during pregnancy. Premenstrual tension first described by Frank (1931) is one of the commonest minor endocrine disorders found in the premenstrual phase of the menstrual cycle in about 40% of otherwise healthy women, Israel (1938) and Bickers and Woods (1951). On the other hand the toxaemias of pregnancy occur in only about 10% of pregnant women. Stander (1945), states that if premenstrual tension is present in a toxaemia case its presence is merely a chance association.

The incidence of eclampsia has been stressed to be higher in single women by some authors, and in this series of 100 eclamptics 30 were single, when they had eclampsia. I thought that the occurrence of the premenstrual syndrome may explain the high incidence of unmarried pregnancies, because, as stated by Israel (1938), there is often a desire to find relief by foolish actions,

difficult./.....

difficult to restrain, and often a transient Nymphomania, in this condition. I therefore tried to find out how many of the cases had this syndrome when they first conceived. Only 7 single women gave a history of premenstrual tension, persistently present from puberty until the time of conception and thereafter, therefore this can be discarded as an important etiological factor in pregnancy in single women. Of the 100 cases followed-up, 61 had a history of premenstrual tension, but in 26 the symptoms disappeared after the eclamptic attack while in 21 the symptoms occurred for the first time following the eclamptic attack. In 14 cases there were premenstrual tension symptoms persistently from puberty until the time of examination. In 39 cases there was no history of premenstrual tension at all.

These facts point out that there is no definite etiological relationship between these two conditions, but a mere chance association if they occur together, or if premenstrual tension develops following a toxaemic or eclamptic pregnancy.

7. <u>THE FAMILY HISTORY OF THE ECLAMPTIC PATIENTS FOLLOWED-UP</u>:

See photograph 10, on page 104, portraying the results of this aspect of the investigation. For the detailed histories refer to the appendix at the end of the thesis in Section VI.

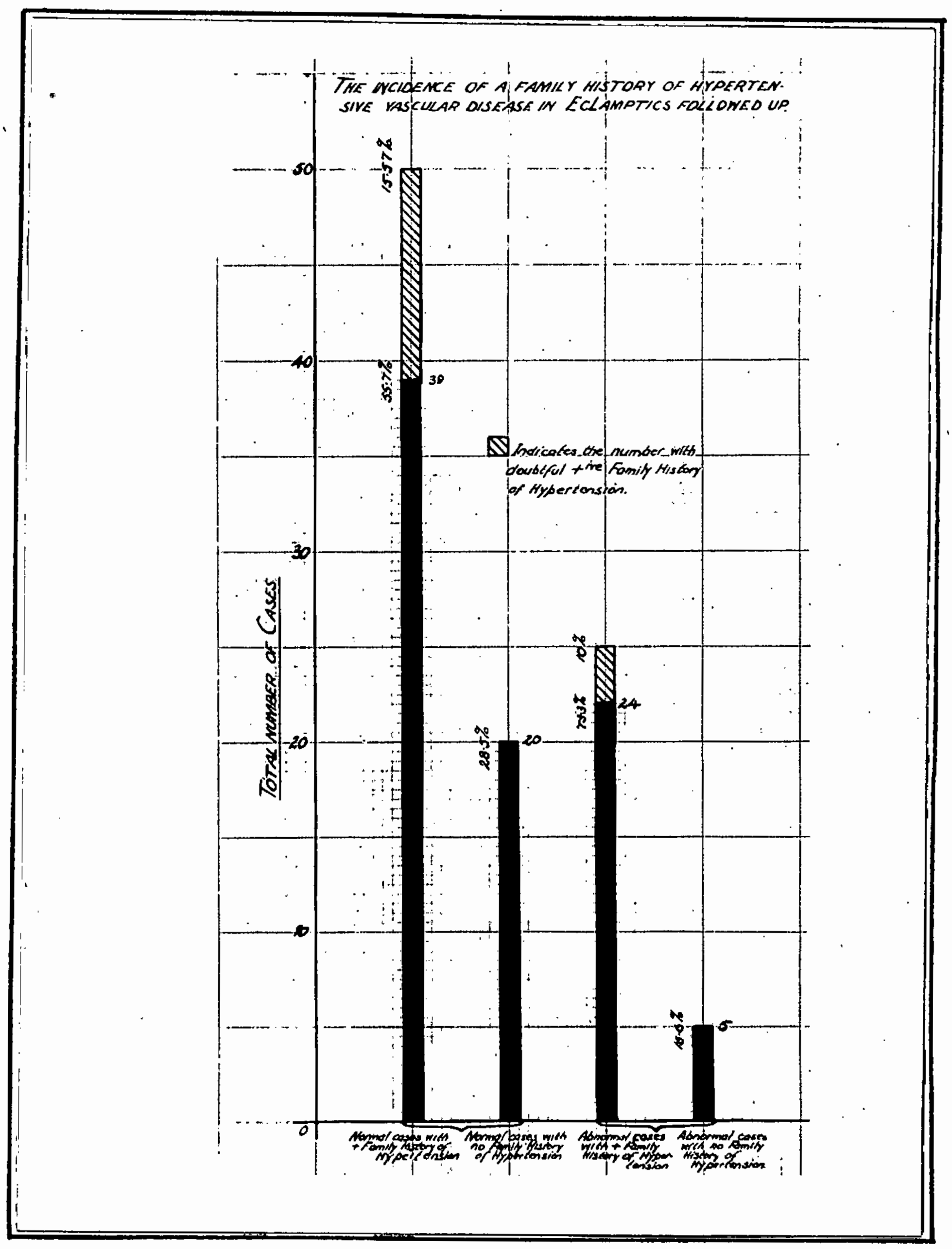
The findings were based on the patients statements and where possible a determination of the blood pressure of relatives, and by referring to Hospital records and Medical Practitioners where the relatives were not available for examination. In cases where the patient's relatives had died, hospital records were consulted where possible, if they had attended there prior to death or during their last illness. In this study a raised blood pressure was taken to mean 140/90 mm. Hg. or higher.

It will be seen from studying the results of this investigation that in some cases the family record and pedigree is incomplete because of difficulty in confirming all the statements by a personal examination of each member of the family.

The./.....

PHOTOGRAPH X:

THIS SHOWS IN SUMMARY FORM A GRAPHIC RECORD OF THE FAMILY HISTORIES OF HYPERTENSIVE VASCULAR DISEASE, OF THE SURVIVING ECLAMPTIC CASES STUDIED.


THE INCIDENCE OF A FAMILY HISTORY OF HYPERTENSIVE VASCULAR DISEASE IN ECLAMPTICS FOLLOWED UP.
TOTAL NUMBER OF CASES
0
10
20
30
40
50
15·57%
35·7%
39
28·5%
20
10%
24
15·6%
5
Indicates the number with doubtful +ive Family History of Hypertension.
Normal cases with + Family History of Hypertension
Normal cases with no Family History of Hypertension
Abnormal cases with + Family History of Hypertension
Abnormal cases with no Family History of Hypertension

(a) THE FAMILY HISTORY WITH REGARD TO THE OCCURRENCE OF ECLAMPSIA IN OTHER MEMBERS OF THE FAMILY:

In the 100 eclamptics followed-up there was a family history of eclampsia in 14 cases. (Namely cases 6, 9, 24, 31, 32, 36, 40, 45, 61, 79, 81, 82, 93 and 98 respectively). This occurred in 6 or 20% of the hypertensive cases, and in 8 or 11.4% of the cases found to be normotensive at follow-up examination. In some of the families there were two, three or more cases of eclampsia. Three cases who had eclampsia twice have a family history of eclampsia. In no case was a family history of epilepsy found; this is rather surprising and contrary to the findings of Maltby and Rosenbaum (1942), who found 58% giving a family history of epilepsy. One of the cases had 5 attacks of eclampsia in succession and is now an epileptic. One other case after having eclampsia once is also epileptic.

From the point of view of a familial incidence of eclampsia, the worst case in this series is a Malay woman (Case 79) who had eclampsia twice at the age of 25 years with her second and at the age of 33 years with her sixth pregnancy. Her history with regard to her pregnancies is as follows:-

Her first pregnancy was toxaemic, second eclamptic, third, fourth and fifth toxaemic, sixth eclamptic, seventh, eighth and ninth again toxaemic. She is now hypertensive, 49 years old and has a family history of hypertension.

The details of her family history are as follows:-

Her mother had eclampsia with the birth of her first child and died in her early forties from hypertensive vascular disease. One of her sisters had eclampsia with her first child and is reported to be well. Another sister had eclampsia with her third child and died during the attack. Her two eldest daughters have had eclampsia (Both included in this series), with their first pregnancies, one of whom has subsequently had a normal pregnancy.

A./.....

A good many reports have appeared of the occurrence of eclampsia in several members of the same family and a tendency to hypertensive disease in relatives of patients with eclampsia and toxaemia of pregnancy has also been noted. Barnes and Browne (1945). Theobald (1933) described a family history in which both parents died of Bright's disease, 5 of their children died of cerebral haemorrhage, one from Angina Pectoris, 1 from tuberculosis and 1 from eclampsia. The surviving daughter had a high blood pressure. In the next generation 1 grandchild died from cerebral haemorrhage, 1 of eclampsia, 1 of tuberculosis and 3 surviving have high blood pressure. Malpas (1938) reported 4 families in each of which there was a high incidence of vascular disease and cases of eclampsia.

Bickenbach and Kronig (1939) and Bickenbach (1939) reported 4 out of 39 eclamptic patients had one, two or more cases of eclampsia in the same family and the incidence of kidney disease and early apoplexy was very definitely increased in these four families. They calculated that this was a much greater familial incidence than would be expected, if it were due to chance alone. Anders (1952) concluded that heredity is of decisive importance in the development of the toxaemias of pregnancy and eclampsia. He found 4 cases of eclampsia with eclampsia in other members of their families. He thought that the disease was transmitted by a gene of low penetrance. In the case mentioned in my series eclampsia occurred in 7 different members of the same family; this must be regarded as a world record because I have not found a single family in the literature with as many occurrences. There is no evidence of renal disease as in the family reported by Theobald; and only her deceased mother, she herself, and her deceased eclamptic sister have or had manifest hypertensive vascular disease.

Barnes and Browne (1945) stated that they could find no hereditary factors in the causation of the hypertension of late pregnancy except in cases where essential hypertension was associated with pregnancy, however it is doubtful if chance alone was

the./.....

the cause of the familial incidence of eclampsia in the 14 families of the 100 eclamptics followed-up, and it should tend to make one think seriously of a hereditary tendency in eclampsia as suggested by Anders of Rostock.

(b) A FAMILY HISTORY OF TOXAEMIA:

A definite family history of toxaemia was found in only 6 cases, but as toxaemia is not as spectacular a condition as eclampsia, a true picture of its incidence cannot be obtained if one has to rely on the statements, observations and memories of relatives. Unless a complete record of all the relatives in all their pregnancies is available, it will not be possible to give an accurate figure in this regard and I have moreover not been able to trace definite figures in the literature for reference. Only generalisations can be quoted e.g. Anders (1947) states that there is a tendency for a higher incidence of toxaemia amongst the relatives of eclamptic cases.

(c) THE INCIDENCE OF A FAMILY HISTORY OF DIABETES MELLITUS:

Twelve out of the 100 cases had a family history of diabetes mellitus, namely cases 1, 3, 4, 11, 21, 47, 51, 59, 73, 86, 90 and 96. This is a much higher incidence of a diabetic family history than usually found and the chances of manifest diabetes in the offspring of such families is one in four according to White and Pincus (1946). This will tend to predispose to vascular degenerative lesions, with or without hypertension in those who develop manifest diabetes, and may thus be responsible for hypertensive vascular changes later on, in such cases who have also had eclampsia. There are 3 patients with diabetes mellitus in the present series but in all 3, its presence was only established long after the eclamptic attack and they are not hypertensive at present. I do not think that there was any definite causative relationship unless the pre-diabetic stage of diabetes mellitus is blamed, but this is hardly tenable, in view of Dieckmann's statement quoted previously.

The./.....

(d) THE FAMILY HISTORY WITH REGARD TO HYPERTENSIVE VASCULAR DISEASE IN THE 30 CASES OF ECLAMPSIA FOUND TO BE HYPERTENSIVE AT FOLLOW-UP EXAMINATION.

In 22 or 73.3% of these cases there was a definite family history of hypertensive vascular disease. In 5 or 16.6% of these cases there was no familial hypertensive history. In 3 or 10% of these cases there was a doubtful positive familial hypertensive history.

(e) THE FAMILY HISTORY WITH REGARD TO HYPERTENSIVE VASCULAR DISEASE IN THE 70 CASES OF ECLAMPSIA FOUND TO BE NORMOTENSIVE AT THE FOLLOW-UP EXAMINATION:

In 39 or 55.7% of these cases there was a definite family history of hypertensive vascular disease.

In 20 or 28.5% there was no familial hypertensive history. In 11 or 15.5% there was a doubtful positive familial hypertensive history.

(f) DISCUSSION OF THE FAMILY HISTORIES OF HYPERTENSIVE VASCULAR DISEASE.

If one adds those with a doubtful positive family history in each group to those with a positive family history in the eclamptic series studied, then, of the cases who are abnormal or hypertensive, 83.3% have a familial hypertensive history, whereas 71.2% of the cases found to be normal have a familial hypertensive history. Although the numbers are small I do think one can conclude that there is not really a markedly higher incidence of a familial hypertensive history amongst those found to be hypertensive years later, than amongst those cases normotensive years later.

This would tend to indicate that a hypertensive family history by itself is not an important factor, or the only factor in determining subsequent hypertension, and that other factors may operate to determine subsequent hypertension in a patient who has had eclampsia. However, the inheritance of hypertension is not

such/.....

such a simple matter as will be seen later, and inter alia genetic penetrance may be a determining factor in whether or not a hypertensive family history is passed on as a hypertensive tendency to the offspring.

One can look upon these findings from another point of view; i.e., that hypertensive vascular disease is extremely common. Bell and Clawson (1928) found hypertension accounted for 14.8% and Fahr (1928) 20% of all deaths in the United States of America in people over 50 years of age, and according to Robinson and Brucer (1940) 40% of the adult population of the U.S.A. are actually or potentially hypertensive. Master et al (1943) found 40% of subjects over 40, 65% to 70% of those over 70 years to have some degree of hypertension with slightly higher figures for women than men. If this is true the chances are that several members of the same family, especially if it be a large family, may suffer from hypertension without there necessarily being any hereditary element, and therefore may be wrongly assumed to have an inherited hypertension or a hypertensive tendency. In particular, this view might be applied to subsequently hypertensive eclamptic patients. On the other hand, according to Platt (1948) essential hypertension could be a hereditary disease conveyed as a mandelian dominant with a rate of expression of more than 90%. This may be an extreme view, but the importance of the hereditary factors although not understood cannot be denied. Thus Ayman (1934) studying 277 families found hypertension in the children in 3.1% of the families when both parents were normal, in 28.3% when one parent was hypertensive and in 45.5% when both parents were hypertensive. Again Hines (1940) found that the children were hyper-reactors to the cold pressor test, in 43.4% when one parent was either hypertensive or a hyper-reactor, and in 95% when both parents had positive findings and were effected by hypertension. Williams (1933) felt that inheritance played a role in hypertensive vascular disease and Bechgaard (1946) Barach (1928), Allan (1933) and others found that up to 77% of patients

with/.....

with essential hypertension have a family history of hypertensive cardiovascular disease. I think that although a familial incidence of hypertension is well known its mode of inheritance is as yet not fully worked out and only general conclusions can be drawn. It is thus possible that inheritance transmitted by a gene with greater or lesser penetrance could possibly explain why eclamptic cases found to be hypertensive at the follow-up examination are hypertensive and why the others are normotensive in spite of a not much greater incidence of a hypertensive vascular family history in the former group than in the latter group.

Other observers, e.g. Diechmann (1952) enquired into the family hypertensive history of 47 eclamptic cases and found that 19% had a positive family history of hypertensive vascular disease. He found a much greater incidence of hypertensive vascular disease, that is, 69% in cases of severe essential hypertension associated with pregnancy. The number of cases and the length of time over which they were studied is not mentioned.

Amongst the 76 subsequently hypertensive cases in a group of 100 non-convulsive toxaemia cases also studied in this thesis, the incidence of a family history of hypertension was 93.4%, whereas amongst the 24 normotensive cases in this non-convulsive toxaemia group 66.6% had a family history of hypertension. This shows that a somewhat greater proportion of essential hypertensives have a family history of hypertension than in the 2 sub groups of eclamptics and pre-eclamptic cases who are normotensive years later.

Barnes and Browne (1945) investigating the relatives of 176 patients with or without pregnancy toxaemia of various types, found some normal cases with relatives who had hypertension, but again it is not stated how long these cases were observed and it must be realised that such cases may eventually develop toxaemia and/or eclampsia in later pregnancies. They had only 5 cases of eclampsia in their series and 3 out of 12 of thdr relatives examined, had hypertension but 9 not. They concluded from this small series that eclampsia occurs in patients who have no

familial/.....

familial predisposition to hypertensive disease, and they deduced from their studies that a familial hypertensive tendency was of little importance in the etiology of pre-eclamptic toxaemia or eclampsia, but in cases of essential hypertension with supperadded toxaemia it was of etiological importance.

I found a higher incidence of a family history of hypertensive vascular disease than the other observers in eclampsia and non-convulsive toxaemia cases. The fact that I studied a larger series of cases and for a longer time after the occurrence of eclampsia or toxaemia, may partly explain the higher incidence because, not only did it give the patient, but also her relatives a chance to grow older, and thus manifest hypertensive vascular disease.

I feel that many cases who develop pre-eclampsia and eclampsia may have a familial hypertensive history, but the proportion with such a history is lower than in the cases with essential hypertension who are pregnant, or cases with latent hypertension who are pregnant and sooner or later become hypertensive. The crux of the problem is that pre-eclampsia and eclampsia occure not only in patients who have inherited hypertension or a latent hypertensive tendency, but also in patients who have not inherited these. It is only in the former group that hypertensive vascular sequelae are found, sooner or later at follow-up examination.

The latter group will henceforth be referred to as the "true" pre-eclamptic or "true" eclamptic cases, and although members of their families may have hypertension, they have not inherited this.

It is evident from the follow-up study that hypertension need not be a factor leading to pre-eclamptic toxaemia or eclampsia but possibly in those cases of pre-eclamptic or eclamptic toxaemia where it is present manifest or latent, toxaemia may recur more readily, and once hypertension occurred, is more likely to be associated with subsequent toxaemic pregnancies.

In other words a hypertensive tendency manifest or latent, if present is constantly present in a given case with a greater

likelihood of toxaemia in subsequent pregnancies. This is confirmed in the present investigation. It was found that such cases seldom if ever have normal subsequent fullterm pregnancies. On the other hand it was found that true pre-eclampsia and eclampsia cases may also have a recurrence of toxaemia, though less commonly in subsequent pregnancies but often have normal pregnancies in between and subsequently and, what is more significant, remain normotensive years later.

In the hypertensive group clinically manifest permanent hypertension develops sooner or later and cases from this group not previously distinguishable are mixed up with the "true" pre-eclamptic toxaemic cases and wrongly included in that group. Thus they fallaciously show up as a percentage of what appears to be true toxaemia cases with residual vascular sequelae.

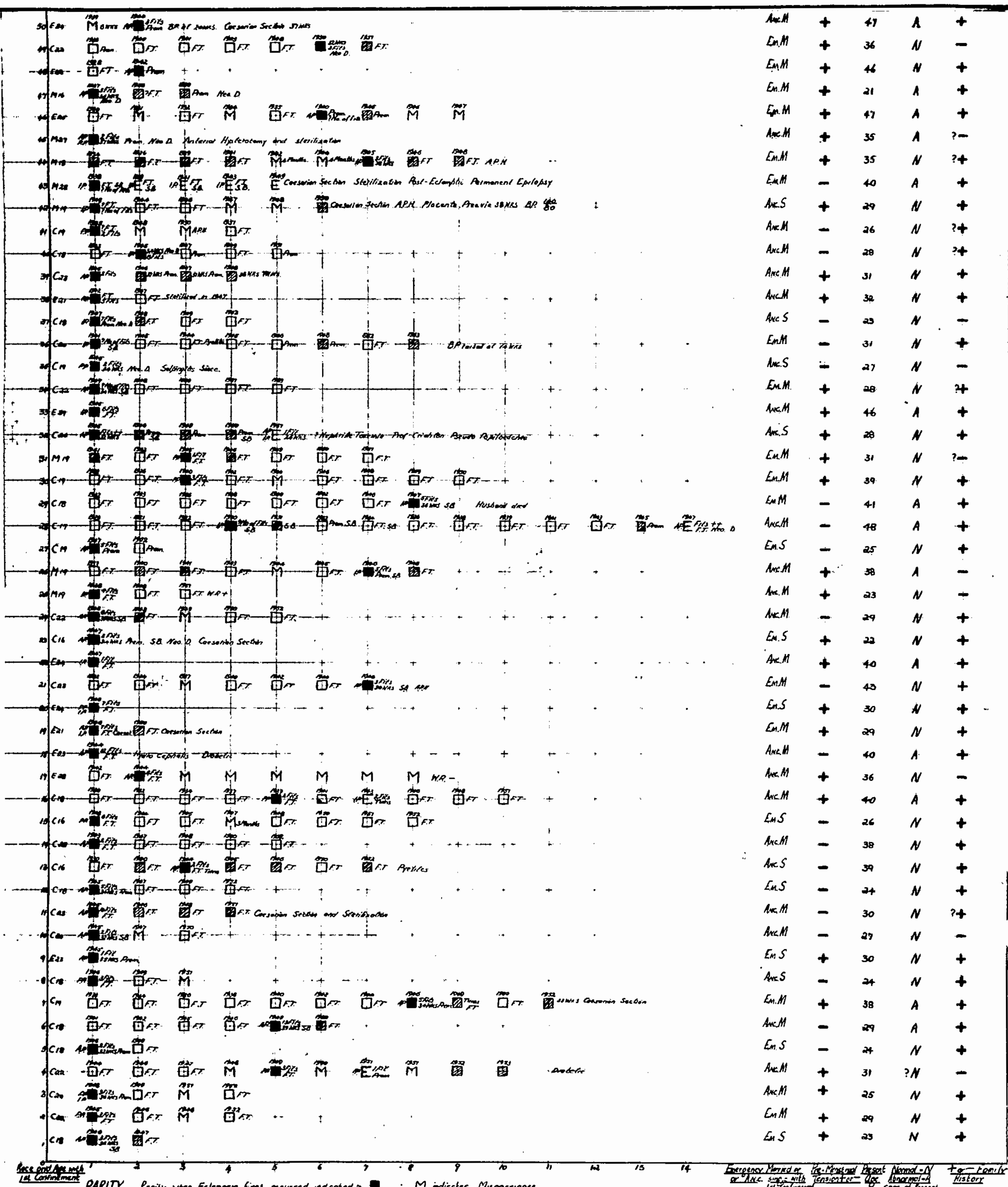
The difficulty is that a possible hypertensive tendency in a given case can only be assessed or determined years later by prolonged follow-up study, as the available diagnostic methods, and the state of our knowledge at present is inadequate to accomplish a diagnosis of latent hypertension.

If in time new methods are devised to distinguish these different groups I am of the opinion that in true pre-eclamptic toxaemia and eclampsia few or no permanent vascular sequelae will be found as a direct result. In my opinion permanent vascular sequelae are not dependant on the duration and severity of the toxaemia before the termination of the toxaemic pregnancy as stressed in the past by Chesley and Browne, Dexter and Weiss and many others but due to the inherited traits of the women.

However, it cannot be denied that the severity and duration of toxaemia may possibly bring out the inherited traits earlier than they would have occurred naturally, had there not been intervening toxaemic pregnancy or pregnancies. This however, is difficult to substantiate by adequate proof.

PHOTOGRAPH XI:

THIS SHOWS A GRAPHIC REPRODUCTION IN SUMMARY FORM, OF THE OBSTETRICAL HISTORY, AGE AND FINDINGS OF THE 100 ECLAMPTIC CASES STUDIED. CASES 1 TO 50 ARE PORTRAYED ON THIS PHOTOGRAPH:



PARITY

Parity when Eclampsia first occurred indicated by ■
Parity when Eclampsia recurred indicated by Black E
Parity when Toxaemia occurred indicated by ▨
Normal previous or Subsequent Pregnancy indicated by □
Toxaemia and Termination by Curettage indicated by ▣

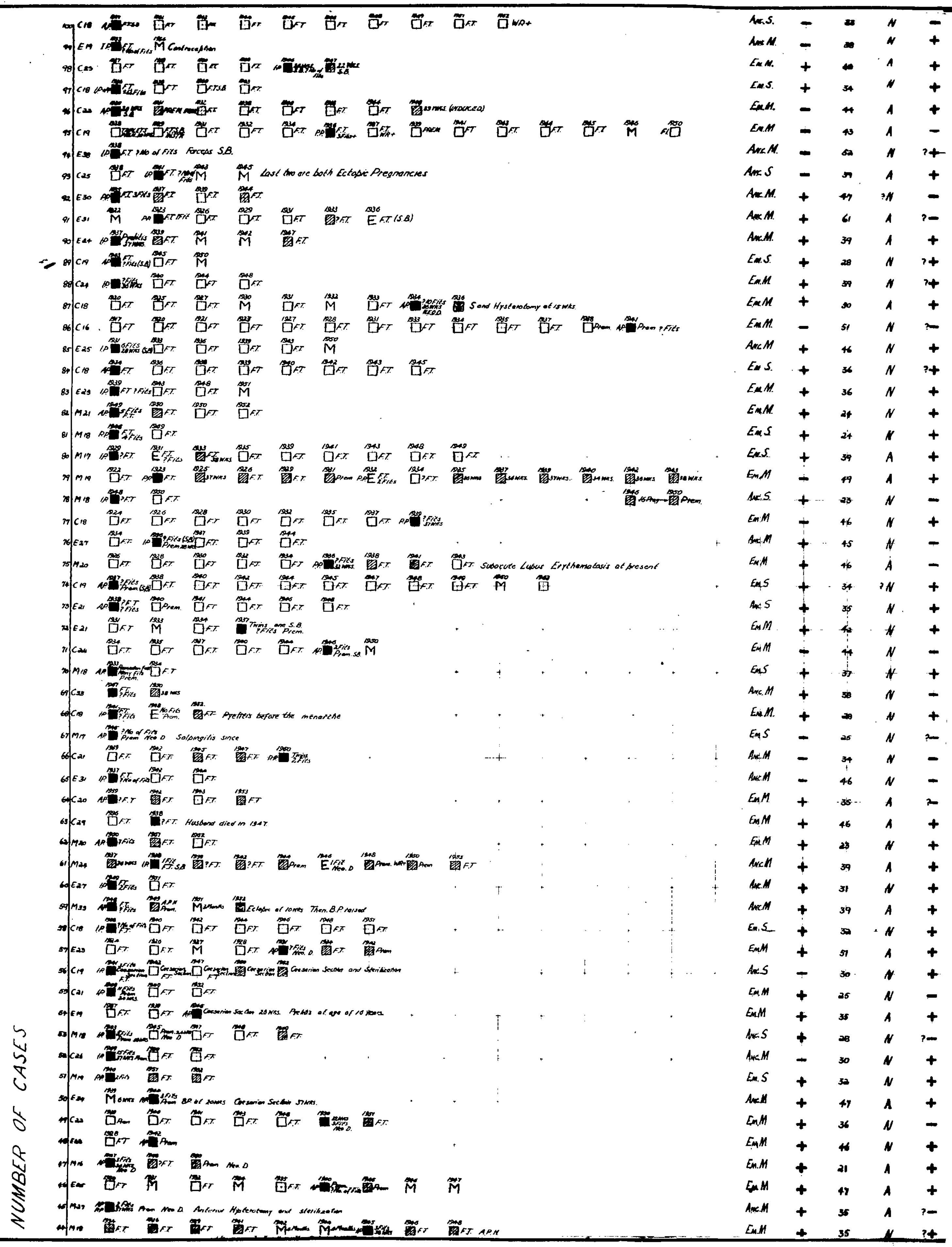
M indicates Miscarriages
S indicates Sterilization
Em indicates Emergency
Anc indicates Ante Natal care

FOLLOW UP STUDY OF ECLAMPSIA CASES INDICATING SUBSEQUENT HISTORY WITH REGARD TO PREGNANCIES, PARITY AND RECURRENCE OF ECLAMPSIA OR TOXAEMIA AS WELL AS RACE, AGE WITH FIRST PREGNANCY, PRESENT AGE, PRESENT STATE OF HEALTH AND FAMILY HISTORY OF HYPERTENSION

PHOTOGRAPH XII:

CASES 44 TO 100 ARE PORTRAYED ON THIS

PHOTOGRAPH:


NUMBER OF CASES

8. THE STATE OF THE CARDIOVASCULAR SYSTEM IN THE 100 ECLAMPTIC CASES FOLLOWED UP :

The peripheral vessels were palpated in each case, but only in cases where cardiovascular disease was gross, did this help in evaluating the vascular system. Funduscopic changes were found to be more reliable and accurate as a method of evaluation.

(a) THE OPTHALMIC CHANGES AT THE TIME OF THE ECLAMPTIC ATTACK:

1. VISUAL DISTURBANCES:

Visual disturbances varying from diplopia, scotomata and sudden blindness occurred in 30% of the cases followed-up before the onset of convulsions. This is in keeping with the incidence from 30 to 50% mentioned by other authors (Dieckmann 1952). These manifestations are probably due to circulatory changes e.g. spasm, in the visual cortex, or local changes in the retina e.g., detachment. In some cases these symptoms preceded the fits by 24 to 48 hours.

All visual disturbances cleared up within two months following the attack and in no case examined was evidence found of the past eye lesions. All cases with visual disturbances had marked hypertension at the time but 50% of these were normotensive at the follow-up examination.

2. THE OPTHALMOSCOPIC FINDINGS AT THE TIME OF THE ECLAMPTIC ATTACKS IN THIS SERIES:

There were 113 eclamptic attacks in this series and the examinations and reports made use of were those of the visiting eye specialist.

In 69 instances the fundi were not remarked on. In 18 the fundi were passed as normal. In 26 instances the fundi were considered to be abnormal. In 14 of these only spasm of the retinal vessels was reported and 7 of them were normotensive while the other 7 were hypertensive at follow-up. In 11 instances there

were./..

were in addition to spasm of the vessels, papilloedema, retinal oedema and in some cases retinal detachment uni or bilateral. Five of these cases were found to be hypertensive subsequently and 6 normotensive. One of the latter cases had a condition called pseudo-papilloedema or pseudo-neuritis, a congenital anomaly, in which the nerve fibres, as well as the accompanying glial tissue at the nerve head produce an elevation of the disc with blurring of the disc margins and disappearance of the physiological cup. The blind spot was not enlarged, the visual fields and a complete neurological investigation was normal. One case was reported as having bilateral papilloedema, marked arterio-venous nipping, flameshaped retinal haemorrhages and a few soft exudates. She was found to be hypertensive at the follow-up examination.

Mylius (1928) and others have proved by photographic study that spasm of the retinal vessels occurs in eclampsia and this is more marked the higher the blood pressure rises above 150 systolic, and with a further elevation haemorrhages and exudates due to anoxia and retinal oedema occur. In 5 fatal cases he found histologically no organic changes in the vessels. This was confirmed by Jones in 1937. Friedenwald (1938) however, found no retinal changes in a number of cases, spasm in others and organic vascular changes in fatal cases. Wagener (1936) found spastic arteriolar changes in 70% of eclamptics and retinitis in 40%. He felt that pregnancy should be terminated in the latter cases else permanent vascular damage would occur. Hallum (1944) agrees with these findings.

According to Dieckmann (1952) retinal haemorrhages and exudates are rare and this is confirmed in the present series. Retinal detachment, the result of retinal oedema, re-attaches itself without operative interference within two months and recovery of vision is good confirming statements by Doggart (1936) and Hallum (1936).

It is evident from the above findings that marked retinal

changes./.....

changes need not be followed by persistent post-eclamptic hypertension especially in young women, except if haemorrhages or exudates are found. Even then the changes may revert to normal, following delivery i.e., retinitis is not necessarily evidence of any pre-existing renal or vascular disease, except if manifest arteriosclerosis is present as well. This agrees with the findings of Wagener (1933), Mittelstrass and Wolfhagen (1948) and the opinion of Gibberd (1951).

Although the prognosis is difficult to assess the deductions from the funduscopic findings do not necessarily indicate or substantiate what will be the sequelae. It seems wiser to terminate a case of toxaemia or eclampsia if haemorrhages or exudates are present.

(b) THE OPTHALMOSCOPIC CHANGES AT THE TIME OF FOLLOW-UP EXAMINATION.

In no case were gross visual disturbances found such as blindness, but many complained of presbyopia. In a few cases visual acuity was impaired because of retinal vascular changes. In none of the normotensive cases were any objective fundal changes detected except in the one case of pseudo-papilloedema already referred to.

The following table illustrates the retinal changes found in the 30 hypertensive cases based on the classification of Wagener and Keith (1939).

TABLE V.

	Grade 0.	Grade 1.	Grade 2.	Grade 3.	Grade 4.
Number of Cases:	2	4	22	2	0

Case 96 had colloid spots visible which are not significant.

Great difficulty was experienced in placing a given fundus in grade 0 or grade 1, and cases rightly belonging to group 1 may

thus./.....

thus have been placed in group O, and vice versa. The table illustrates that grade 2 retinopathy was the most common finding. In no case was papilloedema visible and therefore no case had malignant hypertension. The only case with marked proteinuria had no exudates or haemorrhages and was classified into the grade 2 group. There were 2 cases with grade 3 retinopathy, both with marked hypertensive vascular disease. The one was under treatment for cardiac failure following a recent coronary thrombosis.

Muri (1936) found that amongst 36 cases who had eclampsia many years previously, 13 had changes compatible with grade 1, 14 changes compatible with grade 2, and 9 changes compatible with grade 3 retinopathy using the classification of Keith and Wagener.

Although it seems true in general that cases with marked retinopathy at the time of eclampsia are more liable to persistent hypertension, as indicated by Hallum (1934), it is evident from the present study that in any given case it need not occur, and in most cases the changes seen at the time of the attack are completely reversible.

(c) <u>THE CARDIAC STATE OF THE ECLAMPTIC CASES FOLLOWED-UP</u>:

1. Among the normotensive cases there was only one case with cardiomegaly due to mitral stenosis.

2. Amongst the 30 hypertensive cases there were 8 cases without radiologically demonstrable cardiomegaly, in spite of the fact that the blood pressure was raised appreciably in some of them. Repeated blood pressure readings, and fundal changes though mostly grade 1, confirmed these to be hypertensive cases. This indicates that hypertension may exist for a long time, without necessarily giving rise to obvious anatomical changes in the body. Twenty-two cases showed definite radiological evidence of cardiomegaly, uring the criteria of Evans (1952). Ten of these were of the cardiac kind i.e., cases where enlargement of the left ventricle is associated with only slight changes in the aorta.

Three./.....

9. THE RENAL FUNCTION & STATE OF THE 100ECLAMPTIC CASES EXAMINED:

Without exception the 100 cases examined all had gross albuminuria, oliguria, oedema and hypertension at the time of the eclamptic attack and in 22 cases microscopic haematuria was noted. Fifteen of these were found to be normotensive and 7 werehypertensive at follow-up. Haematuria then, does not appear to be a criterion of subsequent normality or abnormality.

Proteinuria found in 5 of the cases will be discussed later. Glycosuria, confirmed by fasting blood sugar tests as being of a diabetic nature, was found in 3 cases already mentioned.

(a) Amongst the 70 normotensive cases no symptoms or signs of renal impairment were found. None had abnormal chemical constituents in the urine or abnormal microscopical sediments. The modified concentration and dilution test used showed that they could concentrate their urine to specific gravity readings varying from 1022 to 1026 and the dilution test produced readings varying from 1001 to 1006. In all these cases the blood urea was within normal limits and in one case who had antecedent pyelitis the pyelogram was normal.

(b) Besides the 5 cases with proteinuria, one of whom had a fixed specific gravity of 1010, all the other hypertensive cases showed no detectable evidence of disturbed renal function. They had chemically and microscopically normal urines and the concentration and dilution tests showed normal function. In addition the blood urea proved to be normal in all cases and pyelography performed in 3 cases revealed no abnormality. No growth was obtained from catheter specimens of their urines.

The results in the present series are in keeping with those of Chesley and Somers (1941) who found the renal functions normal in over 97% of 141 cases of eclampsia they studied. In the present series there is only 1 case who may possibly have chronic glomerulo-nephritis. The results tend to show that chronic glomerulo-nephritis is a very rare sequel, if it occurs at all as

a./.....

a specific result of eclampsia. None of the cases, besides the 1 mentioned, showed any evidence of manifest impaired renal function after an average period of 10.5 years following eclampsia. In this particular case it seems likely that the renal lesion ante-dated the eclamptic pregnancy as will be pointed out later.

(c) In 1 case who probably suffers from chronic lupus erythematosis with joint pains and a raised sedimentation rate, liver function tests were done, which showed deranged function. She is manifestly hypertensive but had no demonstrable renal lesion, and no LE cells in her blood.

10. THE PHYSICAL BUILD & CONSTITUTION OF THE ECLAMPTIC CASES FOLLOWED UP:

It is said by Draper, Bayer and others (Dieckmann 1952) that a certain personality and body type is predisposed to eclampsia but this is denied by Hinselmann (1924) and others.

The shortest patient amongst the 100 cases was 4 ft. 9 inches and the tallest 5 ft. 9 inches. Their average height was 61.6".

The heaviest patient in the series weighed 197 lbs. and the lightest 90 lbs. Their average weight was 142.13 lbs.

Judging from the figures for weight and height, a tabulation of weight / height ratio and their personalities, I found no evidence of a constant build or type in the present series of eclampsia cases.

The following table illustrates the weight/height ratio of the 100 eclamptic cases in conjunction with their blood pressures.

TABLE 6.

Weight/height ratio:	No. of cases.	% Hypertensive:	% Normotensive:
Less than 1.80 (lean)	30	6.6	93.3
1.81 / 2.60 (Average)	47	38.3	61.5
More than 2.61 (Obese)	23	43.3	56.5

This./.....

This table shows that the higher the weight/height ratio the greater the incidence of subsequent hypertension.

11. THE AGE & PARITY OF THE 100 ECLAMPTIC CASES FOLLOWED-UP:

(a) The Age of the Patients at the Time of the Eclamptic Attack:

The following Table indicates the age at the time of the eclamptic attack, and its relationship to the subsequent cardio-vascular state of the cases.

TABLE 7.

	AGE IN GROUPS:					
	15-20 years	21-25 years	26-30 years	31-36 years	37-42 years	43 years & over.
No. of Cases:	37	18	22	17	4	2
% Subsequently hypertensive	10.8	11.3	50.0	58.8	50.0	50.0
% Subsequently normotensive	89.2	88.7	50.0	41.2	50.0	50.0

The table shows that the older the patient at the time of the eclamptic attack, the more probable will be a finding of hypertension at the follow-up examination.

The mean age at the time of the eclamptic attack of all cases found to be subsequently hypertensive was 29.5 years. The mean age of all the subsequently normotensive cases at the time of the eclamptic attack was 23.3 years.

(b) The Age of the Eclamptic Patients at Follow-up Examination:

The mean age at follow-up examination of all cases was 35.1 years, for those with hypertension 41.7 years, and for those with normotension 32.3 years. The mean age in non-European cases was 33.4 years and in the European cases 40.8 years. The average time elapsed since the eclamptic attack was 10.5 years in all cases, 9.3 years in the normal cases and 13.3 years in the hypertensive cases. The following table illustrates the age at the

time./.....

time of the follow-up study in relationship to the follow-up findings:-

TABLE 8:

Age at follow-up:	21-25 years	26-30 years	31-36 years	37-40 years	41-46 years and over.
Number of Cases:	16	20	20	19	25
% With hypertension:	6.3	5	15	52.7	56
% That are normal:	93.7	95	85	47.3	44

This table illustrates the general tendency of older patients being more inclined to be hypertensive. It must be pointed out however, that this hypertension need not necessarily be the result of the eclamptic attack, but may simply be a manifestation of the wear and tear of life at an older age, or may be due to factors not known, such as is found in the general population, including males. At a later stage I will analyse the hypertensive cases into those directly following the eclamptic attack and those where hypertension supervened some years after the attack.

(c) Parity and its relationship to Eclampsia and its apparent Sequelae:

In 65% of cases the eclampsia occurred with the first pregnancy, which is the usual finding. See photograph 13 on page 124 indicating the parity at the time of the eclamptic attack and its possible relationship with the subsequent findings:-

TABLE 9:

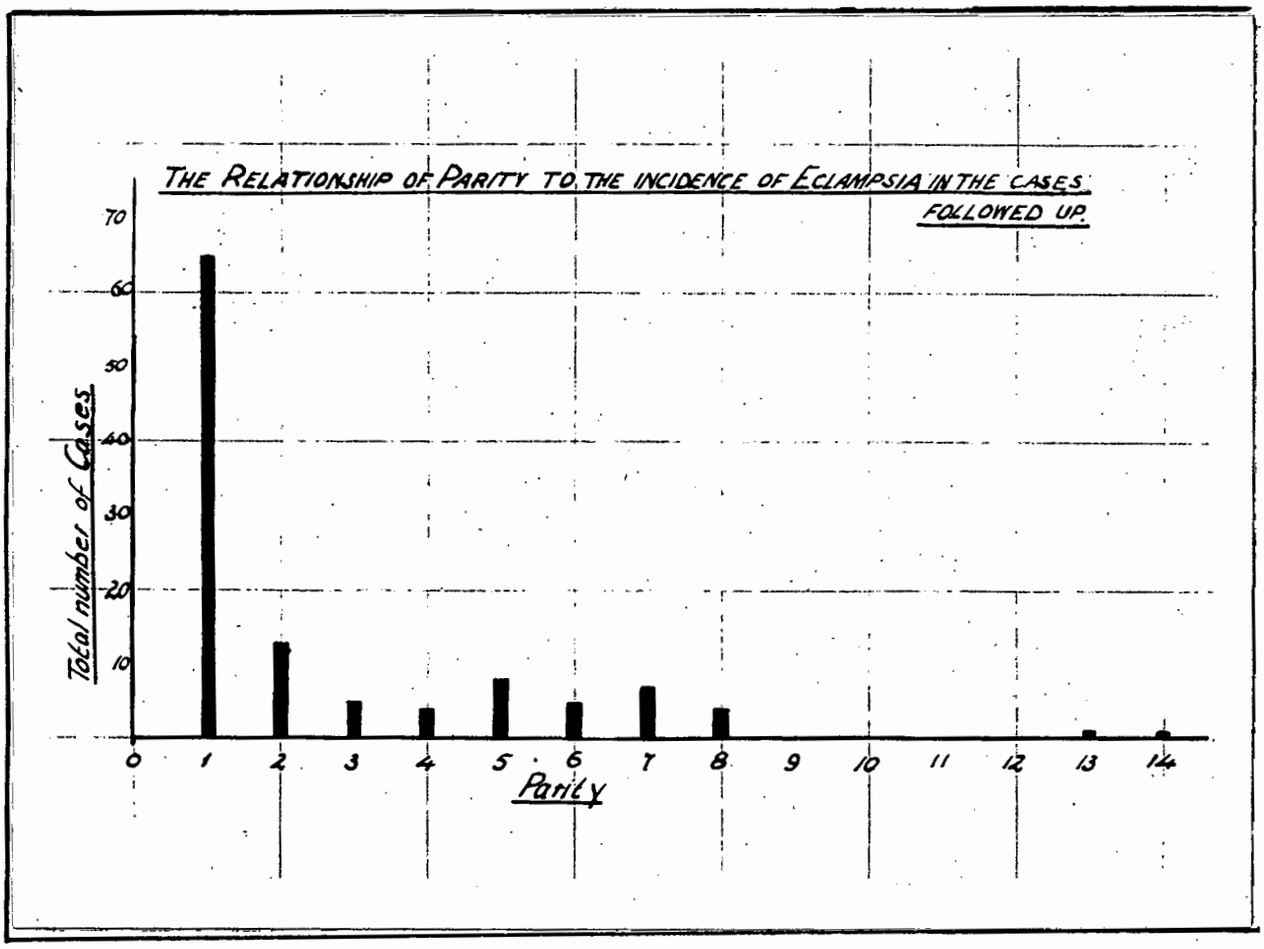
PARITY:	I	II	III	IV	V and more.
Number of cases	65	13	5	4	26
% with Hypertension	16.9	61.6	40	75	61.6
% That are normotensive	83.1	38.4	60	25	38.4

This table shows that there is a tendency towards a higher

incidence./....

PHOTOGRAPH XIII.

THIS SHOWS THE PARITY AT THE TIME OF THE ECLAMPTIC ATTACK AMONGST THE ECLAMPTIC GROUP OF CASES STUDIED. THIS INDICATES THAT THE INCIDENCE OF ECLAMPSIA IS GREATEST IN PRIMIPARAE & SECUNDIPARAE BUT MUCH LESS OFTEN IN THE LATTER GROUP. THERE IS A RAPID DECLINE IN THE INCIDENCE IN MULTIPARAE AFTER THE SECOND PREGNANCY. THIS AGREES WITH THE FINDINGS OF DECIO AND CENTARO (1952)


THE RELATIONSHIP OF PARITY TO THE INCIDENCE OF ECLAMPSIA IN THE CASES FOLLOWED UP.
Total number of Cases
70
60
50
40
30
20
10
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
Parity

incidence of subsequent hypertension in cases of eclampsia with the second or greater parities.

(d) The Parity at follow-up of the Eclamptic Cases Studied:

The following Table illustrates the parity at the time of follow-up of the eclamptic cases examined and the relationship with the blood pressure findings:-

TABLE 10.

Parity at follow-up.	1	2-4	5-7	8-10	11-13	14-20
Number of Cases.	9	40	24	19	2	3
% With Hypertension	44.5	15	20.9	47.4	50	100
% That are Normotensive	55.5	85	79.1	52.6	50	0

This table tends to indicate that multiparity need not be followed by hypertensive vascular disease, and that a woman may have a large family even after an eclamptic attack and, be left normotensive years later.

The average final parity of the normal cases was 4.5 and the average final parity of the hypertensive cases was 6.4. Six normal cases had only 1 pregnancy i.e., 8.5% of the normal cases. Four hypertensive cases - i.e., 13.3% of the hypertensive cases had only 1 pregnancy.

Browne found in a smaller series that all the patients who ultimately recovered were primipara when they had eclampsia. However, in my series this was not the case, and patients having had eclampsia with the second, third, fourth and later pregnancies were occasionally found to be normal subsequently. This latter group included three cases who had eclampsia more than once.

Nevertheless, 83.1% of primiparous eclamptic cases were subsequently found to be normotensive. This confirms that primiparous women show the lesser tendency to develop hypertensive

vascular./....

(b) The Mean Highest Blood Pressure during Pregnancy:

Using Browne's criteria the mean highest blood pressure during pregnancy in the 46 normal cases was 165/107 mm. Hg. and amongst abnormal cases 181/119 mm. Hg. However, if the criteria used in the present series are applied, the mean highest blood pressure amongst the 70 normal cases was 166/110 mm. Hg. and amongst the 30 abnormal cases 190/120 mm. Hg. In other words, the higher the blood pressure during pregnancy, the greater the likelihood of permanent hypertension, which is in keeping with Browne's findings. There are exceptions to this conclusion as exemplified by the case in this series with the highest blood pressure namely 230/140 mm. Hg. during the eclamptic attack. She was found to be normotensive at follow-up examination.

(c) The Blood Pressure on Discharge:

A table (1) showing the results using Browne's criteria, followed by a table (2) using 140/90 mm. Hg. or higher as an index of hypertension:-

TABLE 11 (1) :

Condition at Follow-up.	No. of Cases:	Normal B.P. on discharge		Hypertensive B.P. on discharge		B.P. on discharge unknown.
		Cases	%	Cases	%	
Normal Cases B.P. 130/70 & below.	46	29	63	15	32.6	2
Hypertensive Cases	54	24	44.4	23	42.5	7
T O T A L :	100	53	-	38	-	9

Table 11 (2) :

Condition at Follow-up.	No. of Cases:	Normal B.P. on discharge		Hypertensive B.P. on discharge		B.P. on discharge unknown.
		Cases	%	Cases	%	
Normal Cases B.P. below 140/90	70	41	58.5	26	37.1	3
Hypertensive Cases	30	7	23.3	17	56.6	6
T O T A L :	100	48	-	43	-	9

Using./.....

Using Browne's criteria, the mean blood pressure on discharge was 133/88 mm. Hg. amongst the 46 normal cases and 143/96 mm. Hg. amongst the 54 hypertensive cases. Using my criteria, the mean blood pressure was 133/89 mm. Hg. amongst the 70 normal and 155/100 mm. Hg. amongst the 30 abnormal cases.

It will be seen that a higher percentage of the subsequently normal cases had a normal blood pressure on discharge than the percentage of the subsequently hypertensive cases. (63% As compared with 44%, using Browne's criteria, and 58.5% and 23.3% respectively using my criteria). Also a higher percentage of subsequently hypertensive cases had a raised blood pressure on discharge than normal cases, as the figures of both tables show. However, on the whole the blood pressure on discharge was an unreliable guide to the subsequent behaviour. This is a point stressed by Browne (1939).

(d) <u>The Duration of the Toxaemia and its Relationship to the Sequelae</u>:

Using Browne's criteria, the average duration of Toxaemic symptoms and signs amongst the 46 subsequently normal cases was 3.4 weeks and amongst the 54 subsequently abnormal cases 3.98 weeks. If my criteria are use, the average duration of signs and symptoms amongst the 70 subsequently normal cases was 3.53 weeks and amongst the 30 subsequently abnormal cases 4.22 weeks.

On the whole these figures tend to indicate that the longer the duration of symptoms, the more the likelihood of permanent vascular sequelae but there are exceptions.

Light (1948) states that the duration of the toxaemia has no influence on the development of future hypertension. I believe that cases susceptible to hypertension will tend to develop signs and symptoms of toxaemia earlier in pregnancy than "true" pre-eclamptic toxaemia cases. They therefore inevitably tend to be considered as being toxaemic for a longer period. This is incorrectly interpreted as being the cause of the future hyper-

tension./.....

tension. Cases destined to be permanently hypertensive after toxaemia will be so irrespective of the duration of the toxaemia, because of a latent tendency towards hypertension. I agree with Browne (1951) and others that such cases would develop permanent hypertension sooner or later even if they never became pregnant.

13. FALLACIES ENCOUNTERED WITH REGARD TO CARDIOVASCULAR & RENAL COMPLICATIONS IN THE ECLAMPSIA & NON-CONVULSIVE TOXAEMIA FOLLOW-UP STUDIES & THEIR ELIMINATION:

In view of the fact that all non-convulsive toxaemia and eclamptic cases have hypertension and albuminuria at the time of the attack and usually for some months and even up to 2 years afterwards, or longer, it is best to exclude recent cases. In the series under consideration all cases had toxaemia or eclampsia 4 years previous to the follow-up study, except 3 of the non-convulsive toxaemia cases who recently had recurrent toxaemic pregnancies. Thus cases in the stage of healing were avoided as far as possible.

Another difficulty is that cases seen many years after eclampsia may have been normal for a long time in the interim and only later with advancing age or other intercurrent disease develop hypertensive vascular disease. In such cases it may be difficult, or impossible, to decide whether or not there are etiological or other relationships between eclampsia and the hypertensive disease. In this regard Dieckmann(1952) states that if hypertension develops 5 years later, the antecedent toxaemia or eclampsia cannot be related to the hypertensive vascular disease.

A further fallacy is the inclusion of cases who had hypertensive vascular disease or chronic nephritis prior to the eclamptic pregnancy amongst cases of toxaemia or eclampsia followed-up. If such cases are included they will of necessity indicate an unduly high incidence of vascular or renal sequelae. This error

has./.....

has not been avoided in many of the eclamptic and non-convulsive toxaemia follow-up studies published and consequently a high incidence of renal and vascular complications were reported.

It is essential to know the cardiovascular and renal state prior to the eclamptic pregnancy but, this is not always possible as many women only consult medical men once they have become pregnant and very often only after the 20th week. If they already have a raised blood pressure at this stage they are probably cases of latent or manifest hypertension but, if they become hypertensive later, they are usually regarded as "true" pre-eclamptic toxaemic cases. However, I am convinced that some latent hypertensive cases that mimic "true" pre-eclamptic toxaemic cases are to be found in the latter group. They are, as it were, "the wolves in sheep's clothing."

In the present series 70 of the 100 eclamptic cases were found to be normal from the point of view of hypertensive vascular and renal disease after an average period of 10.5 years and can therefore be assumed to have been normal prior to the eclamptic pregnancy without any doubt. Amongst the 30 hypertensive cases 7 were definitely normal prior to the eclamptic attack, 5 were seen before the 20th week regularly and had blood pressures below 130/80 mm. Hg. Seventeen of the remaining cases had from 1 to 4 normal pregnancies before the eclamptic pregnancy without any intervening disease and can therefore be assumed to have been normal. One case (case 47) aged 16, had no past medical record, and no definite information was available until she presented herself at the antenatal clinic with her first pregnancy, at 30 weeks. She was then already hypertensive with albuminuria and oedema of at least 4 weeks standing and had been feeling ill since conception. Since then she has had persistent hypertension and albuminuria for 5 years and may have been a case of chronic nephritis prior to this. She will be discussed later.

In 7 cases the hypertension developed on an average of 6 to 21 years after the eclamptic attack; probably due to unrelated

causes./....

causes. The nett number with directly related subsequent hypertension is therefore 22.

The above considerations were also applied to the non-convulsive toxaemia follow-up study, as will be shown in a later chapter.

14. SUBSEQUENT PREGNANCIES:

Subsequent to their eclamptic attack, there were 282 pregnancies in 80 women. Thus 80% of cases had at least 1 additional subsequent pregnancy. 58.3% Of the European women had subsequent pregnancies (46 in number) and 86.8% of Coloured women had subsequent pregnancies (236 in number). The smaller number of pregnancies amongst the Europeans is in keeping with the general tendency towards smaller families amongst the Europeans, and is also due to the fact that in many cases preventative measures were adopted, to avoid further issue in view of the previous eclampsia. This is not common practice amongst non-Europeans. The above figures prove that a preceding attack of eclampsia is no bar to further pregnancies. Furthermore, 38 of the 100 eclamptics had no recurrence of toxaemia or eclampsia and had from one to nine further pregnancies. One of these cases was hypertensive at the follow-up examination. Forty-two of the 100 had recurrence of toxaemia or eclampsia once, twice or more times. Of these 21 were found to be hypertensive at the follow-up examination. Sixteen of the 100 cases had normal full term pregnancies between their eclamptic or toxaemic pregnancies. Twenty cases had no further pregnancies and 8 of these were hypertensive at the follow-up examination. See Table 14 page 136 illustrating some of the figures quoted.

15. THE FOETUS:

(a) The foetus at the time of the eclamptic attack or attacks:

Records are available of all 119 of the offspring of the

100 cases at the time when they had eclampsia. The fate of the babies are summarised in the following table:-

TABLE 12:

Weight:	Alive	Neonatal Deaths	Stillbirths	Infantile Deaths	Total:
Under 5 lbs.	8	12	21	1	42
5-6 lbs.	21	6	6	2	35
Over 6 lbs.	31	4	3	4	42
T O T A L :	60	22	30	7	119
PERCENTAGE:	50.45	18.5	25.22	5.88	100

Eclampsia occurred before the 36th week of gestation in 35.3% of cases. The above table indicates that prematurity is an important factor, causing a high foetal mortality. The gross foetal mortality, (i.e., the stillbirth and neonatal mortality) was 43.7%. Congenital hydrocephalus in the child of an eclamptic woman, who subsequently developed diabetes mellitus, was the cause of another fatality. Other factors which may have been causative of foetal mortality were the use of hypnotic drugs and anoxaemia during the fits.

The foetal mortality in eclampsia ranges from 20% to 60%, with an average of 35% (Dieckmann 1952). In Cape Town the mortality rate falls within this range but must nevertheless be considered as being high.

On the following page (page 133) a series of 3 tables (Table 13 A, B and C) indicate the types of eclampsia and their effects on the foetus. A closer study of these reveal that cases with postpartum eclampsia have the largest children and the smallest foetal mortality. Chesley and Somers (1941) found in post-partum eclampsia only 2.2% of the offspring are stillborn.

(b) The Subsequent History of the Children born alive from Eclamptic Patients.

TABLE 13:

TABLES SHOWING THE TYPE OF ECLAMPSIA & ITS RELATIONSHIP TO THE CONDITION OF THE FOETUS :

A.

	FOETUS UNDER 5 LBS.				
	Lived	Neo-Natal Deaths	Still-Births	Infantile Deaths	Total:
Number of cases of A.P. Eclampsia.	5	8	10	0	23
Number of Cases of A.P. & I.P. Eclampsia.	0	0	0	1	1
Number of Cases of I.P. Eclampsia.	3	2	10	0	15
Number of Cases of P.P. Eclampsia.	0	2	1	0	3
T O T A L :	8	12	21	1	42

B.

	FOETUS 5 - 6 LBS.				
	Lived	Neo Natal Deaths	Still-Births	Infantile Deaths	Total:
Number of Cases of A.P. Eclampsia.	6	2	3	1	12
Number of Cases of A.P. & I.P. Eclampsia.	1	1	0	0	2
Number of Cases of I.P. Eclampsia.	4	3	3	0	10
Number of Cases of P.P. Eclampsia.	10	0	0	1	11
T O T A L :	21	6	6	2	35

C.

	FOETUS OVER 6 LBS.				
	Lived	Neo-Natal Deaths	Still-Births	Infantile Deaths	Total:
Number of Cases of A.P. Eclampsia.	5	3	1	0	9
Number of Cases of A.P. & I.P. Eclampsia.	2	0	1	2	5
Number of Cases of I.P. Eclampsia.	8	1	0	1	10
Number of Cases of P.P. Eclampsia.	16	0	1	1	18
T O T A L:	31	4	3	4	42

A.P. = Antepartum; I.P. = Intrapartum; P.P. = Postpartum.

Crichton (1932), in a discussion of Eclampsia, speculated on the subsequent growth, development and intelligence of babies born from eclamptic mothers. There are several reports in which haemorrhages were found in the livers of stillborn babies. Brach (1949) studied the effects of toxaemia on the foetus and newborn child. She found the incidence of stillbirth and premature deliveries to be 10.7%, as opposed to 3.9% from other causes and stated that once the baby was delivered, the chances of survival seemed as good as in the case of healthy mothers' children. The number of women with a raised blood pressure, oedema of the legs and proteinuria, who had premature babies, was higher than in premature births from all other causes. The progress of the former babies, in the first 12 weeks of life, was as good as in the latter cases.

According to Dieckmann (1952), Brown et al (1946), Taylor et al (1949), the consensus of opinion is that once the foetus is born, the maternal condition has no further effect upon it. To verify this statement the children of eclamptic mothers were studied. Most of the data was obtained from the mothers.

At present 51 of the children born alive, are still alive and well, with normal intelligence. Some of them are grown-up, and their occupations range from that of university student to hawker. Besides these, 2 are alive but backward mentally. In both cases the milestones of childhood were delayed and 1 of them only commenced to speak at the age of 5 years. A further 14 have died in addition to the 52 cases included amongst the stillbirths and neonatal deaths, making up the total of 119. Of the 14 deaths, 7 occurred in the first year. These were described by the mothers as delicate and backward children who failed to thrive. They died from gastroenteritis, pneumonia, convulsions, etc. The other 7 children died after the age of 1 year from various causes including tuberculous meningitis, gastroenteritis, pneumonia, etc.

It appears that surviving children of eclamptic mothers behave no differently from other children in general, as far as their physique and intelligence are concerned.

The./..

(c) The Foetus in subsequent pregnancies of Eclamptic Cases Followed-up:

Of the 282 subsequent pregnancies, 224 or 80% resulted in alive infants, and 58 or 20% resulted in either stillbirth or abortion. It is possible that some subsequent abortions were not recalled, or perhaps some criminal abortions were concealed, which may have increased the incidence of the foetal mortality and the subsequent pregnancies as well. Taussig (1936) has proved that no statistics on abortions are entirely accurate; Stander (1945) and Greenhill (1947) also bring out this point. However, figures of one author can be compared with that of another. For instance Stander (1945) reports the incidence of stillbirths as being 2.14% and that of abortions as 10%. Greenhill (1947) gives the incidence of stillbirths in general as 3.98% and that of abortions as 8.2%. Thus it will be seen that in subsequent pregnancies of the eclamptic cases there was a foetal mortality almost twice as great as would normally be expected. (Sym (1929), Rucker (1932) Dieckmann (1941), Chesley and Cosgroves (1946), Bryans & Torpin (1949), have noted a similar high incidence. This agrees with the toxaemic sequence mentioned by Young (1927 and 1937). See page 136, Table 14 illustrating the above figures.

16. SUBSEQUENT TOXAEMIA:

Ninety-three or 33.2% of all subsequent pregnancies were complicated by toxaemia. Of those women with subsequent pregnancies 42 out of 80, i.e., 52.5%, had at least one subsequent episode of toxaemia. Thus the incidence of toxaemia was 4 to 6 times greater than would normally be expected in the general run of pregnancies. This agrees with the findings of Taussig (1936), Dieckmann (1941), (1952), Dexter and Weiss (1941) and Golden, Dexter and Weiss (1943), also Stander (1945). In addition many authors including Young (1927 and 1937), Sym (1929), Gibberd (1931), Rucker (1932), Teel and Reid (1937), Browne and Dodds (1939), Chesley, Somers and Vann (1948), Dieckmann (1952) etc., mention an increase in the number of toxaemias in post-eclamptic./.....

TABLE 14:

ILLUSTRATING THE NUMBER OF PATIENTS, MEAN PERIOD OF TIME COVERED, MEAN AGE AT FOLLOW-UP EXAMINATION & NUMBER OF PREGNANCIES SUBSEQUENT TO THE ORIGINAL ATTACK OF ECLAMPSIA :

	Number of Patients.	Mean No. of years followed	Mean age at time of follow-up.	Number of subsequent pregnancies.	Number of Women who had subsequent pregnancies	% Of Women who had subsequent pregnancies.
European (White)	24	12.44	40.87	46	14	58.3
Coloured	76	9.40	33.48	236	66	86.84
T O T A L :	100	10.56 years	35.12 yrs.	282	80	80%

TABLE 15:

SHOWING THE FOETAL MORTALITY OF SUBSEQUENT PREGNANCIES AND INCIDENCE OF SUBSEQUENT TOXAEMIA :

	% Of subsequent Pregnancies which resulted in still-birth or abortion	% Of subsequent Pregnancies which were toxaemic.	% Of Women with subsequent pregnancies who had subsequent toxaemia.	%Of subsequent Pregnancies which were eclamptic.	% Of Women with subsequent pregnancies who had subsequent eclampsia.
European (White)	28.8	22.2	42.85	2.22	7.14
Coloured	18.29	35.31	54.54	5.1	13.63
T O T A L :	20.0	33.21	52.5	4.64	12.5

eclamptic and post-toxaemic pregnancies. Page and Cox (1938), from collected statistics, state that the incidence is 8 to 10 times higher than that usually found. See Table 14, page 136 illustrating these findings.

Dieckmann (1952) states that if the diagnosis is assured, by following each case of pre-eclamptic toxaemia and eclampsia for 6 months after delivery, so that cases of toxaemia and eclampsia occurring in patients with hypertension and renal disease are separated off, then the remaining cases of "true" pre-eclamptic toxaemia and eclampsia will normally not have toxaemia in subsequent pregnancies. He states that if it recurs in these latter cases, it is very rare. He thinks that cases in which it may possibly recur are either eliminated by death, or prevented from having a recurrence by antenatal care.

I do not believe this to be true, because of the 100 eclamptics followed up, 70 were normal from the point of view of their blood pressure, renal and other functions. After a mean average interval of 10.5 years since the eclamptic attack. Of these 70 normal cases 21 had 1 or more subsequent toxaemic pregnancies, and 3 had eclampsia again.

Thus not 6 months after the first eclamptic attack, but on an average of 10½ years later, they were not yet hypertensive and had no renal lesions. Illustrating without any doubt that what we regard as true pre-eclamptic toxaemia and eclampsia, can recur once or more often in subsequent pregnancies and leave no permanent after effects. These cases account for one variety of recurrent toxaemia to be discussed later. Bryans and Torpin (1949) had similar cases in a follow-up study of 243 eclamptic cases.

The findings are in keeping with a statement by Tillman (1936) that a normal blood pressure in the interim between pregnancies does not guarantee a normal subsequent pregnancy. A further statement based on this follow-up study can be made in this regard, namely that recurrent true pre-eclamptic toxaemia and

eclampsia./....

eclampsia can leave the patient normal from the point of view of hypertensive vascular and renal pathology years later.

Twenty-one out of 30 cases in this series found to be hypertensive subsequently, had from 1 to 9 subsequent toxaemic pregnancies. Thus the incidence of subsequent toxaemia is higher amongst hypertensive cases, than amongst cases found normotensive subsequently.

Twenty cases out of the 100 had no subsequent pregnancies, and 8 of these were hypertensive at follow-up examination. Thirty-eight of the 100 eclamptic cases followed up had 1 or more normal pregnancies without recurrence of toxaemia and only 1 of these was subsequently found to be hypertensive.

These are important findings, as opinions regarding the course of subsequent pregnancies after eclampsia have varied. Besides Dieckmann's own views mentioned previously, it has been taught by some authors in the last 30 years, that eclampsia does not recur and subsequent pregnancies are normal and that eclampsia confers an immunity.

Others have stated that eclampsia nearly always causes permanent damage to the vascular and renal systems and that future pregnancies will be characterised by toxaemia (Dieckmann (1952) quoting other reports).

It is obvious from this follow-up that the course is not grave, and excluding immediate fatalities with the eclamptic attack and soon afterwards, the sequelae that may occur years later are almost entirely hypertensive vascular in nature and occur in 30% of cases. In some of these cases however, the length of time that elapsed after the eclamptic or toxaemic pregnancy, before the hypertensive vascular disease became manifest, makes one doubt if these complications are really attributable to the preceding eclampsia or toxaemia.

In addition it is very likely that not all cases with underlying latent hypertension were excluded and the 30% with vascular

sequelae./....

sequelae may not be "true" eclamptic cases but primarily cases of latent hypertension with superadded toxaemia and eclampsia as indicated in an earlier discussion.

17. SUBSEQUENT ECLAMPSIA:

There was one subsequent attack of eclampsia amongst the white women and 12 subsequent attacks amongst 9 non-European women. The incidence of repeated eclampsia in subsequent pregnancies was 4.64%. 12.5% Of the women with subsequent pregnancies had eclampsia at least twice. (See Table 14, page 136). One of these had eclampsia 5 times. The old idea that eclampsia is never repeated has been repeatedly disproved.

Peters (1937) reports eclampsia 7 times in 1 patient and 6 times in another, 3 times in yet another and twice in 4 further instances. De Lee and Greenhill (1947) state that published reports indicate that in approximately 10% of eclamptic patients eclampsia recurs, Dieckmann (1952) gives this figure as from 0 to 18 per cent. Page and Cox (1938) found a 21% recurrence in 57 patients. Schmechel (1929) estimates eclampsia recurs in 18% of cases. Hinselmann (1924) in a collected series of 10,000 eclamptics from the literature, found it recurred in 1.92% and Eastman (1950) maintains that the recurrence rate is less than 1%. Laun (1928) described a case who had eclampsia 3 times and Clow (1928) mentions a case who had eclampsia 4 times.

Stander (1945) reports the usual incidence of eclampsia to be 0.15% and Dieckmann (1952) states that the rate of occurrence in the United States is 0.66%. However, taking my figure of 0.21% incidence of eclampsia, the incidence of eclampsia in the general population is 22 times as great as the incidence of recurrence of eclampsia. This nearly agrees with the findings of Bryans and Torpin (1949), who found the average ratio of the incidence to be 25 to 1.

Crichton (1952) reported 1 case with eclampsia recurring 5 times. This case is included in the present series (Case 43).

In./.....

In that report she was stated to be normotensive inbetween her pregnancies and also on discharge from hsopital after the fifth eclamptic attack. In this follow-up examination she was found to have developed permanent hypertension and epilepsy subsequently. There was no family history of epilepsy. She developed fits at the age of 39 years after her fifth eclamptic attack, besides of course having had convulsions with each eclamptic attack. There is no doubt that she had true eclampsia with all its signs and symptoms on each occasion. Her mother died of hypertensive heart disease, and one of her sisters had toxaemia of pregnancy. Four years previously, these additional features were not known and in Crichton's discussion of the 3 main theories concerning recurrent toxaemia, he found none of them applicable. He felt that chance alone was not a satisfactory explanation and that if an occult nephritis was the cause, it was surprising that after 5 attacks of eclampsia no nephritishad become manifest, all clinical and laboratory investigations having been normal. There were no placental infarcts present in support of Young's theory and no manifest hypertension in her or her family, to fit in with Browne's theory. It is now known that she became hypertensive and developed a familial hypertensive history, subsequently to Crichton's report. Could the recurrence of eclampsia in her case be explained on the basis of a latent hypertension only evident in the third trimester of each pregnancy ? This is the basis of Browne's hypothesis and is difficult to prove or disprove. However, the fact that she is now hypertensive is evidence in favour of Browne's hypothesis.

Dieckmann (1941 and 1952), states that he has personally never seen a case of eclampsia recur, and Stander (1945) states that it rarely recurs. According to Dieckmann, the high incidence of recurrence reported by other observers and of repeatedly recurring eclampsia, is due to the fact that these cases are not true eclamptic cases but have eclampsia because of underlying vascular and renal disease, and the convulsions are most likely due to hypertensive encephalopathy. Browne (1951) states that if a patient has once had eclampsia, she is more liable to have it

again./.....

again in subsequent pregnancies only if chronic hypertension has succeeded the eclamptic pregnancy.

To disprove these statements made by Browne and Dieckmann the detailed case histories have been analysed and can be referred to in Appendix 3. (See discussion below).

In all these cases other causes of convulsions besides eclampsia e.g. uraemia, pyelonephritis, anaesthesia, epilepsy etc., were excluded.

Seven of the 10 cases with recurrent eclampsia are now manifestly hypertensive and over the age of 39 years. Of the 3 who are normotensive, one is 31 years old, has been known to be diabetic for the past 2 years and neglects her condition. Diabetes Mellitus may be an important predisposing factor to toxaemia and hypertension but she has only suffered from these for 2 years and is normotensive as yet. Her last 2 pregnancies were toxaemic with a rise in blood pressure and albuminuria in the last 4 weeks of each pregnancy. The remaining 2 cases are both 28 years old at present and normotensive but none can prophesy that they will not be hypertensive when they reach the age of 45 to 55 years. Thus it is possible that their present normality is due to their present age. Furthermore, it is difficult to see why eventual hypertension, if they develop hypertension in years to come, should be the cause of recurrent eclampsia.

None of the 10 cases gave a past history of nephritis. One case has pyelitis at the age of 15 years with no recurrence, and has now a normal pyelogram and no abnormal urinary sediment. The blood urea was within normal limits in all the above cases, and there was no evidence of specific gravity fixation. With the dilution and concentration test the maximum concentration varied from 1020 to 1027 and the minimum concentration from 1001 to 1006. The weight/height ratio exceeded 2.4 in all 10 cases indicating an obese plump stocky build, stressed to be the constitutional type in which eclampsia occurs. However, amongst the other 90 eclamptic

cases followed up, there were tall thin and delicately built cases who had eclampsia.

No constant abnormal environmental or dietary factor appeared in these cases except that two Malay women had recurrence of eclampsia during a prolonged religious fast, the Ramazan. I believe that whereas nutrition, personal habits, and climate are more or less constant factors in each pregnancy of a particular woman and though they may predispose they cannot be the factors governing recurrence, as recurrent eclampsia is extremely rarely found with each succeeding pregnancy as in case 43.

The ten cases illustrate that true eclampsia can occur and recur with any parity and preceding normal pregnancy or pregnancies do not rule out the possibility of the occurrence or recurrence of eclampsia in any future pregnancies. There may be normal pregnancies at term in between, and toxaemic pregnancies may precede, intervene or follow recurrent eclampsia, with or without interspersed normal pregnancies in a haphazard way. On the other hand all succeeding pregnancies may be normal or toxaemic. These facts formulate a strong evidence that eclampsia and pre-eclamptic toxaemia are not due to any inherent weakness or disease of any organ, but are more likely due to conditions associated with the immediate pregnancy. Thus first pregnancy, multiple pregnancy, hydatidiform mole, polyhydramnios etc. favour its occurrence but in addition some X factor or factors we do not know as yet must operate. This is probably the reason why investigators are now looking for a cause at the site, function and bloodsupply of the placenta and uterus that leads to secondary widespread effects producing the syndrome or syndromes.

Only three of the ten cases were definitely hypertensive when they had recurrence of eclampsia and so fit into Dieckmann's and Browne's hypothesis. Four became hypertensive only subsequent to the second eclamptic attack, and three are still

normotensive/.....

normotensive. Thus hypertension is not necessarily associated with recurring eclampsia as postulated by Browne and intimated by Dieckmann. Earlier on it was pointed out that inheritance of essential hypertension latent or manifest is far from fully understood and impossible of assessment in a given patient. The truth is only known when a patient has lived her complete life and her blood pressure is recorded from time to time. Furthermore the manifold other causes of hypertension must not be left out of sight, especially in those developing hypertension many years later. I feel that the hypertension and hypertensive tendency hypothesis does not explain the recurrence of toxaemia/or eclampsia in all cases and other unknown factors are causative in the subsequently normotensive cases.

Although true eclampsia occurs commonly in the young and with the first pregnancy, eclampsia may occur and recur at any age in the reproductive period and is therefore not only determined by age. Older patients may be hypertensive as well and for this reason may be more predisposed to encephalopathy.

The incidence of vascular disease and hypertension, taking 140/90 mm. Hg. and higher readings as indicating hypertension, rises rapidly with increasing age (Master, Garfield and Walters 1952) and multiparity parallels increasing age. Thus the two conditions, in some cases at any rate, may be related only by a chance association.

In view of the fact that even in young true eclamptic cases the cause and mechanism of the fits are not known for certain, and when an eclamptic patient is seen it is as yet impossible to say whether she suffers from true eclampsia or hypertensive encephalopathy, I feel that this distinction in the case of the older patient who may have underlying hypertension as well and is called a case of hypertensive encephalopathy, is more of theoretical than practical value in the present state of our knowledge.

In both/.....

In both groups the signs and symptoms of eclampsia are the same and both can have recurrent toxaemia.

If a patient with hypertension and toxaemia is seen for the first time during pregnancy, knowing her family history does not help in deciding whether the vascular system was normal before pregnancy or not and one may wrongly conclude that the pregnancy has produced the hypertension. Such hypertension, if progressive, may be due to a variety of reasons and is often merely revealed by the toxaemic pregnancy.

From this and other follow-up studies it is known that many cases of pre-eclamptic toxaemia and eclampsia are not left with hypertensive vascular disease years later. The question arises why the others should be. I feel that an inherent tendency becomes established in some cases and not in others. After all, a family history of hypertension may be common to both subsequently normal and hypertensive cases. I do not believe that the duration and severity of the toxaemia determines whether or not the person will be normal or hypertensive subsequently but I think that subsequent hypertension is found in those cases where genetic penetrance has ensured the development of an inherited hypertensive tendency.

18. Previous Pregnancies. Previous to the original attack of eclampsia there were 130 pregnancies in 35 women. 37.5% of the white women and 34.2% of the coloured women had at least one or more previous pregnancies. In 8.4% of these pregnancies there was a history and confirmatory clinical evidence of toxaemia. The incidence of previous toxaemia amongst these women was 17.1%, which is higher than the incidence of toxaemia normally found. (Golden, Dexter and Weiss 1941, Stander 1945). This tends to indicate that a woman who has had a toxaemic attack is more liable to develop eclampsia in subsequent pregnancies.

19. The Mortality in Eclampsia.

(a) The mortality in eclampsia at the time of the attack.

The follow-up study naturally cannot indicate the mortality at the time of the eclamptic attack. To arrive at figures in this connection, data was collected from the

Peninsula/.....

Peninsula Maternity Hospital over the period July 1939 to December 1945. During this period 10,901 women were delivered in hospital and 4,566 in the district under hospital supervision and of these 150 were proved eclamptics. Of these, 13 cases died, giving a gross mortality of 8.6%. This is an uncorrected figure. Four of these cases were admitted to hospital in extremis and it is questionable whether any treatment whatsoever would have been of avail. A corrected figure of 9 deaths or 6% is a justifiable deduction if moribund cases are excluded. Twelve of the thirteen deaths were Coloured and Malays admitted as emergencies without previous antenatal supervision. The other, a European, attended the antenatal clinic once and was admitted with severe toxaemia, had a forceps delivery and postpartum eclampsia and died of pneumonia on the third day. The average death rate from eclampsia is approximately 13% in hospitals in the United States, (De Lee and Greenhill 1947), and, according to Browne (1951), accounts for 20% of all deaths from childbirth in England and Wales. Crichton (1932) found the mortality to be 22% in the years 1927-1931 at the Peninsula Maternity Hospital, and Goldberg (1935) found a gross mortality of 24% amongst cases from the same hospital during the years 1925 to 1934. The present figures may thus reflect better antenatal care and more modern methods of treatment, in keeping with the general trend all over the world. Eden (1922) found the deathrate to be 22.5% in Great Britain, Bryant (1935) and Chesley and Somers (1941) in their clinics in America had a mortality of 9.92% and 7.10% respectively. Faulkiner (1947) found the mortality in Dublin over a four year period ending in October, 1943, to be 12.2%. Among their cases Stroganoff and Davidowitch have in recent years brought the mortality down to 3%, a figure which other authors have not been able to equal. The fact that all deaths in cases quoted by me occurred amongst patients who were emergency admissions bears striking testimony to the value of proper antenatal supervision and the early detection and treatment of pregnancy toxaemias.

Table 17/.....

TABLE 16.

SHOWING THE INCIDENCE OF TOXAEMIA IN PREGNANCIES PRIOR TO THE ORIGINAL ATTACK OF ECLAMPSIA.

RACE.	No. of Pregnancies previous to the original attack of eclampsia.	No. of Women who had previous pregnancies.	Per Cent of Women who had previous pregnancies.	Per Cent of previous pregnancies which were toxaemic.	Per Cent of women with previous pregnancies who had previous toxaemia
European (White)	19	9	37.5	0	0
Coloured	111	26	34.2	9.8	23.1
TOTAL:	130	35	35	8.4	17.1

TABLE 17.

ILLUSTRATING THE TYPE OF ECLAMPSIA AND THE MORTALITY IN EACH GROUP.

	Types of Eclampsia.				
	Ante-partum.	Intra-partum.	Post partum.	Mixed.	Unknown.
No. of Cases	31	38	14	37	30
No. of Deaths	1	5	1	3	3

This table illustrates that the greatest number of deaths occurred in cases of intrapartum eclampsia and corresponds with the findings of Mudaliar et al (1940).

However, Greenhill and De Lee (1947) found the highest mortality in antepartum eclampsia, while Browne (1951) finds the highest mortality in post partum eclampsia. The severity of the disease, the period of pregnancy and obstetric difficulties at the confinement will all tend to influence the mortality.

(b) The maternal mortality in Eclampsia cases followed up.

Besides the 100 cases traced and found to be alive, 18 were found to have died since the time of their discharge from hospital in the 4 to 30 succeeding years. (See Tables 18 and 19 on Pages 148 and 149).

Of the 18 patients who died during the period between their attack and the time of the follow-up study, three Coloured women died in subsequent childbirth, one from eclampsia and the others from toxaemia and other complications, an incidence of 16.6% amongst the deaths. Three white and five Coloured patients died of some manifestation of hypertensive cardiovascular disease, an incidence of 44.4% amongst the deaths. One case died in uraemia, an incidence of 5.5% amongst the deaths. As no autopsy was performed it is impossible to give an accurate cause of death in this case. She may have been a case of renal failure in

progressive/.....

TABLE 18

SHOWING PARTICULARS OF THE NINE CASES AMONGST THE EIGHTEEN DECEASED ECLAMPTICS WHO DIED OF CARDIO VASCULAR AND RENAL COMPLICATIONS.

			At the time of Eclamptic Attack.				At the time of Death.		
Name.	Cause of Death.	Race.	Age.	Parity.	Date.	State of Child.	Age.	Parity.	Year of Death
M. B.	Dropsy, Diabetes and high blood pressure.	E.F.	39	10th	1937	Stillbirth	52	11th	1950
L. C.	Stroke and high blood pressure	C.F.	40	16th	1936	Stillbirth	42	16th	1938
J. D.	Stroke and high blood pressure	Malay	31	4th	1946	Neonatal Death	36	4th	1951
L. F.	Stroke and high blood pressure	C.F.	37	4th	1936	Stillbirth	38	4th	1937
W. L.	Stroke and high blood pressure	E.F.	28	1st	1930	Stillbirth	46	4th	1948
L. M.	Poor vision, high blood pressure & stroke	C.F.	34	8th	1946	Child alive	34	8th	1946
M. R.	Congestive cardiac failure with hypertension	Malay	40	12th	1940	Stillbirth	52	12th	1952
F. Z.	High blood pressure and stroke.	E.F.	30	3rd	1944	Neonatal Death	35	4th	1949
M. B.	Uraemia and ? chronic nephritis ? Renal death of progressive vascular disease.	E.F.	31	2nd	1942	Stillbirth	32	2nd	1943

TABLE 19

SHOWING DEATHS DURING THE PERIOD OF FOLLOW-UP STUDY.

	Total No. of Deaths	Percent who died in sub-sequent childbirth	Percent who died of cardio-vascular disease	Percent who? died of chronic Glomerulo-Nephritis.	Percent who died of other unrelated causes.
White	6	0	50	16.6	33.4
Coloured	12	25	41.6	0	33.3
TOTAL:	18	16.6	44.4	5.5	33.5

progressive hypertensive vascular disease or a case of chronic glomerulo-nephritis.

The other deaths were due to unrelated causes, e.g. pulmonary tuberculosis, intestinal obstruction, meningitis and causes unknown, an incidence of 33.5% amongst the deaths.

An unusual incidence of pulmonary tuberculosis in post eclamptic women has been noted by Rucker et al (1952), but this is probably coincidental.

20. Subsequent hypertension in the eclamptic cases studied.

There were nine Europeans and twenty-one Coloureds amongst the 30 cases found to be hypertensive at the follow-up examination. One of these Coloured eclamptic cases may have had chronic nephritis before her first attack of eclampsia. None of the remaining 29 cases were known to have had hypertension before their first eclamptic pregnancy. None of them manifested toxaemia before the 28th week, but this does not preclude a latent hypertension which can, as has been pointed out elsewhere, mimic true pre-eclamptic toxaemia, and only later the patient becomes a clinically manifest case of hypertension.

I am of the opinion that if we had methods of detecting an inherited latent hypertensive trait at the time of the eclamptic attack, the 29 cases with subsequent hypertension would fall into the hypertensive group with superadded pre-eclamptic toxaemia or eclamptic toxaemia as opposed to the cases of "true" pre-eclamptic toxaemia and eclampsia. The remaining 70 eclamptic cases who were normotensive at follow-up are unlikely to have had a latent hypertensive trait and are therefore cases of true eclampsia, unassociated with and unrelated to hypertensive vascular disease. However, as this is not possible to diagnose at the time of the attack, one must accept that 29 apparently normal women who developed eclampsia are now hypertensive. On closer scrutiny of the records of these cases, however, additional proof of the fact that eclampsia does not cause hypertensive cardiovascular disease is obtained. Case 47, who may have had pre-pregnancy nephritis, is excluded.

Thus/.....

Thus, in 22 of the 29 cases, at a mean age now of 43 years, the hypertension arose at the time of the eclamptic pregnancy and has persisted since. In the other 7 cases with a mean age now of 40.7 years, however, the hypertension became manifest only 21, 18, 16, 16, 13, 9 and 6 years later respectively. It is difficult to believe that in these latter cases there was any etiological relationship between the previous eclamptic attack and the hypertension found subsequently.

Therefore in only 22 hypertensive cases was there a definite direct association between eclampsia and subsequent hypertension i.e. in 22 out of the 100 eclamptics followed up. An incidence which is not higher but may in fact be lower that the incidence of hypertension amongst the female population in general at the age of 43 years, which is the mean age of the cases under consideration (Master et al 1943 and 1952 - see below). This points very definitely to the fact that eclampsia is not the cause of subsequent hypertension, but does not exclude the possibility that it may bring out hypertension earlier in a woman who would become hypertensive later in life in any case, whether she had pregnancies with or without eclampsia or no pregnancies at all.

(According to Masters et al (1950) the mean blood pressure amongst women in the age group 40 to 45 is 127.0/79.5 mm. Hg. with a range of 105-150/65-92 mm. Hg. Amongst females in the age group 45 to 49 the mean blood pressure is 130.6/81.5 mm. Hg. with a range of 105-155/65-95 mm. Hg. By these standards the 29 abnormal cases are definitely hypertensive. Thus in the European group the mean blood pressure was 180/105.5 mm. Hg. at the age of 45 with a range of 150-225/90-140 mm. Hg. and in the Coloureds the mean blood pressure was 164.8/98.5 mm. Hg. at a mean age of 40.59 years with a range of 142.5-195/90-125 mm.Hg.

Master et al (1950), Master, Marks and Dack (1943), Robinson and Brucer (1940), showed that over 40% of the adult population in U.S.A. are actually or potentially hypertensive, and there is no evidence that this finding cannot be equally

applied/.....

applied to the population of South Africa, except possibly to natives in the rural areas with whom we are not concerned in this study. Masters et al state that 5% of young adults, 40% of female subjects over 40 and 75% of the females over 70 years have some degree of hypertension.)

TABLE 20:

SHOWING THE INCIDENCE OF HYPERTENSION FOUND AT FOLLOW-UP. ONLY PATIENTS WITH A BLOOD PRESSURE OF 140/90 & ABOVE WERE CLASSIFIED AS HYPERTENSIVE:

	Hypertensive Cases:		Normotensive Cases:	
	No.	Per Cent	No.	Per Cent.
White:	9	37.5	15	62.5
Coloured:	21	27.63	55	72.3
T O T A L:	30	30.0	70	70.0

The gross incidence of hypertension, according to these standards, was 30%. 37.5% among the white women and 27.63% among the coloured women. The nett incidence of hypertension already indicated is 22%.

Different investigators have used different standards to determine hypertension, and of course, the number of patients and the period of time elapsed have also varied, so that comparison with other follow-up studies is difficult. Many of the earlier investigators did not clearly distinguish between hypertensive vascular disease and hypertensive vascular disease with renal vascular involvement on the one hand and chronic glomerulonephritis on the other hand. Also cases were included in the follow-up examinations who had pre-pregnancy hypertension or renal disease and so lead to a false high incidence of post-eclamptic sequelae wrongly attributed to eclampsia.

Bryans and Torpin (1949), using similar standards in a follow-up of 243 eclamptics for 12.3 years, as in the present series, found the incidence of hypertension to be 21.4%; 17.7%

amongst white and 26% amongst the negro women investigated. Teel and Reid (1937) followed 80 eclamptics for 7.6 years, and using a systolic blood pressure of 150 mm. Hg. as a standard, they found an incidence of 27.5% of hypertension. Amongst those known to have a normal blood pressure previous to the eclampsia, they found the rate to be 10%. Reid and Teel (1939) studying pre-eclamptic toxaemia, found hypertension in 51% of cases in which the previous blood pressure was not known, and in those previously normotensive, 21%. Chesley, Somers and Vann (1948), in a study of 240 eclamptic cases followed from 1 to 8 years, found a subsequent blood pressure of 140/90 mm. Hg. or more in 15%. Light (1948) found 30.1% hypertension in a follow-up of non-convulsive toxaemia patients. Dexter and Weiss (1943) state that 25% of patients have hypertension after toxaemia. Page and Cox (1938) reported that in 13,000 cases of toxaemia collected from the literature, the incidence was 43%. Dieckmann and Browne (1938, 1939, 1952), report an average of 27% subsequent hypertension after eclampsia and 34% after non-convulsive toxaemia from the literature. In their own series they found an incidence of 37% and 40% after eclampsia and pre-eclamptic toxaemia respectively. Stander in his text book states that from one-fifth to one-tenth have residual vascular damage. Other authors including Rucker (1932), Herrick and Tillman (1935) Lewis (1940), Corwin and Herrick (1927), Tillman (1936), Browne and Dodds (1939), Reid and Teel (1939), Dexter and Weiss (1941), Dexter and Weiss et al (1943), Mc Clellan et al (1942), Irwing (1947), Breakey (1932), Peckham (1941) and others give figures varying from 13% to 63.4%.

Many authors find a higher incidence of subsequent hypertensive vascular disease in pre-eclamptic toxaemia than in eclampsia. However, cases of hypertension with superadded toxaemia have probably wrongly been included under the group of "true" pre-eclamptic toxaemia cases. Browne and Browne & Dodds find the highest incidence of vascular complications in eclampsia and not in pre-eclamptic toxaemia.

Subsequent./....

21. SUBSEQUENT HYPERTENSION RELATED TO AGE:

The average age of the women with hypertension in this follow-up series of eclamptic cases was 41.7 years. Forty-five years for the European and 40.6 years for the non-European patients. The mean age of all cases at follow-up (including the non-hypertensive cases) was 35.1 years.

TABLE 21:

SHOWING THE ECLAMPTIC CASES BROKEN DOWN INTO AGE GROUPS, WITH HYPERTENSION RELATED TO AGE:

Age Groups:	20-29 years.	30-39 years	40-49 years	50 years & over.
No. of Cases	31	40	24	5
No. Hypertensive	2	10	15	3
% Hypertensive	6.5	25.0	62.5	60.0

The number in each group is rather small to be of statistical value but the results do show the general trend. Of significance is that in the age group 40-49 years (the largest group), 62.5% of the cases were hypertensive subsequent to eclampsia.

This is considerably more than may be expected in a group of women of the same age in the general population. Thus Master, Marks and Dack (1943) found a blood pressure of 140/90 mm. Hg. in 39.27% amongst 6,366 women, mostly white industrial workers, in this age group. The deduction from the foregoing is that eclampsia tends to bring out hypertension at an earlier age than it would normally have occurred. Bearing in mind the 70 cases normotensive at follow-up, I feel that only in the case of patients with a latent hypertensive tendency, or manifest hypertension, will eclampsia have vascular sequelae.

22. PROTEINURIA:

Five of the 100 surviving eclamptic cases had proteinuria

at./.....

at follow-up examination and compares with an incidence of 2.6% of 167 cases followed for a period of 1 - 9 years by Chesley and Somers (1941). All 5 cases were hypertensive, i.e., 16.6% of the total of hypertensive cases, compared with 12.8% of the total hypertensive cases found by Bryans and Torpin (1949) to have proteinuria in a follow-up of 243 eclamptic cases. They, too, found no cases of proteinuria without associated hypertension. Short and Levy (1939) demonstrated proteinuria in 20% of nearly 5,000 women life insurance policy holders and Bull (1946) and many others have written about benign proteinuria. However, none of the above cases fall into this latter category.

In 4 out of 5 there was only a trace of proteinuria, verified by repeat examination of the urine and by catheter specimens, to exclude other causes. In the 5th case there was a significant degree of proteinuria (up to 5 grams per litre). The detailed case histories of the above cases are included in Appendix 4 at the end of the thesis.

In 4 of the 5 cases there was no preceding nephritis. One case had pyelitis at the age of 16 and again at the age of 19 years, the latter in association with her first pregnancy. This was not complicated by toxaemia and was followed by a second normal full term and a third eclamptic pregnancy. Three of the 5 cases had 2 normal confinements before the advent of eclampsia. Four of the 5 cases with only a trace of albumen, have enlarged hearts, retinal changes and signs and symptoms of hypertensive vascular disease, yet no specific gravity fixation, no signs of urea retention or gross renal disease. The youngest of these was 35 years of age and the oldest 51 years. All have a familial hypertensive history and the most likely explanation of the proteinuria is nephrosclerosis occurring perhaps at an earlier age than usual. One of these cases had signs of cardiac failure and they all tend to be obese. None of them have had normal subsequent pregnancies. The fifth case, only 21 years old and

not./....

not obese, with a familial history of diabetes and hypertension, had no objective evidence of cardiomegaly, retinal changes or anaemia and a normal pyelogram. She is hypertensive and has much more marked proteinuria than the other cases. With the concentration and dilution test a specific gravity reading of 1010 was obtained on 3 occasions. The question arises, as to whether she is a case of glomerulonephritis or a case of delayed healing of the renal manifestations of eclampsia, or a case of progressive renal vascular disease in a hypertensive individual. In view of the fact that she has had 2 further pregnancies in rapid succession, this may have acted as a factor in preventing the healing of the renal lesion. Unfortunately, while being investigated, she conceived again and would not co-operate further. I feel that clinically it is impossible to come to any further conclusion at this stage. It is doubtful whether further special renal studies would settle the issue one way or another. She is the type of case that should be followed throughout her life and further pregnancy should be avoided for a while at least, to give the renal lesion time to clear up. If there were to be a progressive deterioration, a Smithwick operation and renal biopsy would be desirable as was done by Dexter, Weiss and others in a few cases they have reported on (1943). In that small group the histology favoured a vascular degenerative renal lesion rather than chronic glomeronephritis and in some cases the histology was that of malignant hypertension, as seen in the kidney.

Although, practically all cases of eclampsia have albuminuria, with or without hypertension, with and after the attack, only a small percentage are subsequently found to have proteinuria with hypertension, and this is the phenomenon of healing first stressed by the German writers and which can take up to 2 years and even longer to occur (Browne 1951).

In conclusion, the clinical findings show that in general the results are in agreement not only with those of other workers

already./....

already referred to, but with a statement by Bell (1932) that a mild degree of change in the renal bloodvessels may often be present after eclampsia from a pathological point of view. This in my opinion occurs only in hypertensive cases destined to be severe. Thus, in only five cases was such a change clinically evident, and in one of these cases glomerulo-nephritis could not be excluded. This case may have had nephritis prior to her first pregnancy and cannot with justification be included in this group.

23. A Comparison of subsequent pregnancies amongst those with and without hypertension.

There were 97 subsequent pregnancies in 22 women in the hypertensive group, and 185 pregnancies in 58 women who were subsequently normotensive at follow-up examination. 73.3 and 82.8 per cent of the women in each respective group had at least one subsequent pregnancy. Among the women in the hypertensive group there was an incidence of abortion or stillbirth of 21.6%. Browne (1945), in a series of hypertensive patients, found the foetal and neonatal mortality to be 16.2 per cent, a figure which roughly corresponds with the findings in this series. The incidence of stillbirths and abortions in the non-hypertensive group was 16.7%, a figure in keeping with a series of pre-eclamptic toxaemia cases, followed over a twelve year period by Browne (1945), who found a foetal and neonatal mortality of 13% amongst them. (See Table 22, Page 159).

This is in keeping with what one expects, that is that cases with hypertensive cardiovascular disease with superimposed toxaemia have a high foetal mortality, as stated by Dieckmann (1952), Dexter and Weiss (1941), Chesley and Annitto (1947) and others. However, Sharkey and Hess (1946) and Bryans and Torpin (1949) found no increased foetal mortality in their hypertensive cases but state that their figures may not be accurate, as they relied mainly on the histories of their patients and not on documentary evidence.

55.6% of the subsequent pregnancies were complicated by toxaemia in the hypertensive group and 21.6% in the normotensive

group/.....

group. 95.4% or 21 women in the hypertensive and 36.2% or 21 women in the normotensive group who had further pregnancies, had at least one further toxaemic pregnancy, which tends to indicate that those who ultimately become hypertensive after an eclamptic attack or attacks are more liable to subsequent toxaemia. This is in keeping with the statement generally accepted that hypertension is one of the factors causative of recurrent toxaemia. However, as recurrent toxaemia occurred in the non-hypertensive group as well, it need not be a factor at all. There were ten subsequent attacks of eclampsia in seven patients amongst those found to be hypertensive at follow-up examination, but in four of these the hypertension only became manifest after the second eclamptic attack (this has already been discussed). In the non-hypertensive group there were three subsequent attacks of eclampsia in three women. The incidence of recurrence of eclampsia was 10.3 and 1.6 respectively in the two groups (See Table 22).

24. A detailed study of cases of recurrent toxaemia amongst the eclamptic cases followed up.

If standard text books on obstetrics are consulted, e.g. Browne, Antenatal Care (1951), Gibberd (1951), Delee and Greenhill (1947) and Williams Obstetrics (1941) etc., very little is said about pre-eclamptic toxaemia recurring in subsequent pregnancies. In fact Dieckmann (1952) states that it seldom recurs and in general cases of toxaemia that recur are immediately spoken of as recurrent toxaemia. Many authors regard these as hypertensive cases. This term was first introduced by Kellogg in 1924, and is defined as the occurrence of toxaemia in 2 or more successive pregnancies, the patient being apparently healthy in between. The following cases manifested recurrent toxaemia and were normotensive at follow-up examination:-

Case	1	Case	42
"	4	"	44
"	11	"	49
"	13	"	51
"	19	"	53
"	24	"	56
"	31	"	62
"	32	"	68
"	36	"	69
"	37	"	82
"	39	"	92

See/.....

TABLE 22

SHOWING A COMPARISON OF SUBSEQUENT PREGNANCIES IN THOSE CASES WITH AND THOSE CASES WITHOUT HYPERTENSION AMONGST THE 100 ECLAMPTIC CASES STUDIED.

	Number of Subsequent Pregnancies	Percentage of women who had subsequent pregnancies	Percentage of subsequent pregnancies resulting in stillbirth or abortion	Percentage of subsequent pregnancies which were toxaemic	Percentage of women with subsequent toxaemic pregnancies	Percentage of subsequent eclamptic pregnancies	Percentage of women with subsequent eclamptic pregnancies.
Hypertensive	97	73.3	21.6	55.6	95.4	10.3	31.8
Normotensive	185	82.8	16.7	21.6	36.2	1.6	5.1

(See Photographs Page 113 and 114 of the case histories in summary form).

Three views are held regarding the significance of this recurrence of toxaemia: (1) Kellogg (1924) suggested that it is due to a concealed nephritis only producing signs and symptoms during pregnancy, with the extra load leading to kidney insufficiency. Gibberd (1928) adopted this explanation and expressed the opinion that pregnancy was the best test of kidney function since "an amount of structural damage insufficient to give rise to signs and symptoms might yet make itself felt during pregnancy". In 1929 he introduced the term occult nephritis to describe the concealed nephritis of Kellogg. Stander and Peckham (1929) introduced the term low reserve kidney for similar cases. (2) Young (1929) stated his belief that the recurrence is due to some unknown factor which, during pregnancy, involves the life of the placenta and hence gives rise to abortion, accidental haemorrhage or toxaemia. The last would only occur if the area of placenta damaged or separated is large enough, and the placenta is retained for a sufficiently long time. (3) Browne found that 60% of the patients he studied who developed recurrent toxaemia had a hypertension of over 130/70 mm. Hg. between the toxaemic pregnancies. Though the patients seemed well, they had a persistent hypertension after the first pregnancy which in the next pregnancy became aggravated, often with the reappearance of albuminuria and oedema. The end was not infrequently abortion or miscarriage. In the remaining 40% the blood pressure, though normal, was borderline, with an instability that in succeeding pregnancies probably predisposed to the occurrence of hypertensive toxaemia. He believes that in these cases there is a familial hypertensive tendency, and that pregnancy does nothing more than to unmask a latent hypertension which in the absence of pregnancy would have developed in any case, though possibly at a somewhat later period. Furthermore he finds no reason to believe that this borderline hypertension and instability of blood pressure which is in his opinion

an important/.....

an important cause of recurrent toxaemia, is entirely a result of the previous pre-eclamptic toxaemia. It is probable that it existed before the first pre-eclamptic toxaemia as a familial hypertensive tendency and predisposed to it. This, he feels, explains the findings of Theobald in 1933 who produced statistical evidence which in his, Theobald's, opinion threw considerable doubt on the accuracy of the view, namely that pregnancy toxaemia could cause chronic nephritis or even disease of the circulatory system, with no significant difference between the mortality rates of these diseases in married and single women up to the age of 55 years.

Also Icenhour et al (1942) examining 900 parous and 900 single women from the age of 20 upwards, found the incidence of hypertension, that is a blood pressure of 140/90 mm. Hg. or over, to be slightly higher in nulliparous women than in multiparous women at all ages. This, Browne feels, shows that to all intents and purposes the patients having hypertension following toxaemia of pregnancy are the same patients who would have developed hypertension had they never become pregnant. These viewswere supported by the findings in a similar study by Barnes and Browne in 1945. However, they do not state how many of the multiparae examined had previous toxaemia. Browne feels that if it is accepted that manifest nephritis does not occur as a sequel of pre-eclamptic toxaemia and eclampsia, then occult or concealed nephritis does not occur either. He states further that this occult nephritis, being a mild form of chronic nephritis, only differs in degree, and if mild forms occur severer forms must also occur. However, as recurrent toxaemia is a frequent phenomenon in obstetric practice, one should see chronic nephritis more often, yet it is only seen rarely. Although all this reasoning sounds logical, many will disagree with Browne's views, especially with his blood pressure standards utilized and the fact that he regards the 40% of his cases with such a low blood pressure as potential cases of hypertension with no substantiating proof. If the cases of recurrent toxaemia in this follow-up series are studied, one

is forced/.....

is forced to disagree with Browne's views. Recurrent toxaemia occurred not only in the group that had subsequent hypertension with a blood pressure of 140/90 mm. Hg. or above, but also in the subsequently normotensive group. It could be argued that if Browne's criteria of a blood pressure of over 130/70 mm. Hg. indicating hypertension were used, many of the present cases will fall into the hypertensive group as did 60% of Browne's cases. Those who do not will fall into a group comparable to the 40% in Browne's series, with a blood pressure which, although normal, is borderline, with an instability and a familial hypertensive tendency. Using my criteria, recurrent toxaemia was found in 55.6% of the subsequent pregnancies of the hypertensive group (21 cases) and 95.4% of the women in this group who had subsequent pregnancies had at least one toxaemic pregnancy. On the other hand recurrent toxaemia was found in 21.6% of the subsequent pregnancies of 21 of the normotensive cases who had further pregnancies (i.e. 36.2% of the normotensive cases who had further pregnancies.) It will be seen then that manifest or previous latent hypertension did not operate in all these cases to produce toxaemia. Other factors against this hypothesis will further be illustrated by the following cases:-

Case 7 amongst the hypertensive cases had seven normal pregnancies, the eighth eclamptic, the ninth toxaemic, the tenth fullterm normal, the eleventh toxaemic, and now, at the age of thirty-eight, she is hypertensive. It would be difficult on the basis of his hypothesis to explain why her tenth pregnancy at term was normal.

Case 16. She had four normal pregnancies at term, a fifth eclamptic pregnancy prematurely, a sixth normal pregnancy at term, a seventh eclamptic pregnancy at term followed by an eighth, ninth and tenth pregnancy, all of which were normal at term, and only now at the age of 40 she is hypertensive.

Case 26, after a normal fullterm pregnancy had two toxaemic

pregnancies/.....

pregnancies, followed by three normal pregnancies and then a seventh gestation which was eclamptic. The next, or eighth, was toxaemic, and now four years later, at the age of 38, she is hypertensive.

Case 28. This patient had three normal fullterm pregnancies, the fourth was eclamptic, the fifth toxaemic, the sixth, seventh, eighth, ninth, tenth, eleventh and twelfth normal, the thirteenth toxaemic and the fourteenth eclamptic. She is now aged 48 and hypertensive.

Case 64. Her first pregnancy was eclamptic, the 2nd. toxaemic and the third a normal fullterm alive birth, and now ten years later she is hypertensive and aged 35.

Case 75. She had five normal pregnancies, the sixth eclamptic, the seventh and eighth toxaemic and the ninth normal at term. She is now aged 46 and hypertensive.

Case 80. Her first and second pregnancies were both eclamptic, the third was toxaemic, the fourth, fifth, sixth, seventh, eighth and ninth were all normal at term and now at the age of 39 she is hypertensive.

Case 91. The first pregnancy was a miscarriage, the second eclamptic, the third, fourth and fifth normal at term, the sixth toxaemic and the seventh again eclamptic. She is now aged 61 and hypertensive.

These cases illustrate that the recurrence of toxaemia may not have been due to hypertension as hypertension only became permanently manifest after several pregnancies. If a hypertensive tendency was an etiological factor, it is difficult to understand why it did not operate in each successive pregnancy. This points to some other factor or factors which in any event did not act constantly.

It is wellknown that in a woman with essential hypertension, a given pregnancy may not change the level of the blood pressure at all, lower it, or aggravate it. (Gibberd 1951 and others). However, in repeated pregnancies in such a case the blood pressure

is bound/.....

is bound to be aggravated sooner or later. Is it possible that a hypertensive tendency could act in a similar way, as Browne suggests? Case 95, now hypertensive, had five normal pregnancies, a sixth eclamptic, and subsequently seven normal pregnancies and a miscarriage. Thus she had eclampsia and although eventually hypertensive, had twelve normal confinements without showing a hypertensive tendency or developing toxaemia, except of course with the sixth pregnancy, which was eclamptic. It is doubtful whether this last named pregnancy had as an etiological factor a possible latent hypertension. I therefore believe that in some cases of recurrent toxaemia neither latent nor manifest hypertension is an etiological factor. Further, in the group with recurrent toxaemia who are non-hypertensive, 21.6% of the subsequent pregnancies were complicated by toxaemia. 36.2%, i.e. 21 of the 58 normotensive cases, had at least one subsequent toxaemic pregnancy. Two of these cases have a labile blood pressure, normal with rest, and one of them has been diabetic for the last two years. Both have a negative family history of hypertension. The 19 remaining cases in this group, after an average interval of 7.9 years since they had eclampsia, are still normotensive and their average age is 31.5 years. In addition, in ten of the 19 there is no family history of hypertension, while in the other nine a family history is present on one parent's side only, which would mean that they have at the most a one in four chance of developing hypertension (Ayman 1933).

The question as to whether or not they will become hypertensive and thus positively manifest a latent hypertension, is nevertheless difficult to answer. Only prolonged follow-up study will clear this issue, but one's opinion based on the facts enunciated above, is that they probably will not. In other words they are cases of recurrent toxaemia without manifest and a very dubious latent hypertension. If one applies Browne's criteria to all the women who had subsequent toxaemia, then 59.5% of the group have hypertension with a blood pressure of over 130/70 mm. Hg. between the toxaemic pregnancies, rising with the toxaemic

pregnancy and followed by albuminuria and oedema. In other words, on a hypertensive basis they have toxaemia, as stated by Browne, who classified 60% of cases in this group. The balance of 40.5% (17 cases) had recurrent toxaemia and in between their pregnancies and subsequently had a blood pressure of 130/70 mm. Hg. or below (40% of Browne's series fall into this group). Thus, using Browne's criteria, there are 17 cases (40.5%) of the present series in this latter group; in other words, a further four cases originally in this group are now, according to this way of reasoning, also regarded as hypertensive, yet none of them have a labile blood pressure. All the cases in this group are normotensive by any standard, with a mean age now of 30.2 years and a mean age when they were eclamptic of 22 years. In 50% of them the family history is negative for a hypertensive tendency. It is felt that neither hypertension nor a hypertensive tendency is responsible for the toxaemia or recurrent toxaemia in these cases. Whether or not a deficient diet, faulty habits, abnormal environment etc. predispose or not, there must be some other factors responsible. This is even more likely to be true if one considers the cases of eclampsia who had subsequent pregnancies without any recurrence of toxaemia at all. In the normotensive group of 70 cases, there were 37 cases without subsequent toxaemia having further issue, that is 63.8% of the normotensive cases as opposed to 21 or 36.2% of the normotensive cases who had subsequent toxaemia.

The above mentioned cases illustrate that in a given case of recurrent toxaemia, normal pregnancies may precede the toxaemic pregnancies, and, what is more difficult to explain, is that in between recurrent attacks a normal fullterm pregnancy may be interposed. (Cases 7, 16, 28 and 96 are examples of this type). Case 79, a similar example, had a normal first pregnancy, then six toxaemic pregnancies and subsequent to this a normal pregnancy followed by eight toxaemic pregnancies.

These cases illustrate that in a definite proportion of recurrent toxaemias neither latent nor manifest hypertension

nor latent nor manifest nephritis is causative. They are thus examples of "true" recurrent pre-eclamptic toxaemia. This entity is therefore not confined to primiparae, nor is it a condition that seldom, if ever, recurs as stated by Dieckmann and others.

Recurrent true pre-eclamptic toxaemia is more common than recurrent "true" eclampsia, in the same way as pre-eclamptic toxaemia on a hypertensive basis is more common than eclampsia on such a basis. Kellar (1945) pointed out that a fair percentage of cases of recurrent toxaemia cannot be explained on the basis of hypertension or nephritis. The analysis of the cases in this series confirms this view, a view that has not been sufficiently emphasised in the literature.

25. A comparison of the previous pregnancies amongst the hypertensive and normotensive groups of eclamptic cases studied.

Previous to the original attack of eclampsia in this study there were 68 pregnancies in 19 women among the hypertensives and 62 in 16 women in those with normal blood pressure at follow-up. Of these pregnancies 4.34% were toxaemic in the first group and 12.9% in the second group. This shows that before hypertension and eclampsia occurred, the number of toxaemic pregnancies in the ultimately normotensive group exceeded those in the ultimately hypertensive group. (See Table 23, Page 167).

TABLE 23:

SHOWING A COMPARISON OF PREGNANCIES OCCURRING PRIOR TO THE ORIGINAL ATTACK OF ECLAMPSIA IN THE HYPERTENSIVE AND NORMOTENSIVE GROUPS:

	Number of previous Pregnancies.	Percent of women who had previous pregnancies.	Percent of previous pregnancies, which were toxaemic.	Percent of women with previous pregnandes who had previous toxaemia.
Hypertensive Cases.	68	63.3	4.34	10.5
Normotensive Cases.	62	22.8	12.9	25.0

CHAPTER 3.

The results of the follow-up study after an average interval of 13.55 years amongst the 100 non-convulsive Toxaemia cases, who had a total of 676 pregnancies, with pertinent discussions in the respective subsections.

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(1) Normal Cases.

Of the total number 24 were normotensive at the time of follow-up and had no retinal changes and no proteinuria. One of these cases, Case 88, had acute Nephritis during pregnancy (Ellis Type 1) and was not really a case of Toxaemia. (See Page 194 for particulars).

(2) Hypertensive Cases.

There were 76 cases out of the total of 100 with a blood pressure of 140/90 mm. Hg. or higher with varying degrees of funduscopic changes at the time of follow-up. Of these 39 had severe hypertensive vascular disease with blood pressures of 180/100 mm. Hg. or more.

(3) Cases with Proteinuria.

There were 6 cases amongst the total of 100 who had Proteinuria. They all had hypertension as well, and are included in the hypertensive group as in none of them was there any evidence of chronic glomerular nephritis. (Cases 3, 8, 31, 36, 53 and 57).

(4) Cases with Diabetes Mellitus.

Four cases, all of whom were hypertensive as well, were found to be diabetic at follow-up examination. (Cases 64, 75, 89 and 93). Two of these had developed signs and symptoms suggestive of intracapillary glomerulosclerosis as first described by Kimmelsteel and Wilson.

(5) Cases with Epilepsy.

One of these cases gave a history of epilepsy, another case had a family history of epilepsy and 6 cases had a family history of eclamptic fits. Thus according to Maltby and Rosenbaum's views, the incidence of a convulsive diathesis would be 8%.

(6) The Premenstrual Tension Syndrome and its association with Non-convulsive Toxaemia.

There/.....

There were 36 cases (15 normal and 21 hypertensive) who had a positive history of premenstrual tension. In 24 of these the syndrome was present before first conception. In 12 its onset followed the toxaemic attack.

In 64 cases there was no history of premenstrual tension. As in the case of eclamptics no etiological association between the incidence of this syndrome and the toxaemias of pregnancy was found.

(7) <u>The family history of the non-convulsive toxaemia cases followed up</u>.

Six of these cases had at least one member in their families who had eclampsia during childbirth.

There was a family history of non-convulsive toxaemia in 23 cases, 20 of whom belong to the hypertensive group.

A family history of Diabetes was found in 9 instances. 8 of these fall in the hypertensive group.

16 of the 24 normotensive cases, that is 66.6%, gave a family history of hypertensive vascular disease, while in 8 or 33.3% this was negative. Amongst the 76 hypertensive cases 66 gave a positive history and 5 a doubtful positive family history of hypertensive vascular disease. That is 71 or 93.4%. In 5 of the hypertensive cases, or 6.6%, the family history was negative from the point of view of hypertensive vascular disease.

See Photographs 14 and 15, on Pages 170 and 171 illustrating the above discussed findings.

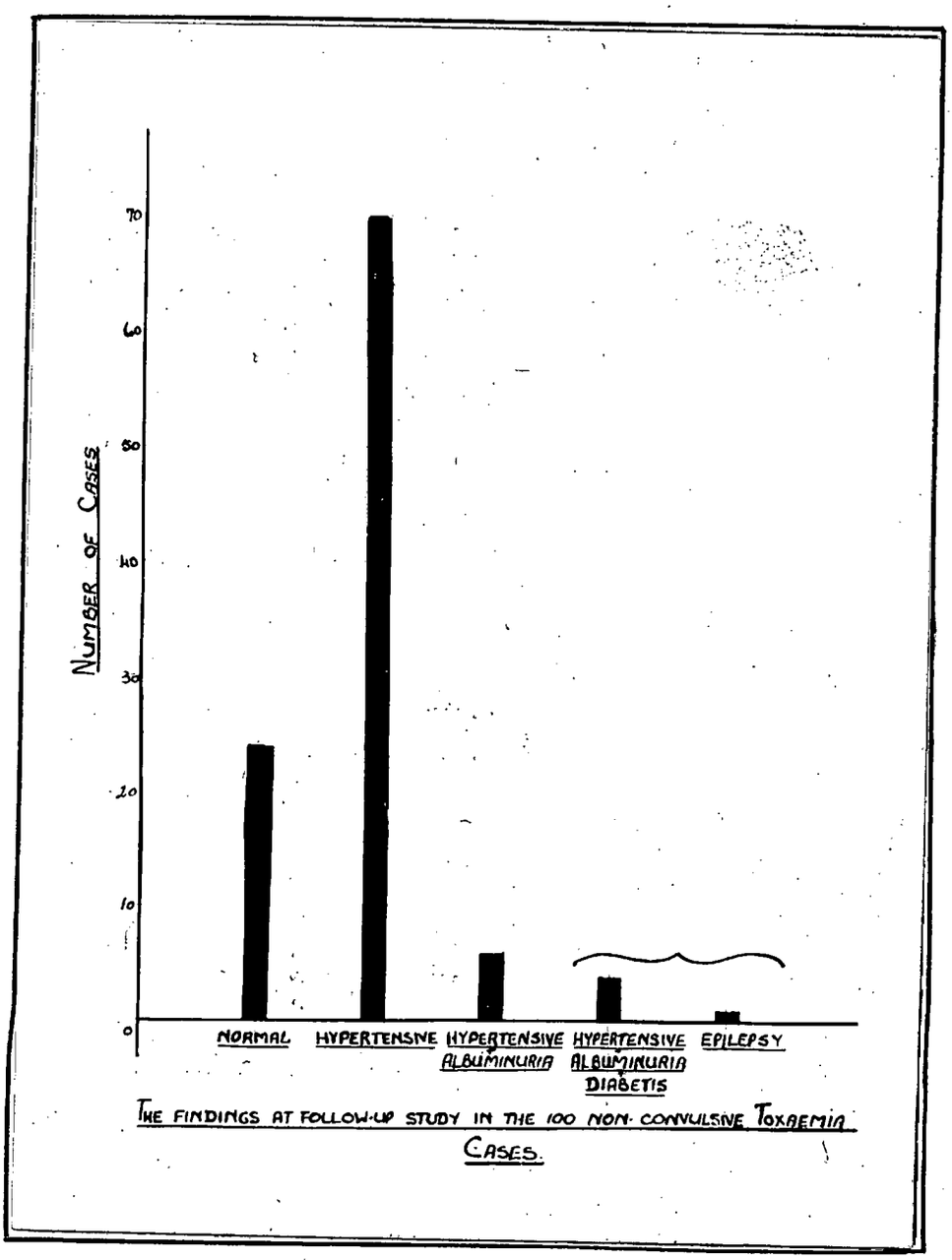
PHOTOGRAPH XIV.

THIS SHOWS A GRAPHIC RECORD OF THE FINDINGS

OF FOLLOW-UP STUDY OF THE 100

NON-CONVULSIVE TOXAEMIA

CASES STUDIED.



THE FINDINGS AT FOLLOW-UP STUDY IN THE 100 NON-CONVULSIVE TOXAEMIA CASES.

PHOTOGRAPH XV.

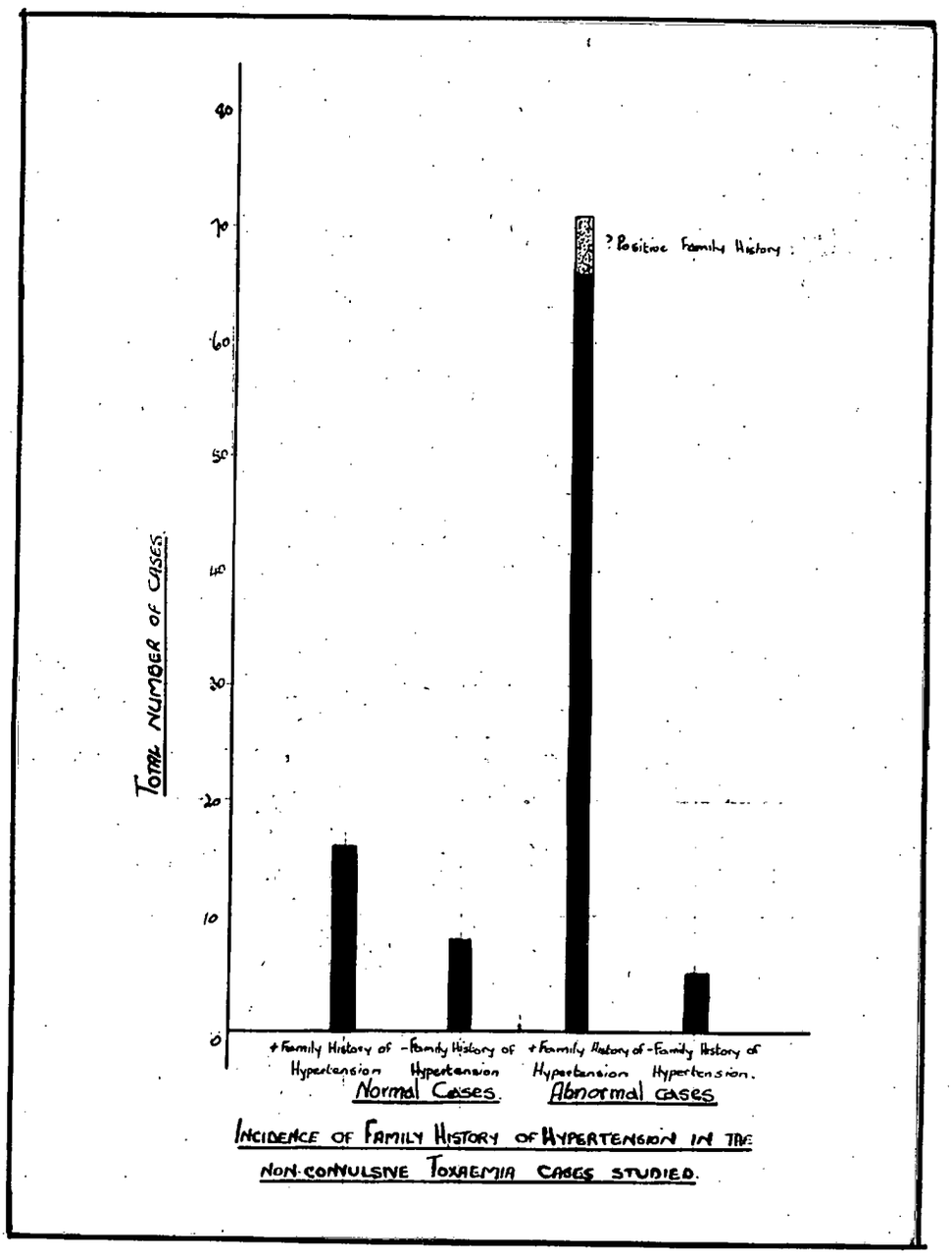
THIS PICTURES IN GRAPHIC FORM THE FAMILY

HISTORY OF HYPERTENSIVE VASCULAR

DISEASE OF THE 100 NON-

CONVULSIVE TOXAEMIA

CASES STUDIED.



INCIDENCE OF FAMILY HISTORY OF HYPERTENSION IN THE NON-CONVULSIVE TOXAEMIA CASES STUDIED.

8. The state of the Cardiovascular system in the 100 non-convulsive Toxaemia cases followed up.

(a) The eye changes at the time of the toxaemia attacks.

(1) Visual Disturbances.

Visual disturbances, e.g. flashes of light, double vision and dimness of vision were uncommon in these cases and was reported in 10% of the cases. These symptoms are thus more common in cases of eclampsia.

(2) Unfortunately the records about the funduscopic findings at the time of the attack are incomplete in many instances. In established cases of hypertension with super-added toxaemia copper wiring, A-V nipping and tortuosity of vessels as well as spasm, with irregularity of lumen and in two cases retinal haemorrhages were noted. In other such cases the funduscopic findings did not help to indicate the fact that there was underlying hypertension. In some cases of true pre-eclamptic toxaemia no fundal changes were seen, while in others spasm of the retinal vessels was noted, and in two instances oedema of the retina and papilloedema. One of the latter was subsequently hypertensive.

It can be concluded from the findings in this series that in general the funduscopic changes are less easily discernible than in eclampsia, but do occur. In cases of manifest hypertension with superadded toxaemia they may aid in the making of a correct diagnosis, only if arteriosclerosis is discernible.

(b) The eye changes at the time of follow-up examination amongst the 100 non-convulsive toxaemias.

Eye changes were confined to the 76 hypertensive cases and Table 24 illustrates these changes in accordance with the classification of Wagener and Keith.

Table 24/.....

TABLE 24.

THE EYE CHANGES ENCOUNTERED AMONGST THE SUBSEQUENTLY HYPERTENSIVE CASES.

	Grade 0.	Grade 1.	Grade 2.	Grade 3.	Grade 4.
Number of Cases	3	15	53	5	0

This illustrates that Grade 2 retinopathy was the common finding. There were no instances of malignant hypertension but five cases showed Grade 3 retinopathy, 3 of whom had congestive cardiac failure. The two others had hypertensive vascular disease in association with diabetes mellitus and possibly intracapillary glumerulosclerosis, but none were definite cases of chronic nephritis. Progressive hypertensive vascular disease was thus the cause of the progressive retinal changes in these five cases.

(c) The cardiac state of the 100 non-convulsive toxaemia cases followed up.

(i) The 24 normotensive cases.

In this group there was one case of mitral stenosis with an enlarged left auricle on Barium swallow, and a mitralised heart without signs of cardiac failure. All the other cases were normal from the point of view of cardiomegaly.

(ii) The 76 hypertensive cases.

There were 37 cases without demonstrable cardiomegaly and 3 of them showed no retinal changes. However, they are definitely early hypertensive cases in spite of this, as repeated blood pressure estimations were abnormal.

39 cases showed radiological evidence of cardiomegaly, and one of these (Case 94) had aortic regurgitation and a negative Wassermann reaction, while another had auricular fibrillation and mitral stenosis in association with hypertension.

Using/.....

Using the criteria of Evans (1952) 16 of these were of the cardiac kind, having had left ventricular enlargement without obvious changes in the aorta. Three were of the vascular kind (including the case of aortic regurgitation) with marked unfolding of the aorta and minimal cardiomegaly. Twenty were of the cardiovascular kind with left ventricular enlargement and aortic unfolding seen side by side. Eight of these had plaques of calcified atheroma in the aortic arch.

This confirms that more than 50% of the hypertensive cases had progressive vascular disease.

(d) <u>The electrocardiographic changes amongst the hypertensive cases of non-convulsive toxaemia.</u>

In 15 cases electrocardiographs were taken as there was no machine available to do graphs of the remainder of the cases when the survey was in progress. The tracings showed the changes of left ventricular strain already referred to when dealing with the eclamptic follow-up, and to avoid pointless repetition will not be discussed further.

(e) <u>The renal function and state of the 100 non-convulsive toxaemic cases studied.</u>

(i) Amongst the 24 normotensive cases, all the renal function tests executed, as specified in the section of methods, were within normal limits. One of these cases was actually a case of acute nephritis during her sixth pregnancy, wrongly called toxaemia at the time, and is now normal as one expects in the majority of cases with Ellis Type 1 nephritis.

(ii) Amongst the 76 hypertensive cases there were 71 whose renal functions were within the limits of normality. The 5 remaining cases had proteinuria, and pyelograms done in two of these cases were found to be normal. The other three had signs and symptoms of congestive cardiac failure and one of these had a blood urea of 56 mg. per cent. The other two had hypertension, Grade 3 retinopathy, and a trace of proteinuria in association with diabetes mellitus and are probably cases of intracapillary glomerulosclerosis.

None/...

None of these two cases showed specific gravity fixation in the dilution and concentration tests.

Two of the cases in whom pyelitis was suspected, no growth was obtained from catheter specimens of urine. The three cases with cardiac failure showed microscopically hyaline and granular casts in their urines.

In can be concluded that in this series there was no evidence that any of the cases had chronic glomerulonephritis as the cause of hypertension.

(9) The physical build and constitution of the non-convulsive toxaemia cases studied.

No constant build, constitution or personality was found, bearing in mind that at least two entities are included in this group, namely "true" pre-eclamptic cases and cases of toxaemia superimposed on underlying hypertension. The shortest patient was 4 ft. 8 ins. and the tallest 5 ft. 7 ins. Their average height was 62 ins. The heaviest patient in this series weighed 260 lbs. and the lightest case weighed 110 lbs. Their average weight was 159 lbs.

TABLE 25.

ILLUSTRATING THE WEIGHT/HEIGHT RATIO OF THE 100 NON-CONVULSIVE TOXAEMIA CASES FOLLOWED UP.

Weight/Height ratio.	No. of Cases.	Percentage with Hypertension.	Percentage Normotensive.
Less than 1.80	16	75	25
1.81 - 2.60	34	58.8	41.1
More than 2.61	50	88	12

This table shows that the higher the weight/height ratio, the greater the incidence of hypertension.

10. The Age and Parity of the 100 non-convulsive toxaemias followed up.

(a) The age when toxaemia first occurred in these cases.

Vide Table 26.

TABLE 26.

INDICATING THE AGE AT THE TIME OF THE FIRST TOXAEMIC ATTACK AND ITS RELATIONSHIP TO THE SUBSEQUENT CARDIOVASCULAR STATE OF THE 100 CASES FOLLOWED UP.

Age in years.	15 - 20 years.	21 - 25 years.	26 - 30 years.	31 - 36 years.	37 - 42 years.	43 years & Older.
No. of Cases	14	24	21	19	14	8
% with hypertension.	50	58.3	76.2	89.5	100	100
Normotensive	50	41.7	23.8	10.5	0	0

This table shows that the older the patient at the time of the first toxaemic attack, the more probably is it that hypertension will be found at follow-up examination. This is to be expected, as we are dealing with a mixed group where, especially in the case of the older patients, a latent hypertension would tend to become manifest. Furthermore, in interpreting the results of this table and Table 27 (to follow), it must be borne in mind that the period that elapsed between the first toxaemic attack and the time of the follow-up study was not a constant, but varied from 4 to 30 years.

The mean age of all cases found to be subsequently hypertensive, when they first had toxaemia, was 31.2 years. The mean age of all the subsequently normotensive cases at follow-up when they first had toxaemia was 22.7 years. The mean age at the time of the follow-up examination of all cases was 43.8 years. In the non-European cases this was 45.3 years and in the European cases 41.3 years.

(b) The age of the toxaemia cases at the time of follow-up.

TABLE 27.

ILLUSTRATING THE AGE OF THE CASES AND ITS RELATIONSHIP TO THEIR SUBSEQUENT CARDIO-VASCULAR STATE AT THE TIME OF THE FOLLOW-UP.

Age at present.	20-25 years.	26-30 years.	31-36 years.	37-40 years.	41-46 years.	47 and more years.
No. of cases	1	7	17	19	20	36
% with hypertension.	0	28.6	56.2	63.2	80	97.2
% normotensive	100	71.4	43.8	36.8	20	2.8

This table shows the same trend of a higher incidence of hypertension amongst older patients, as did Table 26.

The mean age at follow-up examination of those cases with hypertension was 45.35 years, and amongst those subsequently normotensive, 35.6 years. The average time that elapsed since the first toxaemic attack was 13.55 years in all cases, 11.66 years in the normal cases and 14.14 years in the hypertensive cases. The average time that elapsed in European cases since the first toxaemia attack was 12.9 years and in non-European cases 13.9 years.

(c) The parity and its relationship to toxaemia and hypertension. (See Photograph 16, page 178).

Table 28, showing successively the parity when toxaemia first occurred and the parity of the toxaemic cases at present:-

Parity/.....

PHOTOGRAPH XVI.

THIS SHOWS A GRAPHIC RECORD OF THE PARITY

WHEN FIRST MANIFESTING TOXAEMIA

IN THE 100 NON-CONVULSIVE

CASES STUDIES.

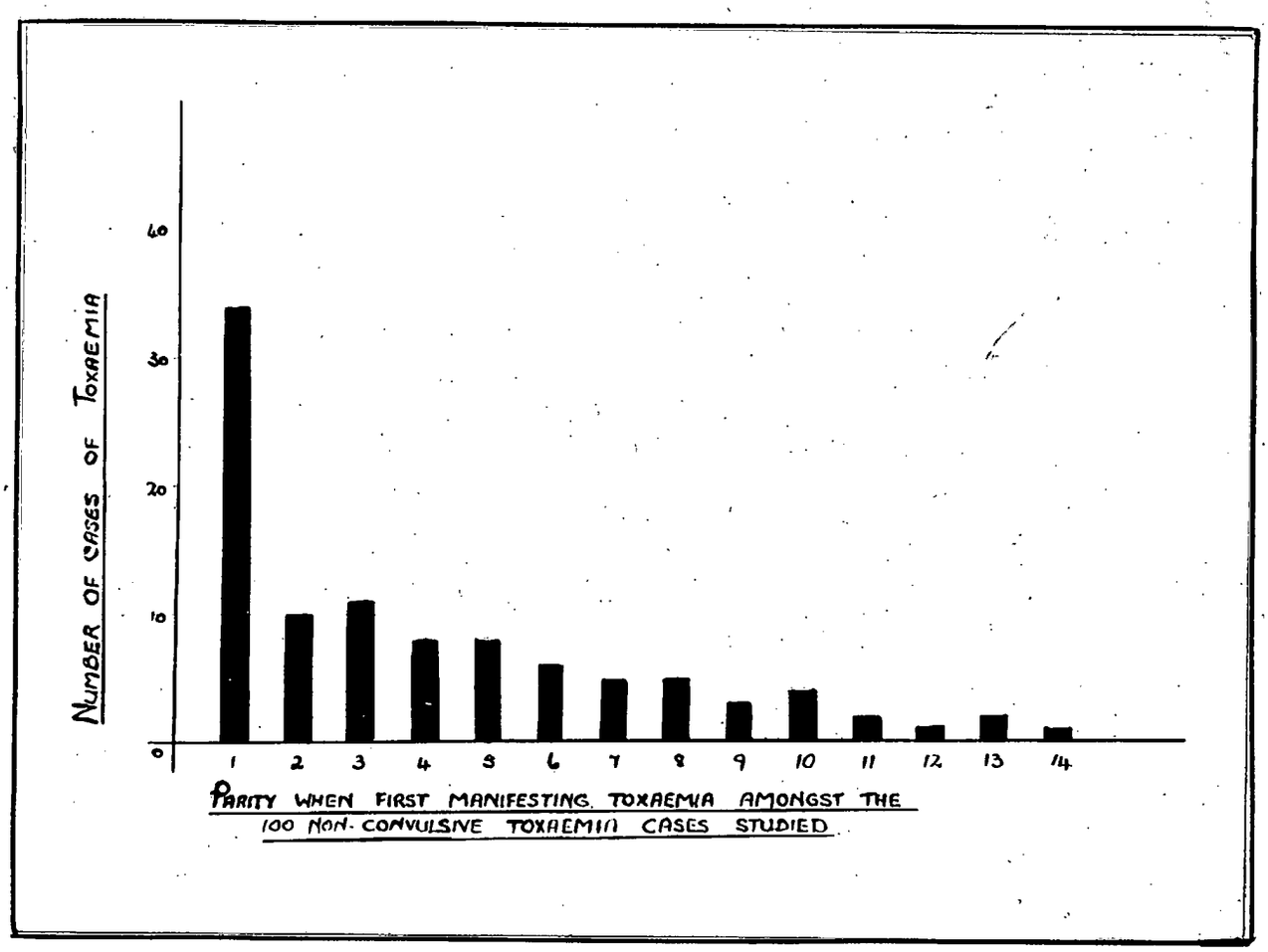

NUMBER OF CASES OF TOXAEMIA
40
30
20
10
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
PARITY WHEN FIRST MANIFESTING TOXAEMIA AMONGST THE 100 NON-CONVULSIVE TOXAEMIA CASES STUDIED

TABLE 28.

SHOWING SUCCESSIVELY THE PARITY WHEN TOXAEMIA FIRST OCCURRED AND THE PARITY OF THE TOXAEMIC CASES AT PRESENT.

Parity.	1	11	111	IV	V and more.
Number of cases	34	10	11	8	37
% with hypertension	52.9	100	81.8	50	91.8
% that are normal	47.1	0	18.2	50	8.2

Parity at present.	1	2, 3 & 4.	5, 6 & 7.	8, 9 & 10.	11,12 & 13.	14-20.
Number of cases	1	30	28	24	12	5
% with hypertension	100	63.4	78.7	79.2	91.7	80
% that are normal	0	36.6	21.3	20.8	8.3	20

The first part of the table shows that there is a tendency for the incidence of post-toxaemic hypertension to increase, as the parity when toxaemia first occurred becomes greater.

The average final parity of the normal cases was 5, and the average final parity of the hypertensive cases was 7.

The second part of the Table shows the tendency that the greater the final parity the greater the incidence of subsequent hypertension, but it is not a sine qua non that women with many pregnancies are necessarily hypertensive years later, because the maximum number of pregnancies in an individual subsequently normal case was found to be 13.

Where the number of cases in a particular age group is small, the calculated percentage of hypertension does not of course assist in pointing to a general trend.

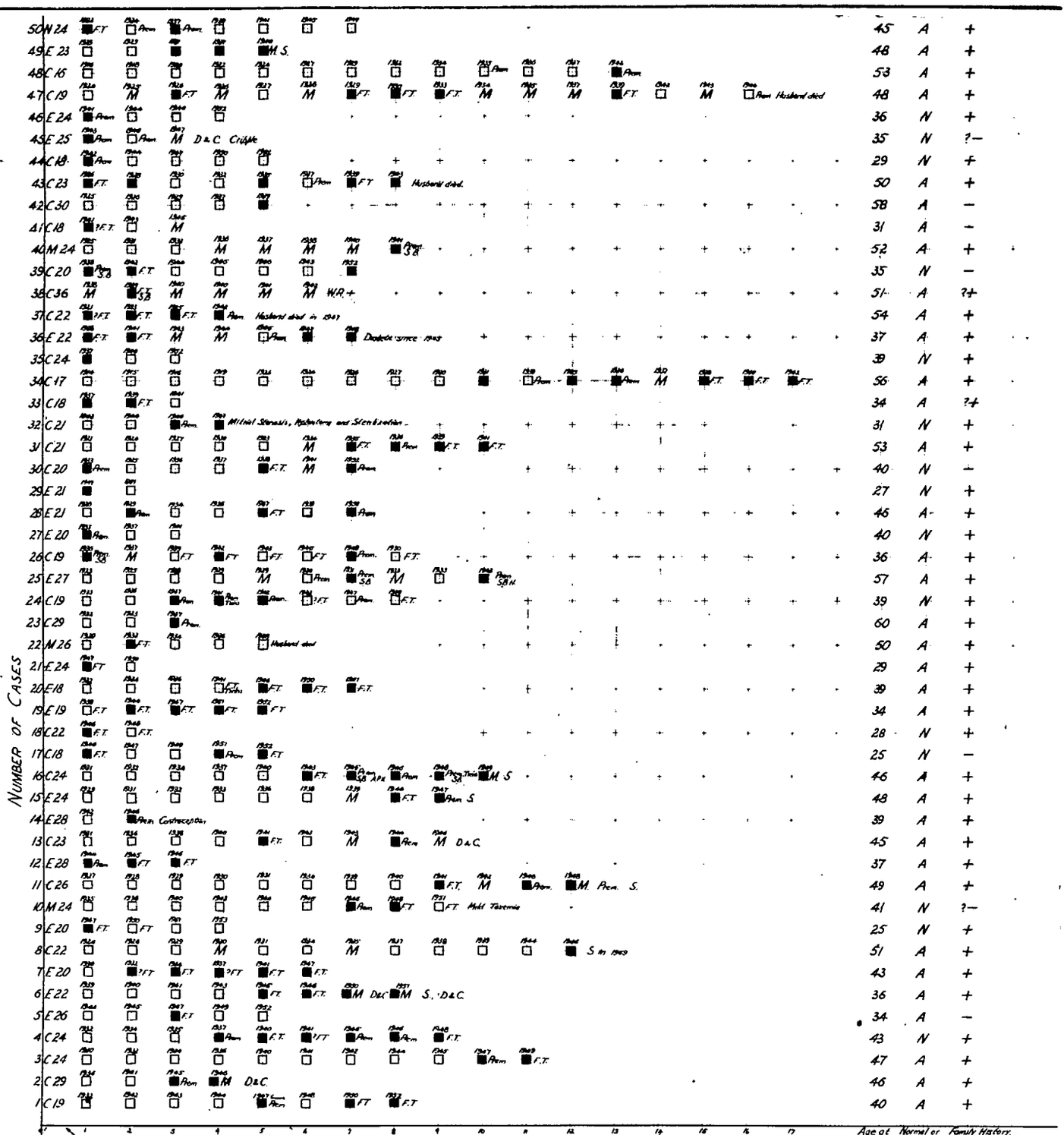
The general conclusion from the foregoing analysis is that

PHOTOGRAPHS XVII and XVIII.

THESE TWO SUCCESSIVE PHOTOGRAPHS PRESENT, IN SUMMARY FORM, THE CASE HISTORIES AND OTHER PERTINENT DATA OF THE 100 NON-CONVULSIVE TOXAEMIA CASES STUDIED.

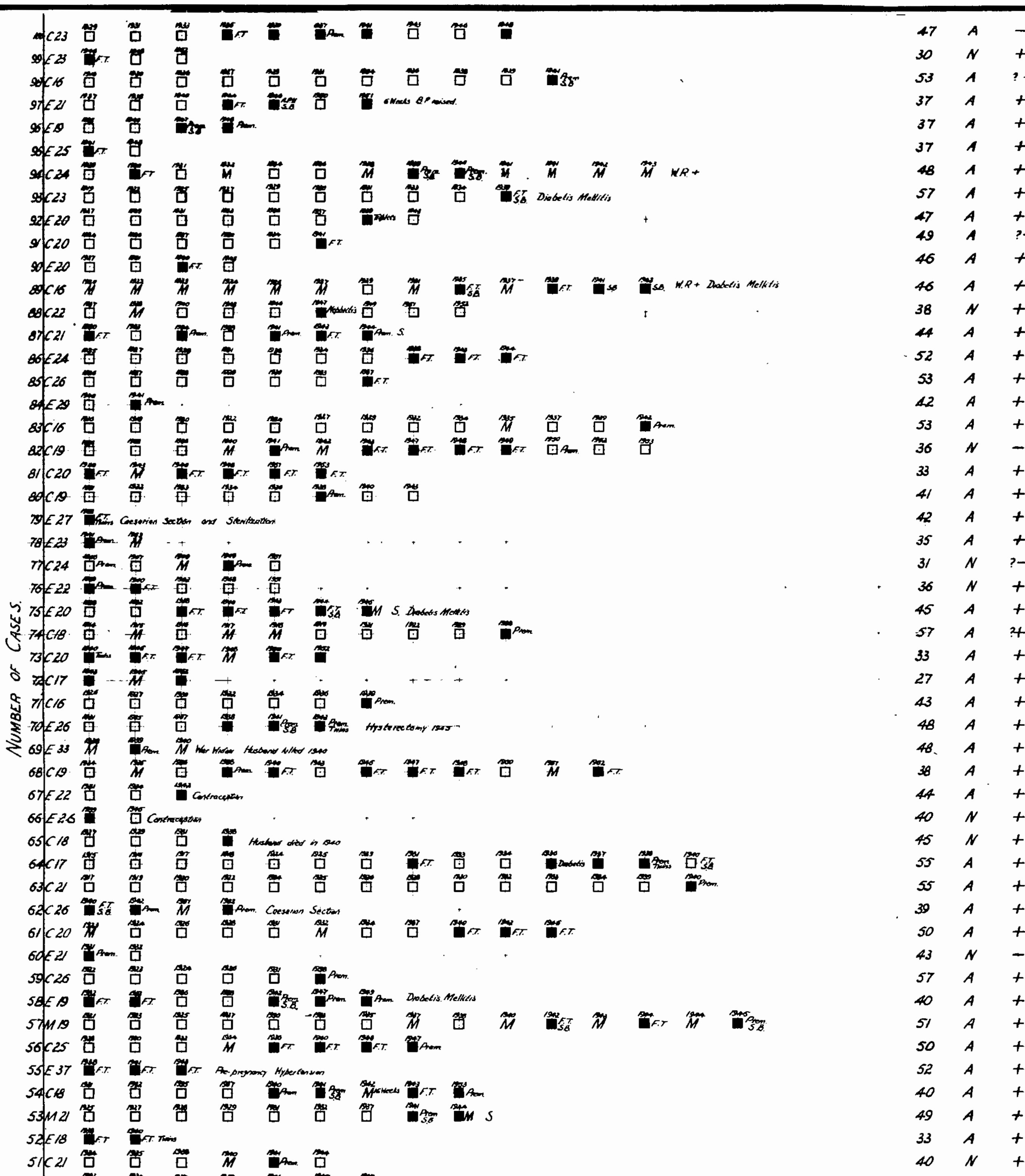
CASES 1 - 50 on PHOTOGRAPH XVII on Page 180.

CASES 50 - 100 on PHOTOGRAPH XVIII on Page 181.



FOLLOW-UP STUDY OF NON-CONVULSIVE TOXAEMIA CASES INDICATING HISTORY WITH REGARD TO PREGNANCIES, PARITY AND OCCURRENCE OF TOXAEMIA AS WELL AS RACE, AGE WITH FIRST PREGNANCY, PRESENT AGE, PRESENT STATE OF HEALTH AND FAMILY HISTORY OF HYPERTENSION

PHOTOGRAPH XVIII:


NUMBER OF CASES.
C23 47 A –
99 E23 30 N +
98 C16 53 A ? –
97 E21 6 Weeks B.P. raised 37 A +
96 E19 37 A +
95 E25 37 A +
94 C24 W.R.+ 48 A +
93 C23 Diabetis Mellitis 57 A +
92 E20 47 A +
91 C20 49 A ?+
90 E20 46 A +
89 C16 W.R.+ Diabetis Mellitis 46 A +
88 C22 38 N +
87 C21 44 A +
86 E24 52 A +
85 C26 53 A +
84 E29 42 A +
83 C16 53 A +
82 C19 36 N –
81 C20 33 A +
80 C19 41 A +
79 E27 Caesarian Section and Sterilization 42 A +
78 E23 35 A +
77 C24 31 N ?–
76 E22 36 N +
75 E20 S. Diabetis Mellitis 45 A +
74 C18 57 A ?+
73 C20 33 A +
72 C17 27 A +
71 C16 43 A +
70 E26 Hysterectomy 1945 48 A +
69 E33 War Widow Husband killed 1940 48 A +
68 C19 38 A +
67 E22 Contraception 44 A +
66 E26 Contraception 40 N +
65 C18 Husband died in 1940 45 N +
64 C17 Diabetis 55 A +
63 C21 55 A +
62 C26 Caesarian Section 39 A +
61 C20 50 A +
60 E21 43 N –
59 C26 57 A +
58 E19 Diabetis Mellitis 40 A +
57 M19 51 A +
56 C25 50 A +
55 E37 Pre-pregnancy Hypertension 52 A +
54 C18 40 A +
53 M21 49 A +
52 E18 33 A +
51 C21 40 N +
50 N24 45 A +

is that primiparae, especially those under 25 years of age, who develop toxaemia are the least likely to develop subsequent hypertensive vascular sequelae.

(See a summary of the case histories of the 100 non-convulsive toxaemia cases studied on Photographs 17 and 18, on Pages 180 and 181).

11. An analysis of the non-convulsive toxaemia cases by applying to them the methods and criteria of Browne and Dodds (1939).

The above analysis involves the correlation of the mean highest blood pressure during pregnancy, the mean highest blood pressure on discharge, and the duration of symptoms of toxaemia in the normotensive and hypertensive groups.

(a) The mean highest blood pressure during pregnancy.

Amongst the 24 normal cases the mean highest blood pressure during pregnancy was 161/106 mm. Hg., and amongst the 76 hypertensive cases 169/111 mm. Hg. This tends to indicate that the higher the blood pressure during pregnancy, the greater the likelihood of hypertension at follow-up examination.

(b) Blood pressure on discharge.

TABLE 29.

ILLUSTRATING THE BLOOD PRESSURE ON DISCHARGE OF THE 100 CASES STUDIED.

Condition at Follow-up.	No. of Cases.	Normal B.P. on discharge. Cases	%	Hypertensive on discharge Cases.	%	B.P. on discharge unknown.
Condition at follow-up.	24	7	29.1	16	66.6	1
Hypertensive Cases	76	4	5.2	68	89.4	4
TOTAL:	100	11	-	84	-	5

The mean/....

The mean blood pressure on discharge amongst the normal cases was 133/91 mm. Hg. and 157/105 mm. Hg. amongst the hypertensive cases. This table shows that a greater proportion of cases subsequently normal have a normal blood pressure on discharge, i.e. 29.1 as opposed to 5.2 per cent. Nevertheless, although a higher percentage of hypertensives had a raised blood pressure on discharge, a rather large percentage of subsequently normal cases also had a raised blood pressure on discharge. This indicates that on the whole the blood pressure on discharge is an unreliable guide to the subsequent behaviour, as pointed out by Browne (1939). One explanation of this discrepancy is that hypertensive cases may still have a normal blood pressure from rest in bed when discharged, but on rising and resuming domestic duties and family worries at home, the blood pressure reverts to hypertensive levels, where it subsequently remains. This occurred in four of the present hypertensive cases.

(c) <u>The duration of the toxaemia and its relationship to subsequent hypertension.</u>

The average duration of toxaemic signs and symptoms amongst the normal cases was 7½ weeks, and 9 weeks amongst the hypertensive cases. This tends to indicate that the longer the duration of the symptoms, the more the likelihood of permanent vascular sequelae. However, it must be pointed out that cases with essential hypertension on conception tend especially to show signs, e.g. a raised blood pressure, either from the beginning of the pregnancy or before the 20th. to the 28th. week, and will tend to have hypertension subsequently in any case. (See discussion in this connection on Page 128). The above group of cases studied are a mixed group and include pre-pregnancy hypertensive cases as well. These will be separated at a later state of the analysis, in order to arrive at a clearer picture.

Subsequent/.....

TABLE 30.

ILLUSTRATING THE NUMBER OF PATIENTS, THE MEAN PERIOD OF TIME COVERED SINCE THE FIRST TOXAEMIC ATTACK & THE MEAN AGE AT FOLLOW-UP EXAMINATION & THE NUMBER OF PREGNANCIES SUBSEQUENT TO THE ORIGINAL ATTACK OF TOXAEMIA.

	Number of Patients.	Mean No. of Years followed-up.	Mean age at time of follow-up.	No. of subsequent pregnancies.	No. of Women who had subsequent pregnancies.	% Of Women who had subsequent pregnancies.
European (White)	38	12.9	41.31	78	37	97.6
Coloured	62	13.9	45.3	190	62	100
TOTAL:	100	13.55	43.8	268	99	99

TABLE 31.

SHOWING THE FOETAL MORTALITY IN SUBSEQUENT PREGNANCIES AS WELL AS IN ALL PREGNANCIES, & THE INCIDENCE OF TOXAEMIA IN SUBSEQUENT PREGNANCIES:

	% of subsequent pregnancies which resulted in stillbirth or abortion.	% Of subsequent pregnancies which were Toxaemic.	% Of Women with subsequent pregnancies who had subsequent toxaemia.	% of all pregnancies which resulted in stillbirth or abortion.	% of all pregnancies which resulted in stillbirth, abortion or neonatal death.	Total No. of pregnancies including abortions amongst the Patients with non-convulsive Toxaemia.
European (White)	17.9	50	51.3	12.6	14.3	174
Coloured	28.9	46.8	59.6	19.5	21.5	502
TOTAL:	25.7	47.7	56.5	17.7	19.5	676

12. Subsequent pregnancies.

There were 268 pregnancies in 99 women subsequent to the first toxaemic attack. 99% of cases had at least one additional subsequent pregnancy. 97.6% of European women had 78 pregnancies and 100% of the Coloured women had 190 subsequent pregnancies, which is in keeping with the smaller families amongst Europeans. In 56.5% of the total number of women who had further offspring, that is 19 European and 37 Coloured women, there was recurrence of toxaemia. It recurred from two to five times in the various cases amongst this group. Nine of these cases were subsequently normal and 47 cases were subsequently hypertensive. This indicates that toxaemia did not only recur in hypertensive cases, but also in normotensive cases, and it must be pointed out that some of these hypertensive cases only became so years later, probably from unrelated caused, and as such were "true cases" of recurrent pre-eclamptic toxaemia, like the normotensive cases with recurrent toxaemia.

In 44 of the 100 cases followed up, there was no recurrence of toxaemia, and only one of these had no further pregnancies.

Amongst the normotensive cases with no recurrence of toxaemia, the number of subsequent pregnancies varied from two to thirteen, while in the hypertensive cases the number of pregnancies varied from 2 to 17, indicating that oft repeated pregnancies is not necessarily associated with subsequent hypertension.

13. The Foetus.

(a) The foetus in the original toxaemic pregnancy.

Because toxaemic pregnancies frequently terminate prematurely, this was the main factor leading to foetal loss, but in two cases abortions were due to syphilitic infection and in 3 other instances diabetes mellitus, in association with toxaemia, was an additional factor leading to stillbirth.

Table 32/.....

TABLE 32.

INDICATING THE FATE OF THE FOETUS AT THE TIME OF THE FIRST TOXAEMIC ATTACK.

Weight.	Alive.	Neonatal Deaths.	Stillbirths.	Infantile Deaths.	Total.
Under 5 lbs.	17	5	8	3	33
5-6 lbs.	32	1	6	0	39
6 lbs. & over	31	1	1	0	33
TOTAL:	80	7	15	3	105
PERCENTAGE:	76.1	6.6	14.2	2.8	100

Amongst the 100 cases one had triplets and three had twin pregnancies, which accounts for the five additional offspring in the Table at the time of the toxaemic attack.

The foetal mortality, that is the stillbirth and neonatal mortality, at the time of the toxaemic attack was 20.8%. This figure is much lower than in the eclamptic series, and the most important factor producing this difference is the use of hypnotic drugs and the anoxaemia during the fits in eclamptic cases. Wellen (1952) found a foetal mortality of 12.4% amongst non-convulsive toxaemia cases, and stressed that the mortality is influenced by the severity of the condition. Severe cases had a four times higher foetal loss than mild cases. The 20.8% mortality in this series is due to the fact that only severe cases were included in this study.

Of the surviving children, one case, that of a European woman, is an imbecile, but the others are all normal and no different from those in the population of children as a whole.

(b) The foetus in subsequent pregnancies.

Of the 268 subsequent pregnancies, 199 or 74.3% resulted in alive infants and 69 or 25.7% resulted in either stillbirth or

abortions/...

abortions. This is a foetal mortality twice as great as is found in the ordinary run of pregnancies and the most important factor in causing this is recurrent toxaemia with prematurity.

14. Subsequent toxaemia amongst the 100 cases followed up.

128 or 47.7% of all subsequent pregnancies were complicated by toxaemia. Of those women with subsequent pregnancies, 56 or 56.5% had at least one further episode of toxaemia. Thus the incidence of toxaemia was four to six times greater than would be expected normally in the general run of pregnancies. This coincides with the results found by other authors, e.g. Bryans and Torpin (1949). Page and Cox (1938) who found the incidence of subsequent toxaemia to be 8 to 10 times higher than that normally found.

Of the 56 cases with recurrent toxaemia, nine are now normal after 13½ years, and although 47 are hypertensive, in some of these the hypertension developed years after their last pregnancy, and cannot with justification be included in the group of recurrent toxaemias due to hypertension. The present series illustrates that pre-eclamptic toxaemia may recur up to six times and leave the patient normotensive years later, e.g. cases 4 and 24 etc. in the non-convulsive group.

However, as a group, the hypertensive cases are more prone to recurrent toxaemia than the normotensive cases.

Forty-four of the 100 cases studied had toxaemia once only, and 15 of them are now normotensive, while 29 are hypertensive. Several of the latter cases only became hypertensive some time after the toxaemic attack. This illustrates that even if toxaemia does not recur, a patient may be hypertensive years later due to other causes than pregnancy or the toxaemic pregnancy in question.

It is evident that the prognosis, from the point of view of vascular sequelae, in pre-eclamptic toxaemia, is good if it occurs in patients without hypertension or a latent hypertensive tendency, but it may be followed by hypertension in the latter type of case immediately or within some years. We have no accurate way of

assessing/.....

assessing a hypertensive tendency in a given case, and only by follow-up examination can it be excluded or confirmed.

In the present state of our knowledge each case should be considered on her own merits after a toxaemic pregnancy, and even then she may be normotensive years later in spite of recurrent toxaemia or a positive family history of hypertension, or she may develop hypertension so long afterwards that it is difficult to relate the hypertension to the foregoing toxaemic pregnancies.

There was no instance of glomerulonephritis following the above series in agreement with the reported results of Browne (1951), Dieckmann (1952) and others.

The general impression and experience (Louw 1952) is that eclampsia and the toxaemias are less common amongst the well-to-do than amongst the hospital class of patient in Cape Town. It is possible that dietary factors, personal habits, socio-economic circumstances or possibly hereditary factors may play a predisposing role to explain this. However, these factors cannot be the exciting cause of toxaemia, else one would expect toxaemia in each succeeding pregnancy, as the above factors tend to remain constant. Moreover in a previous section it was pointed out that the incidence of toxaemias is the same in the European and the non-European population. Therefore it seems unlikely that the above factors play an important part.

This series illustrates that toxaemia may occur and recur with any parity and a preceding normal pregnancy does not rule out the possibility of the occurrence and subsequent recurrence of toxaemia in future pregnancies, even if hypertension, latent or manifest, is excluded. This points to the fact that toxaemia is due to conditions associated with the immediate toxaemic pregnancy with or without predisposing factors like multiple pregnancy or dietary factors, and due to X factors not known to us.

15. Previous pregnancies.

Previous to the first attack of toxaemia there were 308 pregnancies in 65 women. 52.6% of the White women and 72.5% of

the coloured/...

TABLE 33.

SHOWING THE NUMBER OF PREGNANCIES PREVIOUS TO THE FIRST TOXAEMIC ATTACK, THE NUMBER OF WOMEN INVOLVED AND THE INCIDENCE OF MISCARRIAGES:

RACE:	No. of Pregnancies prior to the first attack of toxaemia	No. of Women who had previous pregnancies.	% Of Women who had previous pregnancies.	No. of Miscarriages amongst the previous pregnancies.	% of Miscarriages amongst the previous pregnancies
European (White)	58	20	52.6	3	5.1
Coloured	250	45	72.5	30	12
T O T A L :	308	65	65	33	10.7

the coloured women had one or more previous pregnancies prior to the first toxaemic attack. The incidence of abortion amongst these previous pregnancies was 10.7%, which is the usual incidence of abortion amongst the general population of pregnant women. (Stander 1945).

16. The maternal mortality in non-convulsive toxaemia cases.

The only figures available concern the mortality subsequent to the toxaemic attacks and discharge from hospital. Besides the 100 cases traced and found to be alive, 22 were traced and found to have died (see Table 34 showing causes of death). In addition 269 cases were untraceable. If Table 34 is consulted, it will be seen that 72.6% of these cases died from some or other manifestation of cardiovascular disease, and one case from uraemia. (This case may have had chronic nephritis or may have been a case of hypertensive vascular disease, ending in a renal death clinically impossible of differentiation. Unfortunately, no post mortem to verify this was done.) This patient died some hours after admission to hospital and had fits and a blood urea of 375 mg.%, but unfortunately no other records were available to elucidate the problem.

18.1% of the deaths were due to unrelated causes, e.g. tuberculosis of the lungs. Table 35 gives a detailed record of the 16 cases who died of cardiovascular or renal causes.

TABLE 34.

SHOWING DEATHS DURING THE PERIOD OF FOLLOW-UP STUDY AMONGST THE NON-CONVULSIVE TOXAEMIA CASES.

	Total No. of Deaths.	% who died in sub-sequent child-birth.	% who died of cardio-vascular disease.	% who died of ? chronic Glomerule-nephritis.	% who died of other unrelated causes e.g. T.B.
White	9	11.1	66.6	0	22.2
Coloured	13	7.69	69.2	7.69	15.3
TOTAL:	22	4.7	72.6	4.5	18.1

TABLE 35.

SHOWING PARTICULARS OF THE 16 CASES AMONGST THE 22 DECEASED NON-CONVULSIVE TOXAEMIA CASES, WHO DIED OF CARDIO-VASCULAR AND RENAL COMPLICATIONS:

Name:	Cause of Death:	At the Time of Toxaemic Attack:				At the Time of Death:		
		Race:	Age:	Parity:	Date:	Age:	Parity:	Year of Death:
M.V.	Stroke and raised blood pressure	E.	45	7	1946	46	7	1947
A.W.	Hypertensive congestive cardiac failure.	E.	42	9	1938	46	9	1942
B.L.	Hypertensive congestive cardiac failure.	E.	43	4	1932	49	6	1938
E.M.	Cerebral Haemorrhage and Hypertension and Diabetes.	E.	44	12	1935	50	12	1941
A.M.	Hypertension/Stroke and Diabetes Mellitus.	E.	36	6	1937	45	8	1946
E.R.	2 Successive strokes & hypertension.	E.	40	5	1937	49	5	1946
S.G.	High B.P., Coronary Thrombosis. Died 2 days after Cholecystectomy	C.	45	5	1937	56	5	1948
C.A.	Hypertensive Cardiac Failure.	C.	38	9	1934	48	10	1944
A.A.	Congestive Cardiac failure & Uraemia	C.	35	11	1936	48	12	1949
H.C.	Coronary Thrombosis and Congestive Cardiac failure.	C.	45	8	1941	46	8	1942
S.leG.	Diabetes and Hypertensive Cardiac failure.	C.	37	9	1939	47	10	1949
J.J.	Sudden Death, Hypertensive and Coronary thrombosis.	M.	34	11	1946	36	11	1948
M.M.	Sudden Death ? exact cause.	N.	41	8	1947	41	8	1947
M.H.	Coma and Fits ? Uraemia.	C.	30	2	1947	34	2	1951
J.R.	Stroke.	C.	44	14	1938	49	14	1943
M.S.	Hypertension and Stroke.	M.	47	16	1934	56	16	1943

17. The Incidence of hypertension at follow-up examination amongst the non-convulsive toxaemia cases.

TABLE 36.

ILLUSTRATING THE INCIDENCE OF HYPERTENSION AT FOLLOW-UP.

	Hypertensive Cases.		Normotensive Cases.	
	No.	Per cent.	No.	Per cent.
European	29	76.3	9	23.6
Coloured	47	75.8	15	24
TOTAL:	76	76	24	24

The incidence of hypertension at follow-up was 76%, 76.3% amongst the European, and 75.8% amongst the Coloured cases. At first sight it seems as if the non-convulsive toxaemias produce a higher incidence of cardiovascular sequelae than eclampsia. It must be remembered, however, as previously mentioned, that the present series of non-convulsive toxaemia cases is a mixed group and includes cases with pre-pregnancy hypertension, as well as cases developing hypertension years after the last toxaemic pregnancy and probably due to unrelated caused. (This will be discussed in detail at a later stage).

18. Subsequent hypertension related to the age of the non-convulsive toxaemic cases studied.

TABLE 37.

SHOWING THE NON-CONVULSIVE TOXAEMIC CASES BROKEN DOWN INTO AGE.GROUPS, WITH HYPERTENSION RELATED TO AGE.

Age groups	20-29 years.	30-39 years.	40-49 years.	50 yrs. & older.
No. of cases	7	30	38	25
No. Hypertensive	2	19	30	25
% hypertensive	28.5%	63.3%	78.9%	100%

The average/.....

The average age at follow-up of all the subsequently hypertensive cases was 45.3 years.

The number in each age group is rather small to be of statistical value. However, the results do show the general trend and that is that in all the age groups the incidence of hypertension is considerably more than may be expected in groups of women of the same age in the general population of women (Master Marks & Dack 1943).

One can conclude that toxaemia of pregnancy brings out hypertension at an earlier age than it would normally have occurred in cases who in any case are destined to be hypertensive sooner or later.

19. Proteinuria.

Six of the 100 surviving non-convulsive toxaemia cases had proteinuria at follow-up examination, and in one of these the proteinuria was due to a vaginal discharge. A catheter specimen was shown to be protein free (Case 36). All of these cases were hypertensive as well and made up 7.8% of the hypertensive group. Of the five remaining cases three had signs and symptoms of congestive cardiac failure. Two had severe hypertensive vascular disease with grade 3 retinopathy and a blood pressure of 270/160 mm. Hg. and 280/130 mm. Hg. respectively, and glycosuria. None of them were chronic nephritics as judged by renal function tests done. Proteinuria was probably due to nephrosclerosis, as chronic glomerulonephritis was not found as a sequel amongst these cases.

20. The phenomenon of healing following toxaemia.

One of the normotensive cases (Case 4) took 3½ years after her last toxaemic pregnancy to regain a normal blood pressure and normal results from the renal function tests. She had recurrent toxaemia in the last trimeter of her last six pregnancies. Two and a half years after the last, which was her ninth, she still had a fluctuating blood pressure and a trace of albumen in association with lassitude. Since then her blood pressure has

gradually/.....

gradually dropped, having been 170/120 mm. Hg. a year ago, and now 3½ years later her blood pressure is 130/80 mm. Hg., her fundi, cardiac size and electrocardiogram are normal and the renal function tests completely satisfactory.

In the subsequently hypertensive group there are 3 cases (Cases 72, 73 and 81) who had toxaemic confinements within a period of 6 months prior to the follow-up study and are still hypertensive. They may thus be cases of delayed healing, especially in view of the fact that they are aged 28, 33 and 33 years respectively and 2 of them had no family history of hypertension. This is one of the fallacies to be avoided in a follow-up study, i.e., the inclusion of cases who have recently had a toxaemic pregnancy.

These 3 cases have all had previous toxaemic pregnancies with normal blood pressures in the interim and may thus revert to normal again, a phenomenon often seen in cases of recurrent toxaemia. The first case mentioned appears to be one of the most prolonged cases on record, with delayed healing. The latter 3 cases may possibly take a long time to heal as well and may therefore be wrongly included in the hypertensive group.

One of the normotensive cases in this series (Case 88) appears to have been a case of acute nephritis during pregnancy, wrongly classified as a toxaemia of the non-convulsive type. Her case history is as follows:-

Her first confinement at the age of 22 was normal, the second a miscarriage at the age of 23, the third a normal full term pregnancy at the age of 28 years, the fifth similarly normal at the age of 31. When she was 15 weeks pregnant with her sixth pregnancy at the age of 32 years, following a cold and a sore throat, she developed a headache and puffiness of the eyes after 1 week and slight oedema of the feet. Before this her blood pressure had always been normal but now had suddenly risen to 180/100 mm. Hg. She had marked albuminuria and smoky urine with

red./.....

red blood cells confirmed microscopically. At 17 weeks her blood pressure had dropped to 145/85 with very much less albumen, with a few red cells noted microscopically and some granular casts. At this stage her blood urea was 18 mg.% with a specific gravity of 1004. At 18 weeks the albuminuria had cleared up and no oedema was clinically noticable but her blood pressure was still 145/85 mm. Hg. At 19 weeks, the blood pressure was 130/70 mm. Hg. and the urine chemically and microscopically normal. From then onwards she remained well, with a blood pressure varying between 105 to 120 mm. Hg. systolic and 70 to 75 mm. Hg. diastolic, until the 34th week when she had a premature normal delivery of a 3 lb. 7 oz. alive baby. There was no sign of toxaemia during and after delivery. Subsequently she had 3 further normal full term deliveries at the age of 34, 36 and 37 years respectively. She is now a normotensive case, with a blood pressure of 125/80 mm. Hg., with normal fundi and renal functions.

This case had all the features of an Ellis Type 1 nephritis and has behaved like that subsequently. Haematuria is uncommon in pre-eclamptic toxaemia but more common in eclampsia and the fact that it was present here would not exclude toxaemia. Against this however, and in favour of nephritis, was the period of pregnancy when the signs and symptoms occurred, the absence of marked oedema, the persistence of haematuria and the fact that in spite of the continuance of pregnancy, the signs and symptoms cleared up completely many weeks before labour occurred.

Acute nephritis is rare during pregnancy but the reason for this is not known. Dillon and Schmitz (1947) found the incidence of nephritis to be 0.04% amongst a series of 28,263 pregnant women. Hamilton (1952) found the incidence of acute nephritis in pregnancy to be 0.02%.

21. A COMPARISON OF THE SUBSEQUENT PREGNANCIES IN THE SURVIVING NON-CONVULSIVE TOXAEMIA CASES, AMONGST THE SUBSEQUENTLY NORMOTENSIVE AND HYPERTENSIVE GROUPS:

See./.....

See Table 38 on Page 197 illustrating this aspect.

There were 200 subsequent pregnancies in 58 of the 76 women found to be hypertensive and 68 pregnancies in 24 of the 24 women found to be normotensive at follow-up examination, i.e. 73.7% and 100% of the women in each respective group had at least one subsequent pregnancy. Amongst the women in the hypertensive group there was an incidence of abortion and stillbirths of 28.5% which is in keeping with the experience of Browne and others. The incidence of stillbirths and abortions in the normotensive group was 8.8%, indicating that in true pre-eclamptic toxaemias this figure is much lower than in hypertensive cases.

58% of the subsequent pregnancies in the hypertensive group and 33.8% in the normotensive group were complicated by toxaemia. 61.9% i.e. 47 cases in the hypertensive group of women and 37.5%, i.e. 9 cases, in the normotensive group had at least one further toxaemic pregnancy. These figures indicate that the highest incidence of recurrent toxaemia occurs in the hypertensive cases but subsequently normotensive true pre-eclamptic toxaemia cases may also have a fairly high recurrence rate without there being a hypertensive factor involved.

22. <u>A DETAILED STUDY OF CASES OF RECURRENT TOXAEMIA AMONGST THE NON-CONVULSIVE TOXAEMIA CASES FOLLOWED UP.</u>

(a) The following 9 cases manifested recurrent toxaemia, and were normotensive at follow-up examination with an average age of 36.3 years at the time of follow-up. (Cases 4, 10, 17, 24, 30, 32, 39, 76 and 82 respectively).

The average time that elapsed since the first occurrence of toxaemia in the above 9 cases was 12.8 years, whereas in the 15 normotensive cases without recurrence this period was 10.9 years.

Toxaemia that recurs can do so with second or any parity. Four of the nine cases had toxaemia with their first pregnancy with recurrence in later pregnancies in an irregular fashion. The remainder had normal first pregnancies and toxaemia in subsequent pregnancies haphazardly.

(b) A number of the cases that manifested recurrent toxaemia

were/.....

TABLE 38

A COMPARISON OF THE SUBSEQUENT PREGNANCIES IN THOSE CASES WITH AND IN THOSE CASES WITHOUT HYPERTENSION AMONGST THE SURVIVING NON-CONVULSIVE TOXAEMIA CASES FOLLOWED UP.

Groups of Cases.	Number of subsequent pregnancies.	Percentage of women who had subsequent pregnancies.	Percentage of subsequent pregnancies which resulted in stillbirths or abortions.	Percentage of Subsequent pregnancies which were toxaemic.	Percentage of women with subsequent pregnancies who had subsequent toxaemia.
Hypertensive Group (76 cases)	200	73.7	28.5	58.0	61.9
Normotensive Group (24 cases)	68	100	8.8	33.8	37.5

were normotensive in between attacks and some had subsequent normal fullterm pregnancies. Only years later they became manifestly hypertensive. This group includes 33 of the 76 hypertensive cases with an average age of 43.8 years. However, in sixteen of these cases a hypertensive tendency may have operated as a factor in association with toxaemia because, after their first toxaemic pregnancy, all subsequent pregnancies were toxaemic but in none did toxaemia set in before the 28th. week. These are cases 7, 11, 12, 19, 31, 36, 37, 54, 61, 62, 72, 73, 75, 81, 86 and 89 respectively. The other 17 cases had normal pregnancies subsequent to recurring toxaemic pregnancies and it is unlikely that a latent hypertension was a causative factor. They only became hypertensive on an average of 5 to 20 years after their last pregnancies. These include Cases Nos. 1, 13, 25, 26, 28, 33, 34, 43, 47, 50, 64, 68, 58, 87, 94, 97 and 100 respectively.

(c) The following cases with an average age of 45.1 years manifested recurrent toxaemia and were hypertensive between attacks as well as subsequently. They are Cases 2, 3, 6, 15, 16, 20, 52, 49, 53, 55, 56, 57, 70 and 96 respectively, and formed a group of fourteen of the 76 hypertensive cases. There is no significant difference in the total parity amongst cases with recurrent toxaemia and those who had toxaemia once only.

As was pointed out on Page 151 in the eclampsia follow-up study, eight of the thirty hypertensive cases only became hypertensive years after the eclamptic attack. Recurrent toxaemia in their case was not due to manifest hypertension and difficult to explain on the basis of a latent hypertensive tendency as Browne's hypothesis suggests, because they all had many normal pregnancies interspersed between their toxaemic pregnancies and subsequently. In the non-convulsive toxaemia study 33 of the 76 hypertensive cases who had recurrent toxaemia only became hypertensive years later and manifest hypertension could not have been the cause or a factor causing the recurrence of toxaemia. In sixteen of these cases, following the first toxaemic pregnancy, all subsequent pregnancies were toxaemic, yet in between these pregnancies the

blood/.....

blood pressure was well within the limits of normality. The possibility of a latent hypertensive tendency operating as a factor or an associated factor leading to toxaemia and its recurrence is not excluded in these cases. Only subsequently would such a latent hypertension become a clinically manifest hypertension. (These are the "wolves in sheep's clothing" referred to in a previous section).

In the other 17 cases in this group of 33 many normal pregnancies with blood pressure readings never exceeding 130/70 mm. Hg. were interspersed between toxaemic pregnancies and following them. Therefore it is unlikely that a latent hypertension was operating in these cases and, at that, only selectively in some pregnancies, in spite of the fact that they were full term.

Fourteen of the 76 hypertensive non-convulsive toxaemia cases followed up had toxaemia with each subsequent pregnancy following their first toxaemic attack. Hypertension persisted between the subsequent pregnancies and, following their final pregnancies, all had persistently raised blood pressures. In this group manifest hypertension can be taken to act as a factor or as an associated factor, producing successive toxaemic pregnancies. In the groups of 24 subsequently normotensive cases, 9 had recurrent toxaemia and 33.8% of their subsequent pregnancies were complicated by toxaemia. All 9 of them had at least one subsequent toxaemic pregnancy, but also further normal pregnancies.

Using the same reasons as stated in discussing the corresponding group of post-eclamptic normotensive cases followed up, it is felt that in this group of nine cases, as well as in the 17 cases previously mentioned, who had no hypertension between their toxaemic pregnancies and had intervening normal pregnancies, neither hypertension nor a hypertensive tendency was responsible for the recurrent toxaemia. The X factor or factors conditioned by the given pregnancy producing true eclampsia and pre-eclamptic toxaemia must be responsible in these cases, with or without predisposing factors such as diet, multiple pregnancy, etc.

There/.....

There were 11 hypertensive cases who had further offspring without recurrence of toxaemia, i.e. 14.5% of the hypertensive cases, while 47 cases already mentioned had further offspring with recurrence of toxaemia, that is 61.9%. 23.6%, i.e. 18 cases, had no further offspring.

15 of the 24 normotensive cases had subsequent offspring without recurrence of toxaemia, that is 62.5%, as opposed to 37.5% who had recurrence of toxaemia. Eighteen of the non-convulsive toxaemia cases found to be hypertensive at follow-up had no further offspring after their first toxaemic attack. (See Photographs 17 and 18 on Pages 180 and 181).

To summarise, 26% or 26 of the total of 100 non-convulsive toxaemia cases had no further toxaemia, yet had further pregnancies. This includes 14.5% of the cases in the hypertensive group and 62.5% of the cases in the normotensive group. This indicates that factors other than hypertension can be responsible for recurrent toxaemia and hypertensive cases do not invariable develop recurrent toxaemia.

It must be indicated that it is rare amongst manifestly hypertensive cases to have normal pregnancies between toxaemic pregnancies with the blood pressure falling below 140/90 mm. Hg. and staying at such a level throughout pregnancy, only to rise to hypertensive levels in the puerperium and remain there subsequently. More commonly, the initial raised blood pressure tends to fall in the middle trimester and towards term tends to rise again with or without superadded oedema and albuminuria, changing the clinical diagnosis from hypertension associated with pregnancy to toxaemia superimposed on manifest hypertension. In still other cases the blood pressure remains more or less constant and no oedema or albuminuria occurs, i.e. hypertension associated with pregnancy without toxaemia. However, cases of hypertension may become manifest only during pregnancy, and the blood pressure level, although often initially raised, may sometimes not be raised until the third trimester with or without superadded oedema and albuminuria. Thus they become indistinguishable from true pre-

eclamptic toxaemia. However, such cases will have, with few exceptions, a recurrence of the same sequence of events in subsequent pregnancies producing one form of recurrent toxaemia. Sooner or later such a latent, apparently temporary, hypertension will become manifest as a permanent hypertension. In the present state of our knowledge these cases can only be distinguished from recurrent true pre-eclamptic toxaemia by a prolonged follow-up study of the given patients. If the patient had true recurrent pre-eclamptic toxaemia, examples of which have been mentioned previously in this series, there will be no hypertension years later, at the age when hypertension usually becomes manifest, or, if hypertension occurs, it becomes manifest so long afterwards that it cannot be related to the preceding recurrent toxaemia.

The two follow-up studies, of eclampsia on the one hand, and non-convulsive toxaemias on the other, show that in a very definite proportion of recurrent true toxaemias (eclamptic or pre-eclamptic) neither hypertension nor nephritis are causative. These are thus cases of true recurrent pre-eclamptic toxaemia and eclampsia and are not confined to primiparae, although they show the highest incidence, nor are they conditions that seldom recur, as stated by Dieckmann and others. It must, however, be pointed out that recurrent true pre-eclamptic toxaemia is less common than recurrent pre-eclamptic toxaemia on a hypertensive basis, in the same way as recurrent true eclampsia is less common than recurrent eclampsia on a hypertensive basis. In spite of considerable advances in medical science, the basic etiologies of all these toxaemias are unknown, whether it be a case of toxaemia or eclampsia in a normotensive or a hypertensive pregnant woman or toxaemia associated with a hydatidiform mole or multiple pregnancy in a normotensive or hypertensive woman.

A COMPARISON/.....

23. A COMPARISON OF THE PREGNANCIES PREVIOUS TO THE FIRST TOXAEMIC ATTACK AMONGST THE HYPERTENSIVE & THE NORMOTENSIVE GROUPS OF CASES FOUND IN THE FOLLOW-UP STUDY OF NON-CONVULSIVE TOXAEMIA CASES:

TABLE 39.

ILLUSTRATING THE ABOVE ASPECT:

Groups of Cases.	Number of previous pregnancies	Percentage of women who had previous pregnancies.	Percentage of previous pregnancies which ended in stillbirth or abortion.
Hypertensive Group	276	73.7	11.9
Normotensive Group	32	37.5	15.6

The figures in Table 39 indicate that previous normal pregnancies in a given woman is no criterion that subsequent pregnancies will be normal, nor is it a guarantee that a woman will not eventually be a hypertensive subject, whether or not she has subsequent toxaemia.

24. AN ANALYTICAL SYNOPSIS OF THE FACTS ENCOUNTERED IN THE NON-CONVULSIVE TOXAEMIA FOLLOW-UP STUDY, INDICATING THAT "TRUE" TOXAEMIAS OF PREGNANCY ARE NOT CAUSATIVE OF HYPERTENSIVE VASCULAR DISEASE:

A careful consideration of all the detailed facts concerning the 76 hypertensive cases amongst the 100 non-convulsive toxaemias followed up shows that:-

(1) In 25 cases, at a mean age now of 48.1 years, hypertension arose at the time of the first toxaemic attack and has persisted since. If this is compared with the 22 similar cases in the eclamptic follow-up group, the incidence of subsequent hypertensive vascular disease in true pre-eclampsia and eclampsia is seen to be very nearly the same.

(2) In 48 of the 76 hypertensive cases in the non-convulsive

toxaemia series, with a mean age now of 44 years, the hypertension became manifest from 5 to 20 years after the last toxaemic attack.

(3) In three cases, namely cases 52, 55 and 79, hypertension existed before the first pregnancy, was aggravated temporarily by the toxaemic pregnancies and remained subsequently still at a level above 140/90 mm. Hg. In these three cases the blood pressure was raised in the first trimester and other symptoms, that is superadded oedema and albuminuria, occurred before the 28th. week.

It is therefore evident that in only 25 of the 100 cases was there a direct association between toxaemia and subsequent hypertension, an incidence which is no higher than the incidence of hypertension amongst the female population in general at the same age of 48.1 years. (Master, et al 1943). This indicates that toxaemia is not the cause of subsequent hypertension, but does not exclude the possibility that it may bring out and aggravate hypertension earlier in a woman who would become hypertensive later in life in any case, whether she has pregnancies with or without toxaemia or no pregnancies at all.

If a group of non-convulsive toxaemias which is a mixed group is studied, the higher the proportion of hypertensives or potential hypertensives included amongst them, the higher will be found the subsequent incidence of hypertensive vascular disease at follow-up examination. This will produce the false impression that true pre-eclamptic toxaemia cases show an unduly high incidence of post-toxaemic vascular complications and will also tend to indicate a higher incidence than is found after an eclampsia follow-up study. Therefore, if one excludes cases with pre-pregnancy hypertension and cases developing unrelated hypertension years later, and make allowance for the difference in the mean age at follow-up of non-convulsive toxaemia and eclamptic cases, it is found that the incidence of subsequent hypertension is nearly the same. (25% and 22% respectively in the follow-up studies presented in this thesis).

If one bears in mind that hypertensive vascular disease is a common entity, the association between the toxaemias and subsequent

hypertension may in the first instance be a chance association. However, the fact that pregnancy in manifestly hypertensive individuals is more readily complicated by toxaemia is not denied, but supported by the findings in the present series. In fact, of the 200 cases followed up, 53% were hypertensive.

As methods of diagnosing cases with underlying or potential hypertension become more accurate, this group will be more readily distinguishable. True pre-eclamptic toxaemia and eclampsia, I feel, will be proved not to be the cause of permanent hypertensive vascular sequelae at all. The temporary hypertensive vascular and renal lesions of true pre-eclamptic toxaemia and eclampsia tend to heal within six months to two years, leaving patients normotensive afterwards. This period of healing may take longer in rare cases. Thus, in the present state of our knowledge, postnatal follow-up examinations at intervals for prolonged periods is the only accurate method of separating the true toxaemias from those possibly related to and associated with hypertension.

CHAPTER 4.

A Discussion in summary form of the possible sequelae of eclamptic and non-convulsive toxaemic cases.

The data found and sorted out showed a nett incidence of subsequent hypertensive vascular disease in 22% of eclamptic cases and in 25% of the non-convulsive toxaemia cases studied. If, however, only "true" eclamptic and "true" pre-eclamptic toxaemia cases are considered, it is forecast that the incidence of vascular sequelae will be negligible. For the moment let us consider the opinion of other authors with regard to the relationship of eclampsia and toxaemia to cardiovascular and renal disease.
Many authors, e.g. Peckham (1929), Kellog (1924), Berman (1930), Gibberd (1931), Harris (1924), Peckham and Stout (1931) and others reported an incidence of chronic nephritis in up to 74% of cases in the follow-up studies of eclampsia and toxaemias. However, Dieckmann (1952), Dieckmann & Browne (1939), Dexter and Weiss (1941) Dexter and Weiss et al (1943), Chesley (1941), Corwin and Herrick (1927) and Steiglitz (1926) and others have pointed out that in most cases this diagnosis was made on hypertension and/or proteinuria alone and post toxaemic hypertension with albuminuria was misnamed chronic nephritis. On the other hand Maclean, as early as 1921, pointed out that the presence of albumin and a few epithelial casts is no proof of defective kidneys. Acosta-Sison (1931) reported that the pathological lesion of eclampsia is nephritis and Peters (1937) as well as Addis (1937) stated that eclampsia is identical to glomerulo-nephritis. Bell (1932) and Herrick and Tillman (1935) state that the kidney lesions found in a fatal case of eclampsia and in those who die later on, are of a degenerative rather than an inflammatory nature, i.e. nephro-sclerosis rather then glomerulo-nephritis.

The follow-up studies of Browne and Dodds (1939) and Teel and Reid (1937 and 1939) bear this out. Dieckmann (1952) and Dexter and Weiss et al (1941 and 1943) and others concluded that the

preponderance/.....

preponderance of evidence leaves no doubt that eclampsia is not a nephritis, nor does it cause chronic nephritis. In the present eclamptic series, none gave a history suggestive of nephritis and only five cases had albuminuria in association with hypertension. Four of the five cases had all the features of progressive hypertensive vascular disease with arteriosclerotic changes and nephrosclerosis with no gross evidence of renal impairment i.e. no fixation of specific gravity, no polyuria, no anaemia, no oedema, no rise in blood urea and no definite albuminuric retinitis such as one would expect after an average interval of 10½ years if they were nephritics. In the fifth case chronic nephritis could not be excluded with certainty. She may have been a case of delayed healing after eclampsia, having had two subsequent pregnancies in rapid succession. I feel it is most likely that she was a case of progressive hypertensive and renal vascular disease. Renal biopsy as was done by Dexter and Weiss (1943) is the only way to settle the diagnosis. In their study of cases who had renal biopsies, they concluded that nephrosclerosis is the characteristic histological lesion after eclampsia. It is also significant that amongst the 18 deaths encountered during the follow-up study only one was diagnosed clinically as a case of uraemia. This was in all probability due to hypertension and vascular renal failure. 44.4% of the deaths were due to some or other manifestation of hypertensive vascular disease and arteriosclerosis, namely congestive cardiac failure, apoplexy, or coronary thrombosis.

Similarly, in the non-convulsive toxaemia follow-up, 72.6% of the deaths were due to some or other manifestation of hypertensive cardiovascular disease, and the one uraemic death encountered was probably due to hypertensive vascular diseases with renal failure. This seems to confirm the findings of Dexter and Weiss, Browne and Dodds andothers that toxaemia and eclampsia is not a nephritis, nor does it cause glomerulonephritis.

There is, however, no doubt that a person with chronic glomerulonephritis prior to pregnancy, or one who contracts this during pregnancy, may remain in statu quo, develop toxaemia or

eclampsia and is usually worse off subsequently as mentioned by Dodds and Browne (1939) and Gibberd (1951), Chesley (1950) and others. One case of acute glomerulonephritis during pregnancy was described under the non-convulsive toxaemia group studied.

The possibility of pyelonephritis as a cause of eclampsia and toxaemia put forward by Peters and others (1936) was excluded by the renal studies in this series, in concurrence with the opinion of many authors, namely that there is no such casuel realtionship. Prather (1941) found pyelonephritis in less than 1% of pregnancies and toxaemia in 10%. McLane (1939) also failed to find a nigher incidence of toxaemia amongst his cases of pyelitis than in pregnant women in general. Two of the present series who had pyelitis are hypertensive, but four are normotensive. Pyelitis seems to be a more frequent result rather than a cause of eclampsia, due to repeated catheterisation in the comatosed state of eclampsia. Weiss and Parker (1939) stressed pyelonephritis as an important cause of hypertensive vascular disease, and for that reason those cases with a history of pyelitis were specially investigated, but with negative results. However, cases of pyelonephritis are often only diagnosed with certainty at autopsy.

The next question that arised is whether eclampsia leaves behind some residual vascular damage, and whether it results in subsequent hypertensive cardiovascular disease. Dexter and Weiss (1941) and Dexter and Weiss et al (1943) were convinced that toxaemia often caused irreparable damage. Greenhill (1947), Stander (1947), Gibberd (1931), Harris (1924), Young (1927), Young and Sim (1932), Young (1929), Peckham (1929) and Peckham (1941), Peckham and Stout (1931), Peters (1937), Herrick and Tillman (1935) and many others are proponents of the theory that there are sometimes, or always, residuals. Teel and Reid (1937) and Reid and Teel (1939) conclude that eclampsia causes little damage, but that non-convulsive toxaemias perhaps cause more damage to the cardiovascular system. On the other hand, Dieckmann (1941), Dieckmann and Browne (1938 and 1939) and Dieckmann (1952), who have done a great deal of work in this connection, are equally convinced that the true toxaemias of

pregnancy cause no permanent cardiovascular or renal damage.

Cheeley, Somers and Vann (1948), Light (1948), McClellan et al (1941), Browne and Dodds (1939) and Browne (1951) have all presented follow-up studies which they interpret as confirming the viewpoint that no permanent damage results. Icenhour et al (1942) examined 900 nulliparous women and 900 parous women and found no more hypertension in the latter than in the former group. Barnes and Browne (1945) made a similar study of 915 nulliparous and 1004 parous women with similar results. Theobald (1933) proved by statistical figures that the death rate of cardiovascular and renal disease is no higher in married than in single women up to the age of 55. According to Browne (1951) these figures have not been proved to be incorrect. This present study indicates that eclampsia does not cause hypertensive cardiovascular disease, and the incidence of subsequent hypertension in the group studied is no higher than the incidence of hypertension in the female population in general at the same age (using the figures of Master et al (1943 and 1950). Further, if only "true" eclamptic cases, of which 70 cases found to be normotensive at follow-up are examples, are included in such a follow-up study, then the incidence of subsequent hypertensive vascular disease would be negligible. This will exclude cases with latent or manifest hypertension who form the percentage of hypertensive cases found at follow-up when a mixed group of eclamptic cases are studied.

Bryans and Torpin (1949) assume that the same conclusions apply to pre-eclamptic toxaemia cases as to eclamptic cases, but did not make a follow-up study of non-convulsive toxaemic cases.

The fact that the nett number of cases in the non-convulsive toxaemia group studied had an average age of 48.1 years explains the slightly higher incidence of vascular sequelae in these than in eclamptic cases studied, namely 25 as opposed to 22%.

In general, then, the incidence of hypertension is no higher than the incidence of hypertension at the same age in the general population of females. However, both the mixed group of eclamptic cases and the mixed group of non-convulsive toxaemia cases showed

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significantly higher incidence of hypertension in the younger age groups. Eclampsia and the non-convulsive toxaemias, therefore, tend to bring to the surface a latent hypertension earlier than it would have occurred under normal circumstances. This is in agreement with Browne's views.

If only true pre-eclamptic toxaemia cases such as the 24 subsequently normotensive cases, are included in such a follow-up study, the incidence of subsequent vascular sequelae will be negligible as was indicated when true eclamptic cases were considered

Dexter and Weiss (1943) Peckham (1941), Teel and Reid (1937), Harris (1924), Gibberd (1931), Young (1927 and 1937) and others have done work which can be interpreted as indicating that the duration of the toxaemia is the important factor in causing permanent vascular damage. They feel that the severity of the attack is of secondary importance. It has been pointed out that conclusions in this regard can be fallacious, as the cases considered in making such conclusions are a mixed group, and those with underlying hypertension are bound to have a longer duration of symptoms and a higher blood pressure during the toxaemic pregnancy.

On the other hand, though the word "eclampsia" means to flash forth, implying a condition of sudden onset, it is well known, as Greenhill (1947), Stander (1945) and Browne (1951),have pointed out, that in most cases convulsions are preceded for some time by the signs and symptoms of toxaemia, that eclampsia only very occasionally occurs without premonitory signs, and is nearly always the final result of a long standing or neglected toxaemia.

The entity,post-partum eclampsia, especially when it occurs without hypertension,and/or albuminuria, will, with modern methods of investigation, be found to be due to cerebral venous thrombosis in most cases.

It seems reasonable that if pre-eclamptic toxaemia leaves residual damage, eclampsia should do so as well, and that if eclampsia causes no permanent vascular damage, then neither should

pre-eclamptic toxaemia. This is confirmed in the present investigation.

A reason for the high incidence of subsequent hypertension found in many follow-up studies of non-convulsive toxaemias is, as Dieckmann (1952), Dexter and Weiss et al (1943), Teel and Reid (1937), Reid and Teel (1939), Browne and Dodds (1939), have pointed out that many cases diagnosed as mild pre-eclamptic toxaemias are in reality cases of essential hypertension to begin with.

Dieckmann (1952) believes that true toxaemia seldom, if ever, recurs. He states that those patients who have repeated toxaemia are actually cases of essential hypertension. The information and discussion in the present study does not bear out this belief.

In the subsequently hypertensive group of women following eclampsia, 73,3% had at least one subsequent pregnancy and 55.6% of these were toxaemic. In the non-hypertensive group, following eclampsia, 82,8% of the women had at least one subsequent pregnancy, and 21.6% of these were toxaemic. These latter cases have been followed up for 10.5 years on an average, and are not yet hypertensive. Therefore, not only cases with hypertension have repeated toxaemia or eclampsia, but also cases who are normotensive. In the latter group then hypertension is not an etiological factor and other factors must be responsible, such as environment, diet, etc. which may predispose, plus some X factor or factors, at present unknown, but which certainly are not latent or manifest chronic nephritis or hypertension.

There seems to be no doubt that true eclampsia and pre-eclamptic toxaemia are specific diseases in pregnant women and not manifestations of chronic nephritis nor of manifest or latent hypertensive cardiovascular disease, and although either of these conditions may precede an attack of convulsions with a raised blood pressure, albuminuria and oedema, indistinguishable clinically from true eclampsia and toxaemia, they are separate entities which cannot always be distinguished at the time of the attack but a knowledge of the pre-pregnancy state and a subsequent follow-up will distinguish them. In all these entities

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the same X factor or factors probably operate.

True eclampsia or pre-eclamptic toxaemia does not seem to be a cause of permanent chronic nephritis or of hypertensive vascular disease. However, following an attack, there may be hypertension and albuminuria temporarily for six months to 2 years and even up to 3½ years before healing occurs.

Although patients who have had "true" eclampsia or "true" pre-eclamptic toxaemia more commonly do not have a recurrence of the toxaemia, they are more likely to have subsequent toxaemia than normal pregnant women, but less so than hypertensive pregnant women. A high incidence of stillbirths and abortions may occur, giving rise to the term "the toxaemic sequence", emphasised by Young (1927, 1929, 1937). I do not think that recurrence is due to some morbid constitutional weakness or influence as he suggested, and it is not because they are cases of essential hypertension, as Dieckmann and Brown state, nor is it because the first attack leaves them more susceptible. Rather is it due to some etiological factor or factors conditioned by the pregnancy in question with or without predisposing factors like environment, hygiene, economic factors, diet, latent or manifest chronic nephritis, latent or manifest hypertension, etc. Such factors are likely to remain more or less constant in subsequent pregnancies, which may or may not be toxaemic.

SECTION V:

A SUMMARY OF THE FINDINGS AND THE CONCLUSIONS MADE IN :-

(a) THE ECLAMPTIC GROUP OF CASES FOLLOWED-UP, WITH REFERENCE TO RELATED RESULTS IN THE NON-CONVULSIVE TOXAEMIA GROUP, FOR THE PURPOSE OF COMPARISON.

(b) THE NON-CONVULSIVE TOXAEMIA GROUP OF CASES FOLLOWED UP, WITH REFERENCE TO RELATED RESULTS IN THE ECLAMPTIC GROUP, FOR THE PURPOSE OF ADDITION & FOR COMPARISON.

(a). A summary of the findings and conclusions in the eclamptic group of cases studies, with references to related results in the non-convulsive toxaemia group.

(1) A hundred surviving cases were followed up after an average interval of 10.56 years and had a total of 512 pregnancies.

(2) 70 cases were normotensive and 30 were hypertensive at the follow-up examination. 22 of the latter cases had a blood pressure of 180/100 mm. Hg. or above.

(3) One of the cases may have chronic nephritis, but she probably had this condition before her first pregnancy. Three cases suffer from diabetes mellitus which became manifest in the interim, and one of these is hypertensive as well. Diabetes was not a factor leading to the eclamptic attack in these cases.

Applying the criteria of Maltby and Rosenbaum, a convulsive diathesis was present in 16% of the eclamptic cases in contrast to 8% in the non-convulsive toxaemia group. Two cases developed post-eclamptic epilepsy. The hypothesis of Maltby and Rosenbaum about a convulsive diathesis is not supported by the findings in the present study.

(4) The premenstrual tension syndrome was found to be a chance association and has no etiological relationship to eclampsia or the non-convulsive toxaemias.

(5) There was a family history of eclampsia in 14% of the eclamptic cases and in 6% of the non-convulsive toxaemia cases studied. In one of the eclamptic cases followed up, the history revealed that eclampsia had occurred in seven different members of her family. This is the highest familial incidence found amongst recorded cases in the literature. 83.3% of the 30 hypertensive cases and 71.2% of the 70 normotensive cases in the eclamptic group had a family history of hypertension. In contrast, in the non-convulsive toxaemia cases studied, 93.4% of the 76 hypertensive cases and 66.6% of the 24 normotensive cases had a family history of hypertension. This indicates that a family history of hypertension is not an accurate guide or criterion as to whether or not

hypertension/.....

hypertension will or will not occur subsequently in a given patient.

Nevertheless, the highest incidence of a family history of hypertensive vascular disease was found in the hypertensive cases at follow-up examination. We do not understand the inheritance of hypertension, but there is no doubt that in some eclamptic and toxaemic cases it plays a role and is the determining factor of subsequent vascular sequelae. In the present state ofour knowledge, and with available diagnostic methods, it is not possible to distinguish during pregnancy all cases with underlying hypertension from cases without this tendency. A knowledge of the vascular and renal state before, during and after pregnancy, is helpful, but cases of latent hypertension cannot always be distinguished. They are often associated with recurrent toxaemia, but this occurs in subsequently genuinely normotensive cases as well. However, the former group will sooner or later become hypertensive, and so become recognisable by follow-up study, which is the only final method of differentiation at present.

It is evident that there are four main groups of patients who develop pre-eclamptic toxaemia and eclampsia with pregnancy, namely:-

(1) Clinically manifest or possibly latent glomerular nephritis present before pregnancy and complicated by superadded symptoms of toxaemia and in some cases "eclampsia" or, more rarely, nephritis developing during pregnancy with the same superadded sequence of events.

(2) Manifest hypertension due to various causes present before pregnancy and complicated by superadded toxaemia, and in some cases eclampsia, or hypertensive encephalopathy, as Dieckmann states. (Unfortunately there is no clinical way of separating the cases that will not develop superadded toxaemia and carry a good prognosis when they become pregnant.)

(3) Latent hypertension with superadded toxaemia or eclampsia who will sooner or later, after the first or subsequent toxaemic pregnancies, become manifestly hypertensive.

(4) (a) "True" pre-eclamptic toxaemia and "true" eclampsia

with no association with latent or manifest hypertension, and no predisposition to hypertension or vascular sequelae at all. This is the group that remain normotensive years later.

(4) (b) Some of these cases may become hypertensive years later, and as a result of other factors, e.g. the wear and tear of life, ageing, or factors unknown or due to intercurrent diseases, e.g. polyarteritis, nodosa or acute disseminated lupus erythematosis, unrelated to the preceding toxaemia or eclampsia.

In this thesis cases who have developed hypertension five years or more after their last pregnancy and who were known to be normotensive in the interim, are regarded as falling into this sub-group.

When an eclamptic or toxaemic follow-up study includes cases from groups 1, 2, 3 and 4 (b), they will be the ones who have subsequent vascular and/or renal sequelae, and the results of any follow-up study made will depend on the number belonging to these groups that are included. If all cases studied in a follow-up investigation belong to group 4(a), there will be no permanent vascular or renal sequelae.

(6) Visual disturbances occurred in 30% of the eclamptic cases, usually within 24 hours, as a premonitory sign of convulsive seizures. However, such cases were not necessarily hypertensive at the follow-up examination. In all surviving cases of eclampsia studied, visual disturbances and retinal detachment was found to be reversible and no evidence was left on clinical examination that they had occurred. It is evident that marked retinal changes during an eclamptic attack need not be followed by persistent post-eclamptic hypertension especially in young women, and if haemorrhages and exudates occur at the time, they are reversible. Only where manifest arteriosclerotic changes are present in association with retinitis, is it evidence of pre-existing vascular or renal disease. Gross funduscopic changes at follow-up were confined to cases with advanced hypertensive vascular disease, with or without diabetes mellitus.

(7) 22 of the 30 hypertensive cases and one of the normo-

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normotensive cases with mitral stenosis showed radiological evidence of cardiomegaly. It is evident that manifest hypertension must be present for some time before radiologically evident changes occur.

(8) The electrocardiographic changes conform with those of hypertensive vascular disease at its various stages.

(9) In no case was pyelonephritis found, and one case may possibly have had glomerulonephritis, but because her pre-pregnancy renal state is not known, it is impossible to exclude the possibility that she had preceding glomerulonephritis. The conclusion is that chronic glomerulo-nephritis does not occur as a sequel to true eclampsia, but cases with hypertension who have toxaemia with eclampsia superadded can die subsequently in uraemia as a result of progressive renal vascular disease, and may be clinically indistinguishable from cases of chronic glomerulo-nephritis. One of the cases traced to have died in the interim probably died in this way, but no autopsy was performed, so that the diagnosis was not finalised.

(10) There was no distinctive build, constitution, or personality found amongst the eclamptic and non-convulsive toxaemic cases studied.

(11) "True" pre-eclamptic toxaemia and eclamptic cases are young (usually under 25 years) and most commonly primipara when they have toxaemia. Such cases show a greater tendency to be normotensive subsequently. The older the patient and the greater her parity when toxaemia occurs, the greater the likelihood that toxaemia occurs on a hypertensive basis, and therefore the greater the incidence of vascular sequelae. The older the patient is at the time of follow-up study, the greater is the likelihood of hypertension in the same way, as the incidence of hypertension rises in the general population with advancing age. Multiparity is not necessarily followed by hypertensive vascular disease and a woman who has had eclampsia may have a large family (up to 9 children in this series) and be normotensive subsequently.

(12) In contrast to the findings of Browne, in the present series more fits occurred amongst the subsequently normotensive

than the subsequently hypertensive cases.

(13) In general the higher the mean highest blood pressure during pregnancy, the higher the blood pressure on discharge and the longer the duration of the toxaemia, the greater the likelihood of permanent vascular sequelae. It must be appreciated in these correlations that many of those destined to be hypertensive cases, produce the highest blood pressures during pregnancy and at discharge. They have a raised blood pressure with or without albuminuria and oedema for a longer time during pregnancy than true pre-eclamptic and eclamptic toxaemia cases. They therefore cloud the picture and may lead to fallacious conclusions.

Manifestly hypertensive cases and cases destined to be hypertensive, tend to develop signs and symptoms of toxaemia earlier in pregnancy than "true" pre-eclamptic toxaemic cases. They therefore inevitably tend to be considered as being toxaemic for a longer period. This is incorrectly interpreted as being the cause of the future hypertension.

Cases destined to be permanently hypertensive after toxaemia will be so irrespective of the duration of the toxaemia, because of a latent tendency to hypertension. I support the hypothesis of Browne et al, that such cases would develop permanent hypertension sooner or later, even if they never become pregnant.

(14) There were 282 pregnancies subsequent to the eclamptic attack in 80 women, of which 20% resulted in either stillbirths or abortions. This foetal mortality is almost twice as great as that expected in the general run of pregnancies and is in keeping with the findings of Bryan' and Torpin (1949) and others quoted previously.

The foetal loss at the time of the eclamptic attack was 35.3% i.e., stillbirth and neonatal mortality. The lowest mortality was found in post-partum eclampsia.

The surviving children born from eclamptic mothers at the time of the attack behave no differently from other children in

general./.....

general, as far as their general physique and intelligence are concerned.

Ninety-three (33.2%) of all the pregnancies subsequent to the eclamptic attack, were complicated by toxaemia. Forty-two out of 80 (i.e. 52.5%) of the women who had subsequent pregnancies had subsequent toxaemic pregnancies. The incidence of toxaemia in the subsequent pregnancies was 4 to 6 times greater than is normally found in the general run of pregnancies and agrees with the reported incidence. Twenty-one of the subsequently normotensive cases had recurrent toxaemia and 3 had recurrent eclampsia and, after an interval of 10.5 years are still normotensive. This illustrates that "true" pre-eclamptic toxaemia and true eclampsia can recur once or more often in subsequent pregnancies without leaving any vascular sequelae. This contradicts Dieckmann's statement that true pre-eclamptic toxaemia and eclampsia do not recur and, Browne's statement that there is usually an underlying hypertension. However, recurrence is found less commonly than in the subsequent pregnancies of cases with toxaemia and eclampsia who have under lying hypertension, latent or manifest.

The investigations show that a normal blood pressure between pregnancies does not guarantee normal subsequent pregnancies and that recurrent true pre-eclamptic toxaemia and eclampsia can leave the patient normal from the point of view of hypertension and renal pathology years later.

(15) Eclampsia recurred 23 times amongst 10 of the 100 eclamptics examined. One women had 5 attacks. The incidence of repeated eclampsia in subsequent pregnancies was 4.64% in this series. Seven of the women in the hypertensive group, who had subsequent pregnancies, had subsequent eclampsia, and 3 of the women in the normotensive group had eclampsia again. It has been shown that contrary to Browne and Dieckmann's views recurrent eclampsia is not always due to underlying hypertension or renal disease. In other words so called "true" eclampsia can recur. One of the cases of recurrent eclampsia only became hypertensive

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after the fifth eclamptic attack. The incidence of recurrence of eclampsia was 10.3% and 1.6% respectively in the subsequently hypertensive and normotensive groups.

There were no constant abnormal anvironmental, dietary or other factors except pregnancy in all the cases with recurrent eclampsia. I believe that whereas nutrition, personal habits and climate are more or less constant factors in each pregnancy of a particular woman, though they may predispose, they cannot be the factors governing occurrence and recurrence, especially as recurrent eclampsia is extremely rarely found with each succeeding pregnancy.

Although eclampsia is most common with the first pregnancy, the cases studied illustrate that eclampsia can occur and recur with any parity and preceding normal pregnancy or pregnancies do not rule out the possibility of the occurrence and subsequent recurrence of eclampsia in any future pregnancies. (This applies to true eclampsia as well as eclampsia superimposed on hypertension and renal disease). There may be normal pregnancies at term in between and, toxaemic pregnancies may precede, intervene or follow recurrent eclampsia, with or without interspersed normal pregnancies in a haphazard way. On the other hand all succeeding pregnancies may be normal or toxaemic. These facts formulate strong evidence that eclampsia and pre-eclamptic toxaemia are not due to any inherent weakness or disease or any organ, but are more likely due to conditions associated with the immediate pregnancy. Thus dietary factors, primiparity, multiple pregnancy hydatidiform mole, polyhydramnios, etc. may favour its occurrence but, in addition some other factor or factors unknown as yet, must operate. These factors are probably in the uterus or placenta and produce secondary widespread effects on the renal, vascular and other organs, to produce the syndrome or syndromes which we call toxaemia. It has been pointed out that underlying latent or manifest hypertension or renal disease is only a factor in some cases.

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(16) An analysis of the pregnancies previous to the first eclamptic attack shows that the incidence of previous toxaemia was 17.1%. This is higher than the general incidence of toxaemia. It can be deduced from this that a woman who has had a toxaemic attack, is more liable to develop eclampsia in subsequent pregnancies than other women.

(17) The maternal mortality in eclampsia at the time of the episode was deduced from figures of the Peninsula Maternity Hospital from the 1st July, 1939, to the 31st December, 1945. During this time 150 eclamptic cases were treated, 13 of whom died, giving a mortality of 8.6%. All the deaths occurred with emergency admissions. Amongst the 18 deceased cases traced, 16.6% of the deaths were in subsequent childbirth and 44.4% were due to some or other manifestation of cardiovascular disease. One case died in uraemia, probably from hypertensive renal vascular disease but, as no autopsy was performed, chronic glomerular nephritis cannot be excluded.

(18) The 30 hypertensive cases consisted of 9 European and 21 Coloureds, an incidence of 37.5% amongst the White and 27.6% amongst the Coloured eclamptics studied. It was indicated that one of the Coloureds who is hypertensive may have had nephritis before her eclamptic attack. The remaining 29 cases were apparently normal before their eclamptic pregnancies, but this does not exclude a latent hypertension. Seven of these 29 cases developed hypertension 6 to 21 years after the eclamptic attack and, probably from unrelated causes. The nett number with directly related subsequent hypertension is 22. This incidence of hypertension is no higher than the incidence amongst the population in general, and if the same methods of analysis are applied to the series of 100 non-convulsive toxaemia cases studied, then 25 of them had hypertension directly related at onset to their toxaemic pregnancies. This gives a slightly higher incidence of sequelae amongst the non-convulsive toxaemia cases, in keeping with the results of many similar studies in the literature and, opposed to the results of follow-up studies by Browne and Dodds (1939) and

others./.....

others. As a group the non-convulsive toxaemias were more than 5 years older than the eclamptic cases at follow-up examination and this may be an additional factor determining a higher incidence of hypertension. It is obvious from this follow-up study that the course is not grave and excluding immediate fatalities with the eclamptic attack and soon afterwards, the sequelae that may occur years later, are almost entirely hypertensive vascular in nature. I maintain, however, that if cases with latent hypertension, as well as the manifestly hypertensive and nephritic cases, can be differentiated and excluded at the time of the toxaemic or eclamptic pregnancies, then the incidence of vascular sequelae will be nil both in true pre-eclamptic toxaemia and in true eclampsia cases. Contrariwise the greater the number of latent or manifest hypertensive cases or nephritics included in a series of eclamptics or non-convulsive toxaemia cases studied by follow-up examination, the greater will be the incidence of subsequent vascular and / or renal sequelae. These are the main reasons for the large variation in the incidence of sequelae found in follow-up studies in the literature. Cases of latent hypertension cannot be diagnosed with certainty during pregnancy and the only method available to distinguish them is by follow-up study.

(19) If the eclamptic cases studied are divided into age groups, the numbers with hypertension in each age group, though small, do indicate that in the younger age groups the incidence of subsequent hypertension is higher than in the general population of women in the same age groups. This indicates that eclampsia brings out a latent hypertensive tendency at an earlier age than it would normally have occurred if neither pregnancy nor toxaemia had supervened.

(20) In four of the 5 hypertensive cases who had proteinuria it was explicable on the basis of nephrosclerosis in advanced hypertensive vascular disease with or without symptoms and signs of cardiac failure. The fifth case may have had pre-pregnancy nephritis or delayed healing following eclampsia and rapidly

succeeding./.....

succeeding pregnancies, or hypertensive vascular disease with renal vascular involvement, or chronic glomerulonephritis, but due to difficulties, mainly further conception, a complete study could not be made of her case to finalise the diagnosis. Further study and follow-up along the lines indicated would have to be done to settle the diagnosis. Practically all cases of eclampsia had albuminuria and hypertension and oedema at the time of the attack and the majority of cases were well when followed-up (70 out of the 100 in this series). They all had renal and vascular signs and symptoms for a period after the attack, this period and phenomenon being known as "healing" This was first stressed by the German writers, e.g. Kobes, and according to Browne may take up to 2 years or longer to occur. In my opinion, if healing does not occur, it indicates underlying hypertension or renal disease that has merely become evident at the time of the eclamptic attack and would have occurred sooner or later. Non-healing excludes true pre-eclamptic toxaemia and "true" eclampsia. In other words if only a group of the latter cases are considered in a follow-up study, they will invariably be normal.

(21) Twohundred and eighty-two pregnancies occurred subsequent to the first eclamptic attack in 80 women. 73.3% Of the subsequently hypertensive and 82.8% of the subsequently normotensive cases had one or more further pregnancies, and the incidence of stillbirths and abortions were 21.6% in the former and 16.7% in the latter group. This indicates that underlying hypertension is a factor leading to a greater foetal loss in subsequent pregnancies, and this is mainly due to the higher incidence of toxaemia in their subsequent pregnancies.

55.6% Of the subsequent pregnancies were complicated by toxaemia in the hypertensive group and 21.6% in the normotensive group. Twenty-one women, i.e. 95% of the subsequently hypertensive cases and 21 women (36%) of the subsequently normotensive cases who had further pregnancies, had at least one or more subsequent toxaemic pregnancy. This indicated that those cases with

underlying./....

underlying hypertension tend to be more liable to subsequent toxaemia which is in keeping with the statement that many cases with recurrent toxaemia have underlying hypertension. Obviously as recurrent toxaemia occurred in the normotensive group as well, it need not be a factor at all. Recurrent true eclampsia and recurrent true pre-eclamptic toxaemia are genuine entities without underlying hypertension, contrary to Dieckmann's statements.

It was indicated that even if Browne's criteria and arguments are used, recurrent toxaemia in the subsequently normotensive group is not explicable on the basis of underlying hypertension, especially because they have remained normal after so many years. Neither latent nephritis, nor hypertension explain recurrent toxaemia in a certain group of cases who have all along been referred to as the "true" recurrent eclamptic and "true" recurrent pre-eclamptic toxaemic cases. Recurrent true pre-eclamptic toxaemia is more common than recurrent true eclampsia in the same way as pre-eclamptic toxaemia is more common than eclampsia, on a hypertensive or nephritic basis. This investigation showed that recurrent true pre-eclamptic toxaemia and eclampsia are less common entities. The above grouping into true toxaemias with underlying hypertension or renal disease was further substantiated in the non-convulsive toxaemia cases studied. This is one of the main concepts emphasised in this thesis, a view neglected in the literature of the toxaemias of laterpregnancy. The basic etiology of all toxaemias are unknown. Although hypertension plays a role in some, and may explain the convulsions as being due to hypertensive encephalopathy, while in others nephritis with uraemic convulsions may explain the clinical features, in others we have no definite explanation for the occurrence of the toxaemia and eclamptic fits, except possibly Maltby and Rosenbaum's hypothesis which in my opinion has not been proved.

(22) As indicated previously, previous toxaemic pregnancies in a given woman may make toxaemia and eclampsia a greater subsequent likelihood. However, in every pregnant woman, toxaemia and eclampsia remains a potential danger only to be disproved by

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the test of complete pregnancy. This is why ante-natal care and supervision is essential throughout every pregnancy. Each case therefore, presents her own clinical problem, to be considered on its own merits.

(b) A Summary of the Findings and Conclusions in the Non-Convulsive Toxaemia Group of Cases, with references to related results in the Eclamptic Groups Studied:

The principle facts arising from this investigation of the non-convulsive toxaemias are:-

1. One hundred surviving cases were followed-up after an average interval of 13.5 years and had a total of 676 pregnancies.

2. Twenty-four cases were normotensive and 76 were hypertensive at follow-up examination. Thirty-nine of the latter cases had a blood pressure of 180/100 mm. Hg. or more.

3. There was not a single case of glomerulonephritis but, 4 of the hypertensive cases suffered from diabetes mellitus and 1 case was an epileptic.

The incidence of a convulsive diathesis was 8% as opposed to 16% in the eclamptic series.

4. The incidence of the pre-menstrual tension syndrome was found to have no directly related association with toxaemia.

5. 93.4% of the 76 hypertensive cases and 66.6% of the 24 normotensive cases had a family history of hypertension.

The family history in this regard often lets one down in a given case as an index of the possibility of the occurrence of subsequent hypertension, but nevertheless, the highest incidence of a family history of hypertensive vascular disease was found in the subsequently hypertensive group of cases. Therefore, inheritance of hypertension probably plays an important role in determining subsequent vascular and renal sequelae. (See discussion under Eclampsia).

Visual./.....

6. Visual disturbances are less common in non-convulsive toxaemia cases than in eclampsia cases at the time of the attack.

Funduscopic examination is often not helpful in distinguishing hypertensive cases with toxaemia from "true" pre-eclamptic toxaemia cases. Markedly abnormal funduscopic changes at the follow-up examination were confined to progressive hypertensive cases only.

7. Thirty-nine hypertensive cases showed radiological evidence of cardiomegaly, whereas 37 did not, in spite of the presence of definite hypertension.

8. Multiparity was not necessarily associated with subsequent hypertension, but the older the patient when pregnant, the more likely was there to be toxaemia and subsequent hypertension. This investigation shows that primiparae, especially those under the age of 25 years, who develop pregnancy toxaemia, are in general the least likely cases to develop subsequent hypertensive vascular sequelae.

9. In general, there was a correlation between the age of the patient, her parity, the height of her blood pressure during pregnancy and on discharge, the duration of her toxaemia, and the likelihood of subsequent hypertensive vascular sequelae.

However, many fallacies may enter when these findings are correlated, as the criteria are constantly applied to a mixed group of cases with underlying potential of manifest hypertension in many instances, which cannot be accurately separated from "true" pre-eclamptic toxaemia and eclampsia in the present state of our knowledge except by follow-up study.

10. Toxaemia recurs, not only in the hypertensive and subsequently hypertensive cases but, also in the normotensive cases. On the other hand toxaemia was found not to have recurred in some subsequently hypertensive cases and in many normotensive cases, although by far a larger percentage of the latter had no recurrence

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of toxaemia.

11. The stillbirth and neonatal mortality at the time of the first toxaemic attack was 20.8% in the 100 surviving non-convulsive toxaemia cases, a figure much lower than in eclamptic cases with their attack, where hypnotic drugs and anoxaemia during the fits are additional factors increasing the foetal loss.

The surviving children are no different in health and intelligence from a random sample of the general population of children.

The foetal mortality in subsequent pregnancies was 25.7% and mainly due to recurrent toxaemia with or without underlying hypertension and resulting premature delivery.

12. In 56.5% of women and in 47.7% of their subsequent pregnancies toxaemia recurred. 58% of the subsequent pregnancies were complicated by toxaemia in the subsequently hypertensive group and 33.8% in the subsequently normotensive group of cases.

The incidence of subsequent toxaemia was 4 to 6 times greater than would normally be expected in the general run of pregnancies, which agrees with the findings of other investigators.

13. True pre-eclamptic toxaemia may recur as many as 6 times and leave the patient still normotensive years later. As a group the cases with hypertensive vascular disease, latent or manifest, associated with pre-eclamptic toxaemia are more prone to recurrent toxaemia. Thus 61.9% of the women in the hypertensive goup and 37.5% of the women in the normotensive group in this series had at least one further toxaemic pregnancy. In some of these it recurred many times.

This series also illustrates that toxaemia may occur and recur with any parity, and preceding normal pregnancy or pregnancies do not rule out the possibility of the occurrence and subsequent recurrence of toxaemia in future pregnancies, even if hypertension latent or manifest, is excluded. This points to the fact that toxaemia is due to conditions associated with the immediate toxaemic pregnancy, with or without predisposing factors like multiple./...

multiple pregnancy or dietary factors etc., and due to an X-factor not known to us.

14. Twenty-two non-convulsive toxaemia cases traced were found to have died. 72.6% of the deaths were due to some of other manifestation or cardiovascular disease, and one case died in uraemia, probably a renal death in a case with progressive hypertensive vascular disease.

15. If the non-convulsive toxaemic cases are subdivided into age groups, the incidence of hypertension in the various age groups is definitely higher than is expected in the population of women, in general, in similar age groups. Therefore, the non-convulsive toxaemias tend to bring out hypertension at an earlier age than it would normally have occurred, in cases who in any case are destined to be hypertensive sooner or later.

16. One case with acute glomerulo-nephritis during pregnancy was included in this mixed group of 100 non-convulsive toxaemia cases and described in detail to indicate that nephritis and toxaemia of pregnancy are entirely different conditions, though they may have features in common.

17. The analysis and study of this series also show that true pre-eclamptic toxaemia, just as "true" eclampsia, may occur and recur and that neither hypertension nor a hypertensive tendency is responsible, or a factor in the toxaemia or the recurrent toxaemia. Such cases are still normotensive years later.

It is rare amongst manifestly hypertensive cases to have normal pregnancies in between toxaemic pregnancies with a blood-pressure falling below 140/90 mm. Hg. and staying there throughout pregnancy and labour until the puerperium. (Louw 1953), has mentioned such a case). More commonly the initial raised blood pressure tends to fall in the middle trimester and towards term tends to rise again with or without superadded albuminuria and oedema, changing the clinical picture from hypertension associated with pregnancy to toxaemia superimposed on manifest hypertension.

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Some cases with hypertension may manifest itself only during pregnancy. The blood pressure level, although often initially raised, may not be raised until the third trimester for the first time with or without superadded oedema and albuminuria, thus becoming indistinguishable from true pre-eclamptic toxaemia. The "wolves in sheep's clothing" referred to earlier in the text. However, such cases will have, with few exceptions, a recurrence with the same sequence of events in subsequent pregnancies, producing one form of recurrent toxaemia. Sooner or later such a latent temporary hypertension will become manifest as a permanent hypertension and, in the present state of our knowledge can only be distinguished from recurrent true pre-eclamptic toxaemia by follow-up study of the given patients. If the patient has true recurrent pre-eclamptic toxaemia, examples of which have been mentioned previously in this series, there will be no hypertension years later. In other cases hypertension may occur, but manifest itself so long afterwards that it is hardly possible to relate the preceding recurrent toxaemia to the subsequent hypertension.

This follow-up study also shows that in a very definite proportion of recurrent true toxaemias (eclamptic or pre-eclamptic) neither hypertension, latent or manifest, nor nephritis, latent or manifest, is causative. They are thus cases of "true" recurrent pre-eclamptic and eclamptic toxaemias. These latter conditions are not confined to primiparae, although they show the highest incidence, nor are they conditions that seldom recur as stated by Dieckmann and others. It must, however, be pointed out that recurrent "true" pre-eclamptic toxaemia is less common than recurrent pre-eclamptic toxaemia on a hypertensive basis, in the same way as recurrent true eclampsia is less common than recurrent eclampsia on a hypertensive basis.

In spite of the considerable advances in medical knowledge, the basic etiology of all these toxaemias is unknown. In some cases hypertension is associated and may play a role and, some of these cases may be very difficult or impossible to differentiate

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during the toxaemic pregnancy from those without associated hypertension.

18. The question as to whether or not pre-eclamptic toxaemia and eclampsia produce permanent vascular and renal sequelae is intimately bound up with the problem of hypertensive vascular disease. To settle this issue a careful consideration of all the detailed facts concerning the 76 hypertensive cases amongst the 100 non-convulsive toxaemia cases followed-up was made. This showed that in 25 cases, at a mean age of 48.1 years, did persistent hypertension arise at the time of the initial toxaemic attack, as compared to 22 similar cases in the eclamptic group. The incidence of vascular disease as a complication in the 2 groups is thus nearly the same.

In the other 51 cases pre-pregnancy hypertension or hypertension unrelated and manifesting itself years later, was the cause of their raised blood pressure and, there is therefore no direct association and probably no relationship to the toxaemic pregnancies, in these cases.

The incidence of hypertension, taking into consideration only the 25 cases, is no higher than in the female population in general at the age of 48.1 years, which is their mean age. This tends to indicate that this hypertension is a chance association determined by heredity. Therefore neither is "true" pre-eclamptic toxaemia or "true" eclampsia the cause of subsequent hypertension but, such toxaemia may bring out hypertension earlier in a women who would have become hypertensive later in life in any case.

As methods of diagnosing cases with underlying or potential hypertension become more accurate in future, this group with associated toxaemia will be more readily distinguished, and true pre-eclamptic toxaemia and eclampsia will, I think, be proved not to be the cause of premanent hypertensive vascular sequelae at all.

The temporary hypertensive vascular and renal lesions found almost invariably in "true" pre-eclamptic toxaemia and eclampsia

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tend to heal within 6 months to 2 years, leaving the women normotensive afterwards. This period of healing may take longer in rare cases as indicated by the case in the present series in whom it took 3½ years to occur.

(c) Fields for further Investigations:

There are so many unsolved problems involved in this aspect of medicine that I have from time to time indicated in the text where future research work may be of value in elucidating this complex group of conditions. The following are some of the more obvious examples:-

1. The incidence of cardiovascular and renal disease amongst the various sections of our local multiracial population, to see if this explains the difference in incidence of the toxaemias of late pregnancy.

2. The incidence of the pregnancy toxaemias amongst parous women attending the medical out-patients department; and comparing the incidence, to that of hypertensive vascular disease. In addition, a comparison of the incidence of hypertensive vascular disease in nulliparous women, with the above groups of parous women will be useful information.

3. The reason why the Bantu people have low blood pressure readings during pregnancy, and why the incidence of the pregnancy toxaemias is significantly lower amongst them, compared with the other population groups.

4. A study of accidental antepartum haemorrhage.

5. Electro-encephalographic and other investigations in pregnancy toxaemia and eclamptic cases, to confirm or disprove the hypothesis of Maltby and Rosenbaum.

6. The possibility of new methods in the diagnosis of latent hypertension, besides the pressor test and flicker photometer, that have only a very limited application.

The/.....

7. The subject of oedema in normal and toxaemic pregnancy is a problem that warrants further study.

SECTION VI:

THE APPENDIX (APPENDIX 1,2,3 & 4).

THIS SECTION CONTAINS A REPRODUCTION OF THE FAMILY HISTORY OF THE ECLAMPTIC AND NON-CONVULSIVE TOXAEMIC CASES STUDIED AS WELL AS THE DETAILED HISTORIES OF CASES WITH RECURRENT ECLAMPSIA, & ECLAMPTIC CASES FOUND TO HAVE PROTEINURIA AT FOLLOW-UP EXAMINATION.

APPENDIX I.

1 A. The family history in detail of the 30 cases of eclampsia followed up and found to be manifestly hypertensive.

The following abbreviations will be used in this section:- F.H. +ve., means a positive family history of hypertensive vascular disease.

F.H. -ve., means a negative family history of hypertensive vascular disease.

? Where the history is doubtful a question mark sign will indicate this.

CASE 6: F.H. +ve. Age 29 years and hypertensive. Her father aged 61 is alive and suffers from hypertensive heart disease. (Confirmed clinically). Her mother died at the age of 29 years but the cause of death is not definitely known. She has one sister and 4 aunts alive and well, 1 aunt on her mother's side had fits with her first child and died during labour at the age of 23 years. She is an example of familial eclampsia.

CASE 7: F.H. +ve. Age 38 years and hypertensive. Her mother aged 65 suffers from poor vision, headaches and a raised blood pressure, also confirmed clinically. Father aged 80, alive and well. Grand-parents are both stated to have died from heart failure. One sister aged 47 is stated to suffer from a raised blood pressure. Three sisters and one brother are alive and well. Two sisters died young.

CASE 16: F.H. +ve. Age 40 years and hypertensive. Her father is stated to have died at the age of 47 years from a stroke. Her mother is alive aged 73, has had a stroke and suffers from hypertensive cardiac failure and, has been a patient at the Groote Schuur Hospital. Two sisters died during childbirth but details are not available. One sister aged 26 alive and well. Three brothers aged 48, 52 and 30 years respectively are stated to be alive and well.

Case./....

CASE 18: F.H. +ve. Age 40 years, hypertensive and diabetic. Her mother is aged 77 and is stated to be alive and well. Her father died at the age of 72 years, (confirmed in hospital folder), from hypertensive cardiac failure and, had prostatic obstruction. She has 2 brothers and 2 unmarried sisters younger than herself, are stated to be alive and well.

CASE 22: F.H. +ve. Aged 40 years and hypertensive. Her father was killed accidentally at the age of 40 years. Her mother died at the age of 62 years from coronary thrombosis in the New Somerset Hospital, and was a known hypertensive. She has 1 sister and 2 brothers alive and well. (Her mother had toxaemia with her fourth and last child at the age of 34 years).

CASE 26: F.H. -ve. Age 38 years and hypertensive. She does not know any facts, as she is an orphan and an only child.

CASE 28: F.H. +ve. Age 48 years, hypertensive and post menopausal. Mother died at the age of 60 years, from Asthma and pulmonary tuberculosis. Her father died at the age of 55 from chronic alcoholism, pneumonia and hypertensive vascular diseases. (Confirmed in folder at Groote Schuur Hospital). One sister died from pulmonary tuberculosis and 1 brother died in the 1918 influenza epidemic. Both were still children at the time of their death.

CASE 29: F.H. +ve. Age 41 years, hypertensive. Mother died of pneumonia at the age of 52. Father alive, aged 79, is stated to have high blood pressure. One brother aged 41 has high blood pressure and has had a stroke. Grandfather died of a stroke and Grandmother from old age at 94. Three brothers and 2 sisters are alive and well. One sister died in childbirth at the age of 40 years and is said to have had toxaemia but, I have not been able to trace her records.

CASE:33: F.H. ? +ve. Her mother is stated to have died at the age of 88 years from a stroke. Her father died at the age of 87, also from a stroke. No details are available. She has 1 sister./.....

sister and 6 brothers with ages varying from 44 to 64 and, all are stated to be in good health.

CASE 43: F.H. +ve. Aged 40, hypertensive and suffers from major epilepsy. (Grond mal). Her mother died at the age of 45 years from hypertensive cardiac failure, in the New Somerset Hospital (confirmed). Father aged 65 is stated to be alive and well. She has 3 brothers and 6 sisters stated to be alive and well. One of the sisters had ante-partum haemorrhage and toxaemia with her third child at the age of 32. I have not been able to examine this patient personally.

CASE 45: ? F.H. +ve. Aged 35 and hypertensive. Her mother died at the age of 35 years from eclampsia with her third child. Her father was killed in the 1914-1918 war. Her grandfather died at the age of 73 years from a stroke and high blood pressure (not confirmed). Her grandmother died at the age of 70 from pneumonia. She has 1 brother alive and well.

CASE 46: F.H. +ve. Age 47 years and hypertensive. Mother aged 75, alive but suffers from rheumatism. Father died at the age of 61 from hypertension and cardiac failure, (confirmed from folder notes at Groote Schuur Hospital). One sister aged 52, is stated to be menopausal and afflicted by high blood pressure. One sister and 4 brothers are alive and well. One brother aged 32 died suddenly ? coronary thrombosis.

CASE 47: F.H. +ve. Aged 21 and hypertensive. Her mother aged 40 is a known diabetic for 7 years, but has no hypertension. Her father aged 50 years has been diabetic for 1 year and suffers from high blood pressure and symptoms of early cardiac failure. (Confirmed by examination). She had 1 brother and 1 sister alive and well. Note the family history of diabetes.

CASE 50: F.H. +ve. Aged 47 and hypertensive. Mother aged 62 years, is alive and stated to be well. Father aged 60 years, is suffering from a stroke with aphasia and high blood pressure. Grandmother died at the age of 61 with her third stroke. The

cause./....

cause of death of the grandfather is not known. She has 4 younger sisters and 3 younger brothers alive and stated to be well.

CASE 54: F.H. +ve. Age 35 and hypertensive. Her mother is 55 years of age and has a blood pressure of 200/115 mm. Hg. Her father died at the age of 34 from typhoid fever. She has 1 sister and 4 brothers younger than herself, alive and well.

CASE 57: F.H. ? +ve. Aged 51 and hypertensive. Her father died at the age of 85 years from prostatic obstruction and hypertensive heart disease. (Not confirmed). Her mother is stated to have died from cardiac failure and bronchitis. (Not confirmed). Her only sister is also stated to have died from her "heart" at the age of 63 years, but this I have not been able to confirm.

CASE 59: F.H. +ve. Aged 39 and hypertensive. Her mother aged 60 years suffers from diabetes but her blood pressure is normal on examination. Her father died at the age of 70 years from cardiac failure and hypertension. Three brothers and 4 sisters are alive and well. One elder brother is also stated to have hypertensive vascular disease.

CASE 61: F.H. +ve. Aged 39 and hypertensive. Mother aged 59 alive and well but her blood pressure on examination was found to be 165/95 mm. Hg. She had eclampsia when this daughter (Case 61) was born, this being her first pregnancy. Father alive aged 62 has had a stroke and suffers from hardened arteries and a raised blood pressure, (not confirmed). She has 4 sisters alive who are stated to be well and 1 sister died from rheumatic heart disease while another died from tuberculosis as a child.

CASE 63: F.H. +ve. Aged 46 and hypertensive. Father died at the age of 60 years from a stroke and high blood pressure. Her mother died from hypertensive cardiac failure at the age of 60 (Confirmed from her notes at New Somerset Hospital). She has 1 sister with asthma and 2 brothers in good health.

CASE 64: F.H. ? +ve. Age 35 and hypertensive. Mother died from a carcinoma of the stomach at the age of 53. Her father died at

the./.....

the age of 40 from heart disease but was not known to be hypertensive. She has 2 sisters alive and well.

CASE 75: F.H. -ve. Age 46 and hypertensive. Her mother died at the age of 50 from asthma and her father died at the age of 52 from cancer of the stomach. Her 2 brothers, younger than herself, are alive and well. Her only sister died as a child.

CASE 79: F.H. +ve. Aged 49 and hypertensive. Her mother had eclampsia with the birth of her first child and died in her early forties from blood pressure and her "kidneys". Her father died at the age of 55 from pneumonia. One sister has also had eclampsia and is reported to be well. Another sister had eclampsia with her third child and died. She has 2 daughters who have had eclampsia, the one H.S. had eclampsia with her first child in the Groote Schuur Hospital. The other M. de J. had eclampsia with her first child and a subsequent normal pregnancy.

CASE 80: F.H. +ve. Aged 39 and hypertensive. Her mother died at the age of 50 suddenly from her heart (not confirmed). Her father died at the age of 72 from a stroke, hypertensive vascular disease (confirmed in his folder at Groote Schuur). She has 3 brothers and 6 sisters stated to be alive and well and her eldest daughter has had 4 children normally.

CASE 87: F.H. +ve. Aged 50 and hypertensive. Her father is stated to have died of pneumonia at the age of 60 years and her mother died of a stroke and pneumonia, her notes confirm that she was markedly hypertensive with a blood pressure 250/140. Her brothers and sisters all died young.

CASE 90: F.H. +ve. Aged 39 and hypertensive. Her mother died at the age of 54 from secondary carcinoma of the spine, the site of the primary is unknown (confirmed to be normotensive). Her father died at the age of 67 from diabetes and high blood pressure (confirmed at Groote Schuur Hospital diabetic out-patients notes). Her brother died at the age of 40 from diabetic coma and was hypertensive as well, 1 sister aged 50 years, also a diabetic, and her

remaining./.....

remaining sister is said to have high blood pressure.

CASE 91: F.H. -ve. Aged 61 and hypertensive. She had eclampsia twice at the age of 32 and 45 years. Her father died at the age of 78 from ? carcinoma of the prostate. Her mother died at the age of 40 years; cause of death not known, (unable to trace her folder at the Somerset Hospital). One of her brothers died suddenly at the age of 35, up country. She has 2 sisters and 1 brother stated to be alive and well. Two brothers and 1 sister died as children.

CASE 93: F.H. +ve. Aged 39 and hypertensive. Her mother died during childbirth with convulsions in a twin pregnancy at the age of 40 years. Her father aged 66 years suffers from high blood pressure and attends medical out-patients at Groote Schuur Hospital. She has no brothers or sisters. Note the familial incidence of eclampsia.

CASE 95: F.H. -ve. Aged 43 and hypertensive. Her mother and father are both alive and well, her 2 brothers and 1 sister are also well. Her daughter has had toxaemia with her second and third children.

CASE 96: F.H. +ve. Aged 44 and hypertensive. Her mother died at the age of 40 years from a cardiac failure, diabetes and high blood pressure. Her father died of carcinoma of the large bowel. She has 4 sisters stated to be alive and well and 1 brother died from pneumonia in childhood.

CASE 98: F.H. +ve. Aged 48 and hypertensive. Her mother died at the age of 69 from a stroke and hypertension. Her father died at the age of 67 from cardiac asthma, hypertension and cardiac failure. Her 1 sister had eclampsia with her first child and is still alive but, was not personally examined as she is out of town, however, from the reports one is not able to exclude the possibility of hypertension in her case. She has 2 other sisters who have had children and are alive and well.

1 B. The family history in detail of the 70 cases of eclampsia followed-up and found to be normotensive when examined :

CASE 1: F.H. +ve. Aged 23 and normotensive. Mother aged 50 years stated to be alive and well, father died from a stroke at the age of 47 and had high blood pressure. (Confirmed verbally by private doctor who attended him). She has 1 brother and 1 sister alive and well. One brother died as a child.

CASE 2: F.H. +ve. Aged 29 and normotensive. Her mother aged 54 attends arthritic clinic with osteo-arthritis of the hips and has definite hypertensive vascular disease. Her father died at the age of 34 from pulmonary tuberculosis. She has 4 brothers alive and well and 2 sisters unmarried alive and well. One brother and 1 sister died from tuberculosis as children.

CASE 3: F.H. +ve. Aged 25 and normotensive. Father is blind and has diabetes, carbuncles and high blood pressure at the age of 57. Her mother aged 53 is alive and well. She has 6 sisters and 1 brother alive and well.

CASE 4: F.H. -ve. Aged 31, normotensive but diabetic. Her father died at the age of 30 years from ? pulmonary tuberculosis. Her mother died at the age of 48 from a sarcoma of the humerus. She has no sisters. One brother aged 20 alive and well. One of her aunts is a diabetic aged 47 but normotensive.

CASE 5: F.H. +ve. Aged 24 and normotensive. Father aged 50 years suffers from his kidneys and high blood pressure and her grandfather aged 74 suffers from high blood pressure. Her mother is alive and well, grandmother had carcinoma of the stomach. She has 5 brothers and 2 sisters alive and well, 1 brother and 2 sisters died as children.

CASE 8: F.H. +ve. Aged 24 and normotensive. Father aged 66 hypertensive with repeated epistaxis. Mother aged 43 has headaches with a raised blood pressure. Four sisters and 4 brothers alive and well. (Blood pressure of father confirmed).

CASE 9: F.H. +ve. Aged 30 and normotensive. Her mother aged

58 is obese with a blood pressure of 200/110 mm. Hg. and is menopausal. Her father aged 63 is alive and well. One sister died from eclampsia with her fourth child at the age of 28. She has 4 sisters alive and well without any history of toxaemia. No aunts with a history of fits or toxaemia.

CASE 10: F.H. -ve. Aged 27 and normotensive. Mother aged 65 and father aged 62 alive and well. She has 4 brothers and 4 sisters alive and well.

CASE 11: F.H. ? +ve. Aged 30 and normotensive. Her mother aged 70 and father aged 76 alive and well, her aunt died at the age of 58 from bilateral strokes, diabetes and high blood pressure in the Groote Schuur Hospital One sister aged 40 years is stated to be hypertensive and has had no children. Three brothers are alive and well.

CASE 12: F.H. +ve. Aged 24 and normotensive. Her father aged 69 suffers from high blood pressure. Her mother died at the age of 55 from a stroke (not confirmed). Two sisters alive and well and 1 sister died as a child.

CASE 13: F.H. +ve. Aged 39 and normotensive. Her father died at the age of 60 years from carcinoma of the stomach. Her mother aged 78 had a stroke 18 months ago and is hypertensive, (confirmed in outpatients notes at Groote Schuur). One sister had toxaemia with her sixth pregnancy at the age of 38. One sister alive and well, 2 sisters died as children. One brother suffers from asthma and 1 brother died from Meningitis. One aunt died suddenly ? coronary thrombosis.

CASE 14: F.H. +ve. Aged 38 and normotensive. Mother died aged 48 from hypertensive cardiac failure and her father died at the age of 46 from C.O. poisoning. Three brothers and 1 nulliparous sister alive and well.

CASE 15: F.H. +ve. Aged 26 and normotensive. Mother aged 60 suffers from hypertensive vascular disease (confirmed clinically). Father aged 69 alive and well, 1 brother aged 30 and 1 sister aged

39./.....

39 with 6 children alive and well.

CASE 17: F.H. +ve. Aged 36 and normotensive. Mother died at the age of 66, 5 years ago, from a stroke and hypertension (confirmed). Father died suddenly aged 63 from ? coronary thrombosis. Seven sisters and 3 brothers alive and well. Two sisters and 1 brother died as children.

CASE 19: F.H. +ve. Aged 29 and normotensive. Her mother aged 51 died of coronary thrombosis. Father aged 60 alive but a known hypertensive. Three brothers and 3 sisters alive and well.

CASE 20: F.H. -ve. Aged 30 and normotensive. Father died at the age of 34 from pulmonary tuberculosis. Her mother died from carcinoma of the breast at the age of 44. Three brothers and 1 sister alive and well. Two sisters and 1 brother died as children.

CASE 21: F.H. +ve. Aged 43 and normotensive. Mother died at the age of 71 from high blood pressure and diabetes. Her father died at the age of 63 from dropsy. One brother aged 55 has a blood pressure of 170/100. One sister aged 60 is said to be hypertensive and 2 brothers and 3 sisters are said to be well.

CASE 23: F.H. +ve. Aged 22 and normotensive. Her father aged 52 has hypertensive heart disease and her mother aged 52 is alive and well (a midwife). Seven brothers and 1 sister alive and well.

CASE 24: F.H. +ve. Aged 29 and normotensive. Mother aged 65 alive and well, and father aged 72 has an auricular fibrillation, hypertension and cardiac failure. Three sisters alive and well. One sister had eclampsia with her second pregnancy and died as a result. Two brothers alive and well and 1 brother and 2 sisters died as children.

CASE 25: F.H. -ve. Aged 23 and normotensive. Her father died at the age of 27 from a perforated appendicitis and general peritonitis. Her mother aged 45 is alive and well. No other children in the family.

CASE 27: F.H. +ve. Aged 25 and normotensive. Mother aged 55 varicose./....

varicose ulcer of the leg but otherwise well. Father died aged 50 years from coronary thrombosis and hypertension. Two brothers and 2 sisters alive and well. One brother and 3 sisters died as children.

CASE 30: F.H. +ve. Aged 39 and normotensive. Mother died at the age of 61 from pneumonia. Father died at the age of 70 from hypertensive cardiac failure. Two brothers and 2 sisters alive and well. One brother and 1 sister died as children.

CASE 31: F.H. -ve. Aged 31 and normotensive. Mother died at the age of 30 years from pulmonary tuberculosis. Father died at t the age of 31 from ? poliomyelitis. One sister aged 29 has had toxaemia and eclampsia with her first child. Grandmother has rheumatoid arthritis. One aunt is stated to have hypertension.

CASE 32: F.H. ? +ve. Aged 28 years and normotensive. Had eclampsia twice. Her father died of tuberculosis, at the age of 34. Her mother aged 48 is said to be hypertensive, (not seen personally). Her mother is stated to have had eclampsia twice. One brother and 1 sister alive and well.

CASE 34: F.H. ? +ve. Aged 28 and normotensive. Father is said to have died from a stroke and raised blood pressure. Mother alive and well, 2 brothers and 1 sister alive and well. One sister died as a child.

CASE 35: F.H. -ve. Aged 27 and normotensive. Father aged 58 in good health. Mother died at the age of 38 from asthma. Grandparents died at the age of 80 and 76 but cause not known. Three brothers and 1 sister alive and well. One sister is also asthmatic.

CASE 36: F.H. +ve. Aged 31 and normotensive. Father died at the age of 76 from uraemia due to prostatic enlargement and his notes confirm hypertensive vascular disease (blood pressure 170/110). Mother aged 66 years, is asthmatic and said to be hypertensive. She had eclampsia with the birth of her first child. One sister aged 45 is said to be hypertensive. Five sisters are stated to be alive and well and 1 brother died as a child. No family history of fits.

CASE 37: F.H. -ve. Aged 23. Normotensive. Her father died at the age of 28 years from sarcoma of buttock. Her mother aged 47 is alive and well and one only sister is in good health.

CASE 38: F.H. ? +ve. Aged 32 and normotensive. Her grandmother died at the age of 68 from dropsy and hypertension. Her grandfather died at the age of 78 from gall stones. Her mother aged 56 years is alive and well and her father died at the age of 33 years from ? lymphosarcoma of the stomach. Two sisters died as children, 1 brother alive and well.

CASE 39: F.H. +ve. Aged 31, and normotensive. Mother died at the age of 50 years from hypertension and cardiac failure. Father died at the age of 60 from Miners phthisis. One sister aged 27 is said to be asthmatic.

CASE 40: F.H. ? +ve. Aged 28 and normotensive. Her mother aged 53 years is alive and well, her father aged 55 years is alive and well. Her grandfather died at the age of 65 years from a stroke. Her 1 aunt on her father's side had eclampsia with her third child but was not personally examined. One brother and 1 sister, both died as children.

CASE 41: F.H. ? +ve. Aged 26 and normotensive. Her mother aged 56 is said to be suffering from kidney disease. Her father died at the age of 46 from a perforated ulcer of the stomach. Her grandmother is alive and aged 89 years. She is said to be in good health. Her grandfather died suddenly at the age of 64, heart disease was suspected. Two brothers and 1 sister are alive and well

CASE 42: F.H. +ve. Aged 29 and normotensive. Her mother died at the age of 57 from a stroke and high blood pressure. Her father died at the age of 66 of cerebral haemorrhage (confirmed by autopsy), and had hypertension. Four sisters and 5 brothers are said to be alive and well.

CASE 44: F.H. ? +ve. Aged 35 and normotensive. Her mother aged 60 years is alive and well. Her father died at the age of 32 years from pneumonia. One uncle died of a stroke at the age

of 70 years. Two brothers and 1 sister alive and well.

CASE 48: F.H. +ve. Aged 46 and normotensive. Her father died at the age of 70 years from hypertensive heart disease. Her mother died at the age of 62 from gall bladder disease. One sister aged 53 has hypertension with a blood pressure of 175/115. One brother and one sister are alive and well.

CASE 49: F.H. -ve. Normotensive. No facts known to her as she is an orphan.

CASE 51: F.H. +ve. Aged 32 and normotensive. Mother died at the age of 60 from diabetes, hypertension and cardiac failure. Her father died at the age of 67 from a stroke and ? high blood pressure. Six sisters and 3 brothers alive and well.

CASE 53: F.H. -ve. Aged 28 and normotensive. Her mother aged 65 is alive and well. Her father died at the age of 50 from ? pneumonia. Three sisters are alive and well, 1 brother died as a child.

CASE 52: F.H. +ve. Aged 30 and normotensive. Her mother died at the age of 56 years from pulmonary tuberculosis. Her father died at the age of 73 years from hypertensive cardiac failure in Groote Schuur Hospital. One brother and 1 sister are alive and well and 1 brother and 1 sister died from tuberculosis.

CASE 55: F.H. -ve. Aged 25 and normotensive. Her mother aged 48 and father aged 59 years are alive and well. Her grandfather died at the age of 88 and grandmother at the age of 78 but cause of death unknown. Her two brothers and 2 sisters are alive & well.

CASE 56: F.H. +ve. Aged 30 and normotensive. Mother aged 49 has a blood pressure of 160/100, is obese and asthmatic. Father died at the age of 46 from a stroke. One of her aunts is said to have died from high blood pressure. Two younger brothers and 2 younger sisters are alive and well.

CASE 58: F.H. +ve. Aged 32 and normotensive. Mother died at the age of 70 years from gall stones, hypertension and cardiac failure./....

failure (confirmed). Father died at the age of 52 years ? cause. One sister aged 50 is said to have hypertension. Two brothers and 3 sisters are alive and well. One sister died as a child.

CASE 60: F.H. +ve. Aged 31 and normotensive. Mother aged 59 has hypertension and cardiac disability (confirmed Groote Schuur notes). Father died at the age of 45 years but the cause of death is not known. Three married sisters alive and well, 2 brothers alive and well.

CASE 62: F.H. +ve. Aged 23 and normotensive. Mother alive and well aged 55. Father aged 58 has hypertensive vascular disease (confirmed by private doctor). She has 9 sisters and 2 brothers alive and well.

CASE 65: F.H. -ve. Aged 46 and normotensive. Mother aged 68 and father aged 77 alive and well. Six sisters alive and well. Two brothers died as children.

CASE 66: F.H. -ve. Aged 34 and normotensive. This patient lost both her parents when young, apparently from tuberculosis. She is the only child.

CASE 67: F.H. +ve. Aged 25 and normotensive. Her mother is alive and well, 4 sisters and 1 brother alive and well. State of health of the father not known as he is divorced.

CASE 68: F.H. +ve. Aged 28 and normotensive. Father aged 67 alive and well, mother aged 57 has hypertension and cardiac failure (confirmed Groote Schuur Hospital notes). One sister aged 30 is stated to have had toxaemia and has high blood pressure. One sister and 3 brothers alive and well.

CASE 69: F.H. -ve. Aged 38 and normotensive. This patient could supply no details, she is an orphan.

CASE 70: F.H. +ve. Aged 37 and normotensive. Mother aged 67 was confirmed to be hypertensive, blood pressure 185/110. Father aged 70 is said to be hypertensive. Four sisters and 5 brothers are stated to be alive and well. One sister died as a child.

Case./.....

CASE 71: F.H. -ve. Aged 44 and normotensive. Her mother died at the age of 73 from a stroke and her father at the age of 74 with gangrene of the foot. There is no definite history of hypertension. Five brothers and 2 sisters are stated to be alive and well.

CASE 72: F.H. +ve. Aged 42 and normotensive. Her father died at the age of 52 years from dropsy. Her mother aged 73 years has a blood pressure of 170/100 mm. Hg. Three brothers and 2 sisters are stated to be alive and well. One sister died as a child.

CASE 73: F.H. +ve. Aged 35 and normotensive. Mother aged 54 is a diabetic with a raised blood pressure (confirmed Groote Schuur outpatients notes). Father died at the age of 50, cause of death unknown. She was an only child.

CASE 74: F.H. +ve. Aged 34 and normotensive. Mother aged 57 has a blood pressure of 190/110 mm. Hg. Father aged 67 alive and well. Three brothers and 4 sisters alive and well. One brother and one sister died young.

CASE 76: F.H. -ve. Aged 45 and normotensive. Father died at the age of 32 years from blackwater fever. Mother aged 68 said to be alive and well. Two brothers and 1 sister are stated to be alive and well.

CASE 77: F.H. +ve. Aged 46 and normotensive. Father died at the age of 73, he had a stroke at the age of 70 and again when he died. He was hypertensive (confirmed by private doctor). Mother alive and well aged 75. Three brotheramand 3 sisters are stated to be alive and well.

CASE 78: F.H. -ve. Aged 23 and normotensive. Both parents died young from causes unknown. She was an only child

CASE 81: F.H. +ve. Aged 24 and normotensive. Mother is a known eclamptic included in this series (S.de J.) and is a known hypertensive case. Two of her aunts are also known eclamptics. Her grandmother had eclampsia and died of hypertensive vascular disease. Her sister had eclampsia with her 1st child. Her father is alive and well.

Case./.....

CASE 82: F.H. +ve. Aged 24 and normotensive. Her mother had eclampsia and is a known hypertensive in this series. Her grandmother and two aunts had eclampsia vide case 81. Her sister case 81 also had eclampsia. Her father is alive and well.

CASE 83: F.H. +ve. Aged 36 and normotensive. Her mother suffers from angina pectoris and hypertension aged 59. Her father died of dropsy at the age of 65. Her 1 sister has mitral stenosis 2 sisters and 3 brothers alive and well. One brother and 1 sister died as children.

CASE 84: F.H. ? +ve. Aged 36 and normotensive. Her mother aged 65 years is stated to have hypertension and her father aged 63 is alive and well. She has 2 sisters alive and well. Two brothers died young. Cause of death of grandparents unknown.

CASE 85: F.H. +ve. Aged 46 and normotensive. Her mother aged 84 has had a stroke and suffers from hypertension. Her father died in coma aged 85 ? cause. She has 3 brothers and 2 sisters alive and well, and 1 sister stated to be hypertensive.

CASE 86: F.H. -ve. Aged 51 and normotensive. Her father aged 70 is said to have cerebral arteriosclerosis. Her mother died at the age of 68 from pneumonia, she was blind for 3 years. She is said to have had diabetes. This patient is a diabetic herself with cataracts and pulmonary tuberculosis. She is in the Westlake Sanatorium. She has two sisters and 3 brothers alive and well.

CASE 88: F.H. ? +ve. Aged 39 and normotensive. Mother alive and well. Father died at the age of 75 was said to have had asthma and high blood pressure. Three sisters alive and well. One sister died as a child.

CASE 89: F.H. ? +ve. Aged 28 and normotensive. Mother aged 54 alive and well, her father died at the age of 60 from cardiac failure and ? hypertension. She has 4 sisters and 3 brothers stated to be alive and well.

CASE 92: F.H. -ve. Aged 47 and normotensive. Father aged 73

alive./.....

alive and well. Mother aged 69 also alive and well. One brother and 1 sister alive and well.

CASE 94: F.H. ? +ve. Aged 52 and normotensive. Mother died at the age of 74 from a stroke. Father died suddenly at the age of 84 from his 'heart!' Three brothers and 1 sister alive and well.

CASE 97: F.H. +ve. Aged 34 and normotensive. Father died at the age of 47 from delirium tremens. Mother aged 56 has a blood pressure of 195/115 (confirmed personally). She has 2 sisters and 1 brother alive and well.

CASE 99: F.H. +ve, aged 38 and normotensive. Father died at the age of 53 from carcinoma of the stomach. Mother aged 70 years is a known hypertensive. One sister aged 50 years is said to be hypertensive. Six sisters and 4 brothers are alive and stated to be well.

CASE 100: F.H. -ve. Aged 38 and normotensive. Her father is alive and well, her mother aged 63 is in the mental hospital. There are 6 sisters and 3 brothers alive and well and no family history of hypertensive vascular disease.

APPENDIX II.

THE FAMILY HISTORY OF THE 100 NON-CONVULSIVE TOXAEMIAS FOLLOWED-UP

A. The family history of the 24 Normotensive Cases:

The following abbreviations will be used in this section:- F.H. +ve means a positive family history of hypertensive vascular disease. F.H. -ve means a negative family history of hypertensive vascular disease.

? Where the history is doubtful, a question mark sign will indicate this.

CASE 4: F.H. +ve. Coloured normotensive, age 43 at present. Her mother is aged 65 years and has a clinically confirmed hypertension. Blood pressure 175/110. Her father died at the age of 60 years. The cause of death is stated to be hypertension and a stroke. One of her sisters is a known hypertensive who had her eighth pregnancy terminated because of toxaemia. Five other sisters have all had children and are alive and stated to be well. One brother died at the age of 38 from Bright's disease, and another at the age of 43 is stated to have died from his "heart and kidneys". Two brothers are alive and well.

CASE 9: F.H. +ve. European normotensive, age 25 at present. Her father aged 57 years is stated to be hypertensive and mother aged 52 years is alive and well. Her aunt aged 55 suffers from hypertensive cardiac failure. Blood pressure 190/120 mm. Hg. No brothers or sisters.

CASE 10: F.H. -ve. Malay normotensive, age 41 at present. Mother aged 64 alive and well. Father died at age of 28 years from influenzal pneumonia in 1918. One brother and one sister also died as infants during this epidemic. One brother alive and well.

CASE 17: F.H. -ve. Coloured normotensive. Age 25 at present. Mother aged 50 years alive and well. Father aged 52 alive and well. Five sisters, 2 of whom have had normal pregnancies and,

three./...

three brothers, all alive and well.

CASE 18: F.H. +ve. Coloured, normotensive, age 28 at present. Her mother aged 59 has a blood pressure of 185/110. Her father aged 60 years and 4 brothers alive and well. One sister died young.

CASE 24: F.H. +ve. Coloured, normotensive, age 39 at present. Mother aged 62 has a blood pressure of 165/100 but is otherwise well. Her father is stated to have died at the age of 69 of a heart attack ? coronary thrombosis. She has 4 brothers alive and well and 1 sister who has had only normal pregnancies.

CASE 27: F.H. +ve. European, normotensive, age 40 at present. Mother aged 65 has a blood pressure of 185/100 and complains of headaches and shortness of breath. Her father, brother and sister alive and well.

CASE 29: F.H. +ve. European, normotensive, age 27 at present. Her father aged 55 is a hypertensive subject with a blood pressure of 185/105 mm. Hg. Her mother aged 53 is alive and well. Of her 2 sisters the one is multiparous, alive and well. No brothers.

CASE 30: F.H. -ve. Coloured, normotensive, age 40 at present. Mother aged 55, father 58 and 1 brother aged 19 all alive and well. Seven brothers and 1 sister died as children.

CASE 32: F.H. +ve. Coloured, normotensive, age 31 at present. Her mother aged 67 is a hypertensive subject with a blood pressure of 210/115 mm. Hg. Her father is stated to have died of dropsy at the age of 44. One sister died of congenital heart disease. Five sisters all had normal confinements, they are alive and well.

CASE 35: F.H. +ve. Coloured, normotensive, age 39 at present. Father died at the age of 40 from Miners Phthisis. Mother died of hypertensive cardiac failure in 1943 at the age of 48. Two sisters, both of who are multiparous, are alive and well. One sister died of tuberculosis.

CASE 39: F.H. ? -ve. Coloured, normotensive, age 35 at present.

Mother died at the age of 48 from carcinoma of the stomach. Father died at the age of 58 from tuberculosis. Four sisters alive and well, 1 of whom had toxaemia with her first pregnancy.

CASE 44: F.H. +ve. Coloured and normotensive. Aged 29 at present. Mother died of cerebral haemorrhage at the age of 60 with associated hypertension. Father died of cirrhosis of the liver at the age of 56. One brother is stated to be nephritic.

CASE 45: F.H. ?-ve. European. Normotensive. Age 35 at pregent. Her father at the age of 33, mother aged 31, both died from pneumonia in 1918. She has 4 married sisters alive and well. One sister died from tuberculosis.

CASE 46: F.H. +ve. European and normotensive. Age 36 at present Labile blood pressure. Mother aged 67 years is a known hypertensive with blood pressure 210/115 mm. Hg. Father alive and well. Four sisters alive and well, all of whom have had children.

CASE 51: F.H. +ve. Coloured. Normotensive. Age 40 years at present. Her mother died at the age of 60 years from coronary thrombosis and , according to the records at Groote Schuur, was hypertensive with a blood pressure of 170/100. Father aged 65 years is alive and well. One brother is alive and well and 1 sister died of tuberculosis.

CASE 60: F.H. -ve. European. Normotensive. Age 43 at present. Mother aged 65 alive and well. Father died at the age of 32 years of tuberculosis. No brothers and sisters.

CASE 65: F.H. +ve. Coloured. Normotensive. Age 45 at present. Her mother died at the age of 41 years from hypertension, blood pressure 220/120 mm. Hg. and a stroke. Her father died suddenly at the age of 60 years. Cause not definitely known. She has 3 brothers alive and well. Two sisters died as children. One daughter is one of the cases of eclampsia in the present series.

CASE 66: F.H. +ve. European, normotensive, at present aged 40 years. Her mother died of diabetic gangrene of the foot at the age of 53. She had hardened arteries and hypertension as well.

Her father died at the age of 93 from a stroke. Her mother died at the age of 70 from carcinome of the stomach. Her 1 sister had toxaemia with her 7th child. One other sister and 2 brothers are alive and well. One uncle on her mother's side died of hypertensive cardiac failure in Groote Schuur Hospital.

CASE 77: F.H. ? -ve. Coloured. Normotensive. At present 31 years. Has no contact with her family. Her father died when she was young ? cause. Mother, is alive, but lives up country. No details known about her family.

CASE 82: F.H. -ve. Coloured. Normotensive. At present aged 36. Mother alive and well, age 58. Father died at the age of 30 in an accident. One brother alive and well.

CASE 88: F.H. +ve. Coloured. Normotensive. At present aged 38. Mother aged 63, has had 3 strokes and a blood pressure of 230/120.mm. Hg. Father aged 65 alive and well. Two brothers both have tuberculosis. One sister alive and well.

CASE 99: F.H. +ve. European. Normotensive. At present aged 30. Mother died at the age of 63 from hypertensive cardiac failure. Blood pressure 240/120 at the time of death. Father died at the age of 26 from pneumonia. Two unmarried sisters alive and well. One brother died as a child.

SUMMARY:

Sixteen of the normal cases have a positive family history, i.e., 66.6%. Eight of the normal cases have a negative family history, i.e. 33.3%.

B. The family history of the 76 cases found to be hypertensive at the follow-up examination ;

CASE 1: F.H. +ve. Coloured. Hypertensive. At present aged 40. Her father died at the age of 50 years from apoplexy. Her mother died with the birth of her 13th child in the Peninsula Maternity Hospital from eclampsia. She has 3 younger sisters and 2 brothers alive and well.

CASE 2: F.H. +ve. Coloured. Hypertensive. At present aged 46. Her mother died at the age of 74 from a stroke and had a raised blood pressure. Father aged 80 alive and well. Two of her mother's sisters both died of strokes at the age of 56 years and 72 years respectively. She has 2 brothers alive and well, 4 died during childhood, her 3 sisters are stated to be alive and well. One of these had toxaemia with her first child and 3 sisters died whilst still children.

CASE 3: F.H. +ve. Coloured. Hypertensive. At present aged 47. Father died at the age of 76 years from pneumonia. Mother died at the age of 65 from a stroke and hypertension (confirmed by private doctor). Two sisters alive and well. One sister died as a child. Seven brothers alive and well.

CASE 5: F.H. -ve. European. Hypertensive. At present aged 34. Father aged 60 and mother 56 are both alive and well. Three unmarried sisters alive and well.

CASE 6: F.H. +ve. European. Hypertensive. At present aged 36. Mother died at the age of 62 years from a stroke and high blood pressure. Father died at the age of 58 years from gangrene of the left leg. One brother aged 37 is hypertensive. Five brothers are alive and well. One brother died of mitral stenosis and cardiac failure. Four sisters are alive and well.

CASE 7: F.H. +ve. European. Hypertensive. At present aged 43. Father died at the age of 54 years from a cerebral tumour. Mother died at the age of 68 from diabetes and hypertensive cardiac failure. Blood pressure 225/125 mm. Hg. She had toxaemia with 2

pregnancies./...

pregnancies, the one being triplets and the other twins. Four sisters alive and well, 1 of whom had toxaemia with her first child

CASE 8: F.H. +ve. Coloured. Hypertensive. At present aged 51. Mother died at the age of 50 years in 1918 from pneumonia. Father died at the age of 70 years from hypertensive cardiac failure, according to her sister who is a trained nurse. Three sisters a alive and well, 1 of whom is stated to have had toxaemia with her fourth child. Three brothers alive and well.

CASE 11: F.H. +ve. Coloured. Hypertensive. At present aged 49. Father died at the age of 83 from pneumonia. Mother died at the age of 73 from cerebral haemorrhage, blood pressure 261/130 mm.Hg. Two sisters died from tuberculosis, 1 sister is stated to be hypertensive at the age of 51 and had toxaemia with her fourth and last pregnancy which was a twin pregnancy. One brother at the age of 42 has intermittent claudication. Ten younger brothers and sisters died as children.

CASE 12: F.H. +ve. European. Hypertensive. At present aged 37. Father died at the age of 63 from hypertensive cardiac failure and diabetes. Mother died at the age of 79 from dropsy and hypertensive caridac failure. No brothers or sisters.

CASE 13: F.H. +ve. Coloured. Hypertensive. At present aged 45. Mother died of stroke at the age of 68. Father died from cerebral haemorrhage at the age of 63 in Groote Schuur Hospital, blood pressure 225/120. Three brothers and 2 sisters alive and well.

CASE 14: F.H. +ve. European. Hypertensive. At present aged 39. Mother died at the age of 54 from a stroke and high blood preasure. Her fatherdied at the age of 72 from secondary carcinoma of the liver. Five sisters alive and well, 1 had toxaemia with her second and last pregnancy and is stated to have high blood pressure now. One brother alive and well.

CASE 15: F.H. +ve. European. Hypertensive. At present aged 48. Mother died at the age of 78 from hypertension and arterial sclerosis and cerebral haemorrhage (confirmed by private doctor). Her

father./.....

father died from a coronary thrombosis at the age of 60. Three sisters alive and well. One sister died at the age of 30, puerperal sepsis.

CASE 16: F.H. +ve. Coloured. Hypertensive. At present aged 46. Mother died at the age of 40 with her 12th confinement from eclampsia. Her father died at the age of 50 years from cardiac asthma. She has 4 sisters alive and well. Two sisters and 6 brothers died as infants.

CASE 19: F.H. +ve. European. Hypertensive. At present aged 34. Mother died of hypertensive cardiac failure at the age of 55 years and had eclampsia with her first and second pregnancy. Her father aged 59, is alive and well. Her sister had eclampsia with her first pregnancy and hysterotomy and sterilization with her second pregnancy because of toxaemia. One other sister alive and well who had normal pregnancies.

CASE 20: F.H. +ve. European. Hypertensive. At present aged 39. Mother aged 65 attends medical outpatients department with hypertensive cardiovascular disease. Her father aged 68 alive and well. Three brothers alive and well.

CASE 21: F.H. +ve. European. Hypertensive. At present aged 29. Mother aged 60 years in good health. Father aged 67 a symptomatic hypertensive, blood pressure 180/100 mm. Hg. One sister had 2 children and toxaemia with them both.

CASE 22: F.H. +ve. Malay. Hypertensive. At present aged 50. Mother died of a stroke at the age of 70 years and her father at the age of 72 from cerebral haemorrhage. One sister and 3 brothers alive and well.

CASE 23: F.H. +ve. Coloured. Hypertensive. At present aged 50. Mother died of dropsy at the age of 65 years and is stated to have had hypertension. Father died from a heart attack at the age of 73. One sister died of a stroke at the age of 51 and had toxaemia with her last three pregnancies. Two sisters and 1 brother are alive and well.

Case./.....

CASE 25: F.H. +ve. European. Hypertensive. At present aged 57. Mother died at the age of 89 from hardened arteries and heart failure. Father died at the age of 80 from cerebral haemorrhage. One sister, aged 54, is stated to be hypertensive. One sister alive and well. One brother is stated to have hypertension. Three other brothers alive and well.

CASE 26: F.H. +ve. Coloured. Hypertensive. At present aged 36. Mother died of hypertensive cardiac failure at the age of 46 years and had toxaemia with her last 3 pregnancies out of a total of 8. Her father died of asthma at the age of 70 and was stated to be hypertensive. Six sisters are alive and well, one of whom had toxaemia with her first child. One sister died of tuberculosis.

CASE 28: F.H. +ve. European. Hypertensive. At present aged 46. Mother died with the birth of her second child ? postpartum haemorrhage at the age of 22. Father alive, aged 69, suffers from hypertensive cardiac failure, blood pressure 220/150 mm. Hg. One sister is alive and unmarried. Two younger stepbrothers and 6 stepsisters alive and well.

CASE 31: F.H. +ve. Coloured. Hypertensive. At present aged 52. Mother died at the age of 22 from cerebral haemorrhage. Her father died at the age of 60 from ? pneumonia. One brother is stated to have died from coronary thrombosis, at the age of 50 years. One only sister died from asthma.

CASE 33: F.H. +ve. Coloured. Hypertensive. At present aged 34. Mother died at the age of 72 from asthma and pneumonia and is stated to have had hypertension as well. Her father died of intestinal obstruction at the age of 50. One sister is alive and well. A sister and brother died as children from tuberculosis.

CASE 34: F.H. +ve. Coloured. Hypertensive. At present aged 56. Her mother died at the age of 65 from a stroke and had hypertension as well. She had toxaemia with 2 of the 3 pregnancies. Her father died at the age of 67 from dropsy. Her brother, aged 46, is stated to have Bright's disease. Her only sister died of pneumonia.

One./.....

One of her daughters is pregnant, and under treatment for toxaemia

CASE 36: F.H. +ve. European. Hypertensive. At present aged 37. Her father died of hypertensive cardiac failure at the age of 57 in Groote Schuur Hospital. Her mother died at the age of 27 from tuberculosis. Two brothers are alive and well.

CASE 37: F.H. +ve. Coloured. Hypertensive. At present aged 54. Her mother died of asthma at the age of 73 years. Her father aged 83 has chronic bronchitis and hypertension. Three sisters are alive and well. One sister died of peritonitis and another of carcinoma of the uterus.

CASE 38: F.H. ? +ve. Coloured. Hypertensive. At present aged 51. Her mother aged 76, is said to be alive and well. Her father at the age of 63 died from ? hypertensive cardiac failure in England. No brothers or sisters.

CASE 40: F.H+ ve. Malay. Hypertensive. At present aged 52. Her Mother died at the age of 65 from carcinoma of the uterus. Her father died at the age of 33 from cardiac failure, associated with hypertension. Blood pressure 190/95 mm. Hg. Four sisters are alive and well.

CASE 41: F.H. -ve. Coloured. Hypertensive. At present aged 31. Her father aged 54 has chronic bronchitis. Her mother died at the age of 29. She has no brothers or sisters.

CASE 42: F.H. -ve. Coloured. Hypertensive. At present aged 58. Her mother died at the age of 80 years from carcinoma of the stomach. Her father died at the age of 69. No brothers or sisters

CASE 43: F.H. +ve. Coloured. Hypertensive. At present aged 50. Her mother aged 73 has hypertensive cardiac disease associated with marked obesity. Blood pressure 240/120 mm. Hg. Her father died of congestive heart failure at the age of 60 but, it is not known whether he was hypertensive or not. She has 4 sisters and 6 brothers alive and well.

CASE 47: F.H. +ve. Coloured. Hypertensive. At present aged 48. Her mother aged 73 is blind from bilateral glaucoma and a known

hypertensive./....

hypertensive cardiac. Blood pressure 225/125 mm. Hg. Her father succumbed in a motor car accident at the age of 65. Her sister had eclampsia with her second child. Two other sisters are alive and well.

CASE 48: F.H. +ve. Coloured. Hypertensive. At present aged 53. Her mother died of cardiac asthma and hypertension at the age of 53. Her father died of carcinoma of the colon at 63. Her only sister is said to have hypertension at the age of 48 years.

CASE 49: F.H. ? +ve. European. Hypertensive. At present aged 48. Her father died of pneumonia in 1918. Her mother died at the age of 54 from pneumonia as well and is stated to have had repeated epistaxis and severe headaches which the private doctor put down to hypertensive vascular disease. No brothers or sisters. Cause of death of grandpertents not known.

CASE 50: F.H. +ve. Native. Hypertensive. At present aged 45. Her father died at the age of 40 years from ? coronary thrombosis. Her mother died at the age of 60 years from a cerebral vascular accident. One sister is alive and well.

CASE 52: F.H. +ve. European. Hypertensive. At present aged 53. Her father died at the age of 52 from broncho pneumonia. Her mother is alive and well. Her father's brother died at the age of 65 years from hypertensive cardiac failure at the Groote Schuur Hospital. Blood pressure 195/115. Her grandfather died of a stroke. Two brothers alive and well. Two sisters alive and well. The one has had two children with toxaemia on each occasion.

CASE 53: F.H. +ve. Malay. Hypertensive. At present aged 49. Her mother died at the age of 72 from dropsy and hypertension confirmed from notes at Groote Schuur Hospital. Blodd pressure 230/130. Her father died of carcinoma of the stomach at the age of 73. Three younger sisters alive and well.

CASE 54: F.H. +ve. Coloured. Hypertensive. At present aged 40. Her father died of pneumonia at the age of 67. Her mother died at the birth of the 3rd child, of toxaemia. One sister is a known hypertensive at the age of 42. Blood pressure 195/110 mm. Hg.

One./.....

One sister is alive and well.

CASE 55: F.H. +ve. European. Hypertensive. At present aged 52. Her father died at the age of 85. He was a known hypertensive with calcified arteries. Her mother was killed in the last war (1939 - 1945). No brothers or sisters.

CASE 56: F.H. +ve. Coloured. Hypertensive. At present aged 50. Her father is alive and aged 70, is known to be hypertensive. Blood pressure 210/110. Her mother suffers from arteriosclerosis aged 68. Two younger brothers are alive and well.

CASE 57: F.H. +ve. Malay. Hypertensive. At present aged 51. Her father died of diabetes, hypertension and coronary thrombosis at the age of 65. Her mother, aged 70, is alive and well. Two sisters and 3 brothers are alive and well.

CASE 58: F.H. +ve. European. Hypertensive. At present aged 40. Her mother, aged 70, is a known hypertensive attending the Provincial Hospital, Port Elizabeth. Her father died at the age of 60 from coronary thrombosis. Two brothers are alive and well. Two sisters are alive and well, one has had toxaemia twice.

CASE 59: F.H. +ve. Coloured. Hypertensive. At present aged 57. Her mother aged 76 is a diabetic, asthmatic, hypertensive with a blood pressure of 185/95. She is amazingly bright after having had 20 children. Her father died at the age of 62. He had diabetes and carcinoma of the stomach. One sister, aged 49, is stated to have high blood pressure with severe headaches. One sister aged 42, had toxaemia with her 10th child. One sister aged 37, had toxaemia with her 7th child. Four brothers are alive and well. Six brothers and seven sisters died as children.

CASE 61: F.H. +ve. Coloured. Hypertensive. At present aged 50. Her mother died at the age of 60 from asthma and pneumonia. Her father died at the age of 67 from cerebral haemorrhage and hypertension. A brother and sister died of pulmonary tuberculosis and 1 is suffering from tuberculosis at present. Three other sisters are alive and well. One of them had toxaemia with her 1st child and her eldest daughter again had eclampsia.

CASE 62: F.H. +ve. Coloured. Hypertensive. At present aged 39. Her mother died of hypertensive cardiac failure and diabetes at the age of 62. Her father is alive and a known hypertensive. Blood pressure 210/110 mm. Hg. Her brother died of subarachnoid haemorrhage at the age of 36.

CASE 63: F.H. +ve. Coloured. Hypertensive. At present aged 55. Her mother is stated to have died at the age of 74 from hypertensive cardiac failure. Her father died at the age of 70 from a stroke. One sister aged 49, is stated to be hypertensive. Two brothers are alive and well.

CASE 64: F.H. +ve. Coloured. Hypertensive and diabetic. At present aged 55. Her mother, aged 63, is asthmatic and hypertensive with a blood pressure of 210/115. Her father is alive and well, ag aged 74. Two brothers and 1 sister are alive and well.

CASE 67: F.H. +ve. European. Hypertensive. At present aged 44. Her mother died at the age of 61 from coronary thrombosis and hypertension. Her father died at the age of 77 from carcinoma of the colon. One brother died of cirrhosis of the liver. One sister is alive and well.

CASE 68: F.H. +ve. Coloured. Hypertensive. At present aged 38. Her mother died at the age of 65 following a second stroke. She was known to be a hypertensive. Her father died at the age of 60 years from coronary thrombosis. One sister aged 35 had toxaemia with her 10th child.

CASE 69: F.H. +ve. European, hypertensive, at present aged 48. Her mother is a known hypertensive aged 68 with a blood pressure of 200/115. Her father died at the age of 57 from myocarditis, bronchitis and asthma. Two brothers and 1 sister are alive and well

CASE 70: F.H. +ve. European, hypertensive, at present aged 48. Her mother aged 68 is alive and well. Her father aged 73 is alive and a known hypertensive with a blood pressureof 210/115 mm. Hg. One sister aged 40 years is stated to be a hypertensive. Two sisters and 5 brothers are alive and well.

Case./.....

CASE 71: F.H. +ve. Coloured, hypertensive, at present aged 43. Her mother died at the age of 52 from hypertension and coronary thrombosis. Her father died at the age of 65 from pneumonia. One daughter has had toxaemoa with her first child.

CASE 72: F.H. +ve. Coloured, hypertensive, at present aged 27. Her mother had toxaemia with her 8th and last pregnancy. She is now 52 and a known hypertensive. Blood pressure 180/110. Her father died of a stroke at the age of 60. Three brothers and 2 sisters are alive and well. Two sisters died during childhood.

CASE 73: F.H. +ve. Coloured, hypertensive, at present aged 33. Her mother aged 53 is a known hypertensive with a blood pressure of 170/100. Her father died of asthma at the age of 64. One sister died of rheumatic heart diesase at the age of 24. One sister aged 36 is stated to be hypertensive following toxaemia with her 5th child. One sister and three brothers are alive and well.

CASE 74: F.H. ? +ve. Coloured, hypertensive, at present aged 57. Her mother died of pneumonia at 49. Her father died of peritonitis at the age of 52 and was said to have been hypertensive. One brother aged 55 suffers from angina and hypertension. Three sisters are alive and well.

CASE 75: F.H. +ve. European, hypertensive and diabetic. At present aged 45. Her mother aged 67 is diabetic with peripheral neuritis and hypertension. Her father aged 69 suffers from gallstones, angina and hypertension. Four sisters are alive. One died of cardiac failure ? rheumatic heart.

CASE 78: F.H. +ve. European, hypertensive, at present aged 35. Her father, aged 70 is hypertensive, ith a blood pressure of 175/100 mm. Hg. Her mother, aged 65, is alive and well. One sister and 2 brothers are alive and well.

CASE 79: F.H. +ve. European, hypertensive at present aged 42. Her mother died at the age of 62 from diabetes and hypertensive cardiac failure. Her father died at the age of 60 from a 2nd stroke.

One./.....

One brother aged 50, is stated to be hypertensive. One brother and sister is alive and well.

CASE 80: F.H. +ve. Coloured, hypertensive, at present aged 41. Her mother aged 62 is alive and well. Her father died at the age 62 from cerebral haemorrhage. Blood pressure 230/120 mm. Hg. One sister aged 45, is stated to have hypertension.

CASE 81: F.H. +ve. Coloured, hypertensive, at present aged 53. Her mother died at the age of 24 from tuberculosis. Her father, presumed to be well, is aged 56. Her grandmother on mother's side died from a stroke and hypertension at the age of 76 years in Groote Schuur Hospital. One sister died suddenly from subarachnoid haemorrhage at the age of 27.

CASE 83: F.H. +ve. Coloured, hypertensive, at present aged 53. Her mother died of congestive cardiac failure and hypertension at the age of 53. Her father died at the age of 60 from cardiac asthma and coronary thrombosis. One sister is alive and well.

CASE 84: F.H. +ve. European, hypertensive, at present aged 42. Her mother, aged 74, has a blood pressure of 210/115, had had 18 pregnancies with toxaemia associated with the last two. Her father aged 76, is alive and well, except for bronchial asthma. One sister had toxaemia with her first child. Other brothers and sisters well.

CASE 85: F.H. +ve. Coloured, hypertensive, at present aged 53. Her mother died of hypertensive cardiac failure at the age of 70. Her father died of meningitis at the age of 40. One brother died of carcinoma of the colon.

CASE 86: F.H. +ve. European, hypertensive, at present aged 52. Her mother died in a diabetic coma at the age of 59 and was a hypertensive as well. Her father died of hypertensive heart disease at the age of 70. One sister is stated to have high blood pressure.

CASE 87: F.H. +ve. Coloured. Hypertensive. At present aged 44. Her mother died at the age of 81 from heart block and cardiac failure./.....

failure. Her father died at the age of 63 from hypertensive cardiac failure. One sister had eclampsia with her fourth and fifth pregnancies and died in the latter pregnancy.

CASE 89: F.H. +ve. Coloured. Hypertensive and diabetic. At present aged 46. Her mother, aged 68, has a bloodpressure of 175/100. Her father is alive and well. One sister died from uterine haemorrhage following an abortion. Four brothers died as children.

CASE 90: F.H. +ve. European. Hypertensive. At present aged 46. Her mother died at the age of 52 from intestinal obstruction. Her father died at the age of 68 from hypertensive cardiac failure. Three brothers and 3 sisters are alive and well.

CASE 91: F.H. ? +ve. Coloured. Hypertensive. Aged 49. Her mother died from causes unknown at the age of 69. Her father died at the age of 79 years from a stroke and high bloodpressure. No brothers or sisters.

CASE 92: F.H. +ve. European. Hypertensive. At present aged 47. Her father died from coronary thrombosis and hypertension at the age of 65. Her mother died at the age of 75 from hypertensive cardiac failure. Three sisters are alive and well.

CASE 93: F.H. +ve. Coloured. Hypertensive and diabetic, aged 57. Her father died of high bloodpressure and cardiac failure at the age of 65. Her mother is alive and well and aged 82. Her mother's sister died at the age of 70 from a stroke. One brother died of coronary thrombosis, at the age of 58, one from a stroke at the age of 51 and one died following an intercranial operation while another is alive and well.

CASE 94: F.H. +ve. Coloured. Hypertensive. At presen t aged 48. Her mother died at the age of 68 from a stroke and hypertension. Bloodpressure 230/120. Her father died of tuberculosis at the age of 50, one brother died of tuberculosis at the age of 20, while one sister is alive and well.

CASE 95: F.H. +ve. European. Hypertensive. At present aged 37.

Her mother died following her second stroke at the age of 58 and was a ? hypertensive. Her father died of coronary thrombosis at the age of 62, and had hypertension as well. Four sisters are alive and well. A fifth suffers from epilepsy since the age of 21.

CASE 96: F.H. +ve. European. Hypertensive. Aged 37. Her mother aged 60 is under treatment for hypertensive cardiac failure. Her father died suddenly at the age of 48. Cause of death unknown. Two brothers and two sisters alive and well.

CASE 97: F.H. +ve. European. Hypertensive. At present aged 37. Her mother aged 62 is alive and well. Her father aged 60 is a known hypertensive cardiac case with a bloodpressure of 220/110. One sister at the age of 31 is a chronic nephritic. The rest of the family normal.

CASE 98: F.H. ? neg.- Coloured. Hypertensive. Age 53. Mother died of tuberculosis at the age of 62. Father killed accidentally at the age of 50. Two sisters are alive and well. One sister had toxaemia with her 8th child.

CASE 100: F.H. neg.- Coloured. Hypertensive. At present aged 47. Mother and father alive and well, although this does not exclude a symptomatic hypertension. Two brothers and two sisters are alive and well.

SUMMARY.

Family history of abnormal cases = 76 cases.

66 have a positive family history.

5 have a doubtful/positive family history.

71 are taken to have a positive family history = 93.4%

5 have a negative family history = 6.5%

76 = 99.9%

APPENDIX 3.

The Detailed Histories of the Cases with Recurrent Eclampsia.

The following are the detailed features of the cases with recurrent Eclampsia:-

CASE 4. This patient gives no past history of pyelitis or nephritis and had three normal confinements with no rise in bloodpressure and one miscarriage before the first eclamptic pregnancy, at the ages of 22, 24, 25 and 26 years respectively. Her family history is negative from the point of view of a hypertensive vascular tendency, but she had a diabetic family history and has always been obese. With the first eclamptic attack at the age of 27 years her bloodpressure and urine were normal until the 39th week, but she had oedema of the feet from the 34th week and three postpartum fits. She then had a miscarriage followed by another eclamptic pregnancy at the age of 29 years, with symptoms from the 36th week for three weeks, and intrapartum fits. Since then her blood pressure and urine has been normal except with two subsequent toxaemic pregnancies, when she again had symptoms for the last seven weeks in each case. In the last two years she has developed diabetes mellitus. Can one explain the recurrence of eclampsia in her case on the basis of hypertension and occult diabetes as an aggravating factor? I doubt this, as she has a bloodpressure of 110/70 now at the age of 31, with a fasting blood sugar of 145 mgm. %. percent. However, in view of her diabetes she is likely to become hypertensive in years to come, but can this hypertension which will manifest years later be responsible for the recurrent eclampsia? Niether Dieckmann nor Browne's hypotheses hold water in this case and some other factor or factors must be responsible.

CASE 32. She had eclampsia with her first pregnancy at 32 weeks eight years ago at the age of 20 years. Her bloodpressure was normal before this and is normal now. Her second pregnancy, one year later, was complicated by toxaemia, so was the third, fourth, and fifth. This last one was again eclamptic at 28 weeks. It is of interest that she has pseudopapilloedema, which was wrongly interpreted. She has a positive family history of hypertensive vascular disease and is now 28 years old with a bloodpressure of 110/75 mm. Hg. Can the events be explained on Dieckmann's or Browne's hypothesis? I suppose on flimsy grounds it could be argued, in view of her family history, that a hypertensive tendency exists, only manifesting itself during pregnancy, and thus predisposing to toxaemia and fits. However, I feel that some other factor or factors operated.

CASE 43. A Malay, who has had eclampsia five times. The first attack at the age of 28, the second at the age of 29. During this period the state of her bloodpressure and urine was not known. However, since then her bloodpressure was always found to be below 130/80 mm. Hg. in between pregnancies. Inspite of this, her next three pregnancies ended in eclampsia with toxaemic signs in the last trimester on each occasion, and on discharge from hospital after the fifth pregnancy, her urine and bloodpressure were normal. In the interval, during the last four years, she has become manifestly hypertensive and a permanent epileptic. In addition a family history of hypertension has become evident. The first four pregnancies were from her first husband, who died, the fifth from her second husband. Here again, it could be argued that a latent hypertensive tendency only manifest in the last trimester of each pregnancy, was the cause of the toxaemia and eclampsia. However, this cannot be proved or disproved, and it seems likely that other factors could also have operated.

CASE 16. Her first four confinements were normal with no rise in bloodpressure, oedema or albuminuria, at the ages of 18, 20, 22 and 25 respectively. Her fifth confinement, at the age of 27, ended in eclampsia preceded for four weeks by oedema and a raised

bloodpressure, and albuminuria for two days. The fifth occurred immediately postpartum. The next pregnancy under hospital supervision, was completely normal. With the seventh pregnancy there was a rise in bloodpressure in the first twelve weeks, which disappeared, and at 36 weeks she had intrapartum eclampsia with oedema and bloodpressure of 130/80 and albuminuria. This was a twin pregnancy. Her subsequent three pregnancies have all been normal. She has a positive family history of a hypertensive vascular tendency, and now, at the age of 40 years, manifest hypertensive vascular disease. Could one explain the recurrence of eclampsia in this case on a hypertensive vascular basis? This is difficult especially in view of the fact that she had a normal pregnancy between the two eclamptic attacks and three subsequent normal pregnancies. One would expect a hypertensive tendency to be a constant factor if present. Possibly the twins, a known association of toxaemia, was a factor, but could not have been the only factor, as it does not explain the first eclamptic attack, which was a singly pregnancy. Neither Browne's nor Dieckmann's hypothesis holds and other factors, unknown to us, must have been operating.

CASE 28. Her first three confinements were normal at full term at the ages of 17, 18 and 20 respectively. Her fourth pregnancy at the age of 27 ended in intrapartum eclampsia at full term, with a stillbirth, after four weeks of pre-eclamptic toxaemia. Her fifth pregnancy at the age of 28 years was complicated by toxaemia and a stillbirth near term, and so was the sixth. The 7th, 8th, 9th, 10th, 11th and 12th were normal at term. With the 13th pregnancy her bloodpressure became elevated in the first trimester and she later had toxaemia with a premature stillbirth. The fourteenth and last pregnancy was again associated with a raised bloodpressure throughout pregnancy with superadded toxaemia in the last 3 weeks and terminating in a premature stillbirth with eclampsia at the 35th week. Her bloodpressure was raised between the 13th and 14th pregnancies, and since then the manifest hypertension has been at a higher level. She is now postmenopausal with

a doubtful positive family history of hypertensive vascular disease, and suffers from bronchial asthma for the last four years. I believe that she was hypertensive and that this may have been a factor in the production of recurrent eclampsia as stated by Dieckmann and Browne.

CASE 61. A Malay - with her first pregnancy at the age of 24 ending in a premature alive birth at 32 weeks with toxaemia from the 28th week. The second pregnancy was eclamptic with symptoms from the 28th week and ending near term with a stillbirth and postpartum eclampsia. At the age of 25 her third pregnancy was again toxaemic from the 34th week, but ended in an alive birth at term. The fourth, at the age of twenty-nine, was toxaemic for three weeks and ended in an alive birth at full term. The fifth at the age of thirty-one, again toxaemic from the 36th week, ended at full term with an alive birth. Between all these pregnancies her bloodpressure was normal. She then had her sixth pregnancy ending in eclampsia, at 33 weeks her bloodpressure was 120/80, and when delivered at 37 weeks 220/140. The infant died in the neonatal period. Since then her bloodpressure has been raised in between pregnancies and her seventh, eighth and ninth pregnancies were all complicated by toxaemia near term. She has a family history of hypertensive vascular disease and is now 39 years old and suffering from manifest essential hypertension. She may thus fit into Dieckmann's hypotheses as the hypertensive vascular disease became manifest with the second eclamptic attack, and has been persistently present since. Her Wassermann reaction is positive, but I do not think that this is a factor, as she has had adequate therapy right from the first pregnancy, and has no stigmata clinically.

CASE 68. An eighteen year old coloured girl - with her first pregnancy she had eclampsia with an alive birth at full term after two weeks of preceding toxaemia. Her second pregnancy, at the age of 25, was complicated by toxaemia from the thirtieth week, and again ended in eclampsia at term with an alive birth. Her third pregnancy at the age of twenty-eight years, was again complicated by toxaemia

from the thirtieth week, and again ended in eclampsia at term with an alive birth. Her third pregnancy, at the age of twenty-eight years, was again complicated by toxaemia from the 34th week and ended in an alive birth at term. She has a positive family history of hypertensive vascular disease and had pyelitis at the age of fifteen, which has not recurred. Her bloodpressure was known to be normal between her pregnancies. She is now 28 years old and normotensive. Has she developed recurrent eclampsia on the basis of a hypertensive vascular tendency as Browne and Dieckmann believe, or was it due to other factors?

CASE 79. A Malay - her first pregnancy occurring at the age of 19 was at full term and ended in an alive birth without any toxaemia. Her second pregnancy ended in postpartum eclampsia at the age of twenty near term with one week's history of pre-eclamptic toxaemia. Her third pregnancy, at the age of 22, was complicated by toxaemia in the last eight weeks, so was the fourth at the age of 23 years, and both the fifth and the sixth at the ages of 26 and 28 years respectively were similarly complicated by toxaemia near term. The state of her bloodpressure between these latter pregnancies is not known to me. With her seventh pregnancy at the age of 29 years, she had post-partum eclampsia at term, preceded by four weeks of toxaemic symptoms. Six months after this, her bloodpressure was 120/80 and her urine normal. Her eighth pregnancy at the age of thirty-one was a normal hospital confinement. With the ninth she had toxaemia for the last three weeks, but delivered at term at the age of 33. The tenth at the age of 35, the eleventh at the age of 37, the twelfth at the age of 38 and the thirteenth at the age of 40, as well as the fourteenth at the age of 41 and the fifteenth at the age of 44, were all toxaemic and delivered near term after a few weeks of symptoms. The sixteenth was premature at 34 week with preceding toxaemia for six weeks. Her bloodpressure has been known to be raised above 140/90 mm. Hg. in between the last eight pregnancies. She is now 49 years old and manifestly hypertensive with bronchial asthma, and has a positive family history of hypertensive vascular disease. In this case Dieckmann's hypothesis is unlikely

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to be correct, because it will not explain the normal fullterm eighth pregnancy. This, in fact, is the type of case to be considered when one wants to explain all the features by any theory. Is it possible for a hypertensive tendency to manifest in one pregnancy and not in another?

CASE 80. A Malay, who at the age of 17 years with her first pregnancy had intrapartum eclampsia preceded by toxaemia for one week with an alive birth at term. Her second pregnancy at the age of 19 ended at term but was preceded by toxaemia for three weeks and complicated by postpartum eclampsia. She had an alive birth. At the age of 21 her third pregnancy ended with two weeks of toxaemia before termination at 40 weeks with an alive birth. The fourth at the age of 23 years was normal, so was the fifth at the age of 27, the sixth at the age of 29, the seventh at the age of 36 and the 8th at the age of 37. These were fullterm pregnancies. She is now 39 years old and known to be hypertensive for the last twelve months with a positive family history of hypertension. Again, does Dieckmann's hy: hypothesis hold in this case, especially in view of the fact that the last five pregnancies were normal? I am inclined to think that other factors were operating which led to a recurrence of eclampsia.

CASE 91. A European who had a miscarriage at the age of 32 years with a bloodpressure of 110/65 at this time, and with her second pregnancy, at the age of 32 preceded by one week of toxaemic signs at term an alive birth with postpartum fits. Her third, fourth and fifth pregnancies were all full term normal ones and the sixth was complicated by a raised bloodpressure in the last trimester at the age of 42 years. Since this time her bloodpressure has been raised, and with the 7th pregnancy in the first trimester her bloodpressure was raised, but normal in midpregnancy, with a secondary rise in the last trimester and superadded toxaemic signs ending in intrapartum eclampsia at term with a stillbirth. She has been hypertensive since and is now aged 61. The family history is

negative from the point of view of a hypertensive vascular disease. This is one of the cases where Dieckmann's and Browne's hypothesis prove true with eclampsia recurring in a hypertensive subject.

In all the above cases other causes of convulsions besides eclampsia in pregnancy can be excluded. Even in Case 61 who had a positive Wassermann reaction this can be excluded as the cause of fits as she had repeated treatments with each pregnancy from her first.

APPENDIX 4.

Eclamptic cases followed up and found to have proteinuria, as estimated by the sulpho-salicylic acid method.

The following is a brief summary of the history of the 5 cases with proteinuria.

Case 47. A Malay at present aged 21 with hypertension and albuminuria and a positive family history of hypertensive vascular disease on her father's side. In addition both her parents are diabetic. Her first pregnancy at the age of 16 years was complicated by toxaemic signs from the 30th. week, but in spite of rest and diet at 34 weeks she had antepartum eclampsia with a blood pressure of 160/110 mm. Hg. which was 140/80 on discharge from hospital with persistent albuminuria. Six months later her blood pressure was 140/85 with albumen a trace. One year later at the age of 17, with her second pregnancy, at the seventh month, she had a re-exacerbation of symptoms with toxaemia, and delivered at 36 weeks. With her third pregnancy at the age of 19 she had similar signs in the last eight weeks before term. She delivered a premature infant at 35 weeks who died in the neonatal period. Her blood pressure rose to 175/130 mm. Hg. with marked albuminuria and oedema. At the follow-up examination which was two years later although symptomless except for general lassitude, her blood pressure was 140/100.mm. Hg. proteinuria 5 grams per litre with a specific gravity fixed at 1010 on three occasions. A pyelogram however revealed no abnormality and the blood urea was 37 mgm.%. However, there were no retinal changes and no radiological evidence of cardiomegaly. Her weight/height ratio was 2.14, her haemoglobin 12.5 grams percent and her P.C.V. 40%. Microscopy of the urine showed granular casts and transitional epithelial cells only. While being investigated she became pregnant once more and could not be investigated for further renal studies as she was not co-operative and in view of the pregnancy.

The question in this case is to decide whether she was a

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nephritic or if her vascular renal manifestations were the result of the eclampsia, and subsequent toxaemias with delayed healing. It was felt that with the data on hand one was not able to finalise this issue.

Case 50. A European female whose first pregnancy at the age of 34 years ended in a miscarriage at 3 months. Her blood pressure at this time was 125/80 mm. Hg. and she was obese. Her second pregnancy at the age of 39 was complicated by hypertension after the 20th week, rising to a level of 230/120 mm. Hg. at the 35th. week with marked albuminuria and oedema, and culminating in antepartum fits. She was delivered by Caesarean section of an alive baby. Her blood pressure on discharge was 270/120 mm. Hg. with albumin a trace in 1944. In 1952 at the age of 47 she is obese with weight/height ratio of 3.22 and complaining of dyspnoea on exertion. Her blood pressure was 220/140 mm. Hg. with a grade 2 retinopathy. However, her urine showed a maximum concentration of 1021 and a minimum concentration of 1005 with albumen a trace and her blood urea was 33 mgm. %. Pyelogram revealed no abnormality, but a Roentgen photograph of the chest revealed definite cardiomegaly. In addition there was a positive family history of hypertensive vascular disease. The diagnosis of hypertensive vascular disease with its onset at the time of the eclamptic pregnancy with some degree of remission following this and now progressive hypertension with some renal vascular damage appears the most likely in her case.

Case 54. A European aged 35 at present with a family history of hypertension and pyelitis at the age of 16 years, had her first pregnancy at the age of 19 years. This was a normal full term confinement with an alive birth and at 20 weeks a recurrence of the pyelitis. Her second child at the age of 21 years was born at full terms, alive, and the pregnancy was uneventful, With a blood pressure of 120/80 mm. Hg. as the highest recording. With her third child at the age of 27 years in 1945 she started with oedema at the 28th week and was found to be hypertensive with a reading of 200/110 mm. Hg. and within a few days in spite of

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treatment in bed developed ante-partum eclampsia with a highest blood pressure of 180/125 mm. Hg., marked oedema and albuminuria. A Caesarean section was performed at this stage (29 weeks) and a premature 3 lbs. baby born, that died the next day. She had retinal oedema and exudates with hyaline and granular casts and red cells in the urine. Two weeks later she was albumen free with a blood pressure of 160/110 mm. Hg. Six months later she had a trace of albumen and a blood pressure of 170/100 mm. Hg. At follow-up examination, six years later, her blood pressure is still 230/140 mm. Hg. and her weight/height ratio 2.5. She had grade 2 retinopathy and radiologically a cardiomegaly with an unfolded aorta. The maximum concentration of her urine was 1023 and the minimum concentration 1008. Pyelography was normal and no growth of bacilli obtained from a catheter specimen of urine. Her blood urea was 32 mgm. %. She is another example of hypertensive vascular disease becoming manifest after eclampsia with some renal vascular involvement.

Case 57. A European aged 51 at present with a family history of hypertensive vascular disease. She had her first pregnancy at the age of 23 years at full term, normal and uneventful, with antenatal care. The second, at the age of 25 years, as well as the fourth at the age of 27, were likewise full term and normal. The third was a miscarriage at 8 weeks, when she was 26 years old, from causes unknown. Her fifth pregnancy, at the age of 30 years, was normal until the 30th week when toxaemic signs arose. At the 34th week in spite of diet and rest she had ante-partum eclampsia with a premature infant who died in the neonatal period., Since this time her blood pressure has been raised and during pregnancy a further rise with albumen occurred as well as some minimal oedema. Thus, with the 6th pregnancy, this occurred at the 34th week and labour was induced at the 37th week, with an alive birth. The seventh pregnancy, at the age of 41 years was characterised by a fall of the blood pressure in the middle trimester to 130/80 mm. Hg., but at the 35th week was 165/100 mm. Hg. and two weeks later 210/130 mm. Hg., with marked proteinuria and some oedema. She was induced and

5 lb. 4 oz. alive child born. Her blood pressure on discharge was 180/120 mm. Hg. with a trace of albumen. This was in 1942. Ever since then she has been a known hypertensive, but since 1949 she has been under treatment because of symptoms and in 1951 had a proven attack of coronary thrombosis with electrocardiographic changes. Since then she has been living a very quiet life, resting almost half of each day, and complains of tiredness, dyspnoea on minimum exertion and has had some oedema which was treated with mersalyl injections. On examination at the follow-up, her blood pressure is 190/120 mm. Hg., and she has a grade 2 retinopathy and a cardiomegaly confirmed radiologically. The maximum concentration of the urine was 1019 and minimum concentration 1005, with proteinuria a trace, but no formed elements on microscopy. Her blood urea was 33 mgm. % and pyelogram normal. Her weight/height ratio was 2.8. In view of her symptoms and a raised venous pressure of + 2 cm., one can conclude that she has hypertensive vascular disease with signs of cardiac failure and some renal involvement, which again became manifest after the eclamptic fifth pregnancy at the age of 30 years.

Case 98. A Coloured aged 48 years at present with a family history of hypertensive vascular disease and a familial incidence of eclampsia. Her first pregnancy at the age of 23 years was a full term uneventful normal one with an alive birth and antenatal care. The second, at the age of 25 years, the third at the age of 26 years, and the fourth at the age of 34 years, were all similarly full term normal with alive births and normal blood pressure and urine. With her fifth pregnancy at the age of 42, when seen at two months she was normal, and her blood pressure 120/75 mm. Hg. At the 30th. week, when seen again for the first time, she had headaches and a raised blood pressure and oedema, but in spite of rest and diet, developed ante-partum eclampsia within four days and had a stillbirth. This was in 1946. Unfortunately she did not attend a post-natal clinic and was only seen with her sixth pregnancy when 20 weeks, because of oedema and headaches since the 18th week. She was found to have a blood pressure of 170/110 mm. Hg. and two flame-shaped retinal haemorrhages. A few days later her blood pressure had risen

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to 220/120 mm. Hg., albuminuria had increased and oedema was generalised, so that a surgical induction was done and she delivered a 1 lb. 12 oz. stillborn child. Three weeks later, on discharge, her blood pressure was 170/100 mm. Hg. and albumen free. She was not seen again since then (1947) until the time of the follow-up examination in 1952. Her weight/height Ratio was found to be 2.78 and she has been asthmatic for four years. She complained of dyspnoea on severe exertion and had a clinical cardiomegaly confirmed radiologically with a grade 2 retinopathy. In addition to a trace of albumen, the maximum concentration of the urine was 1024 and the minimum concentration 1008. The blood urea was 30 mgm.% and nil abnormal was found on microscopy. A pyelogram was not done, but no growth was obtained from a catheter specimen of urine examined bacteriologically.

The diagnosis in her case on clinical grounds is again hypertensive vascular disease with the trace of proteinuria pointing to some renal vascular involvement.

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