IMMINENT ECLAMPSIA.

THE CLINICAL STATE

AND

THE TREATMENT WITH AVERTIN

OF

100 CASES.

A

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IMMINENT ECLAMPSIA.

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INTRODUCTION.

The term eclampsia is derived from the Greek eklampien meaning a flash, and its etymology suggests the acute onset of the convulsions. On the surface, therefore, it would appear paradoxical to define any state as being one of "imminent eclampsia". However, although the aetiology is unknown, sufficient knowledge of the preceding history and manifestations of eclampsia has accumulated to justify such a specific term. In a subsequent chapter, these symptoms and signs will be assessed and discussed in detail.

Where the net of antenatal care is widespread and where such services are accepted and utilized by all who are pregnant in a community, the incidence of severe toxaemia and eclampsia is minimal. Few obstetricians in highly developed, civilized areas are afforded the opportunities for studying and treating any large numbers of cases of imminent eclampsia. In 1955 in Great Britain, Keller[82] who was leading a discussion on this subject, said "that none of us has had the opportunity of carrying out any sort of real clinical trial of the various methods, say, of inducing normotension."

In Cape Town antenatal care is available for all sections of the population. Ignorance, lack of fares for transport and occasionally superstition, are some of the reasons why these facilities are not used, or only occasionally used, by many pregnant women. As a result, severe toxaemia of late pregnancy is relatively frequently seen.

A study of the Clinical Reports of the Department of Obstetrics of the University of Cape Town for the year 1953 to 1959[164-169] inclusive, showed that in cases of eclampsia many patients have their first convulsion whilst in hospital. (Table 1).

TABLE 1.

Year.	Cases of Eclampsia.	First convulsion in hospital	
		Number.	Percentage.
1953	47	19	40
1954	54	23	43
1955	53	29	55
1956	41	16	39
1957	35	23	66
1958	37	19	51
1959	44	21	48
Total	311	150	48

The table indicates that approximately half the cases of eclampsia seen over a seven year period had a first convulsion while in hospital. The majority of these patients presented signs and symptoms of sufficient severity to forewarn of the impending convulsion. A logical conclusion, therefore, is that these manifestations were not correctly assessed or that if correctly assessed the treatment administered was inadequate, ineffectual or both. A retrospective review of these 150 cases of proven imminent eclampsia was considered but abandoned for the following reasons:

1. Retrospective surveys produce fewer and less conclusive findings than prospective surveys.

2. The clinical records of individual cases may be missing or may contain insufficient data.

3. A planned programme of management to include a method of relieving angiospasm would not be possible.

During the seven years 1953 to 1959, the treatment of severe toxaemia of late pregnancy was almost without exception by means of sedatives.

From the aforegoing the impression may have been gained that the problem of imminent eclampsia as recorded by the number of first convulsions occurring in hospital, was greater in Cape Town than in other centres. Table 11 (page 3) reveals that a similar picture is prevalent in many other centres throughout the world. Table 11 was compiled from a random selection of clinical reports of different maternity units and from a personal communication.[59]

TABLE 11.

Country	Hospital.	Year.	Cases of Eclampsia	1st Convulsion in hospital	
				Number	Percentage.
England	Queen Charlotte's[135,59].	1949-1958	41	41	100%
England	Princess Mary Maternity[134].	1957	6	2	33⅓%
New Zealand	Department of Obstetrics University of Otago[170]	1955	3	1	33⅓%
England	Liverpool Maternity[98]	1954	2	1	50%
Australia	The Royal Women's, Melbourne.[161]	1955	26	16	61%
Scotland	Royal Infirmary, Edinburgh[151]	1957	9	7	78%
Uganda	Makere College Medical School[103]	1956-1958	17	8	47%
England	Kingston Hospital[91]	1958	5	2	40%
Ireland	Rotunda[138]	1959	7	7	100%
		Total	116	85	73%

On the figures as shown in Table 11, which are all of fairly recent origin and taken from scattered areas on three continents, 73% of cases of eclapmsia have their first convulsion while in hospital. (More recent clinical reports available have been published in an abridged form and this particular facet of eclampsia is not revealed.) The figures from Cape Town and those in Table 11, provide a sufficient justification for this survey. A pertinent statement by the late W. J. Dieckman[46] is worth repeating:- "if the maternal and foetal mortality are to be kept at a low rate, a plan of procedure for all obstetric complications is necessary, and particularly for the patient with eclampsia and severe pre-eclampsia."

The Prospective Survey.

It was decided that a prospective survey of one hundred successive cases of "imminent eclampsia" treated in part by means of tribromoethyl alcohol (Avertin), should be undertaken. Criteria for the severity of the toxaemia in those patients who were to receive avertin were defined. As it was expected that the majority of patients in the survey would be non-booked admissions, it was agreed that no attempt would be made to classify which specific toxaemia of late pregnancy was present prior to the commencement of therapy. Patients less than 28 weeks' pregnant are not usually accepted for admission to the maternity units of the Department of Obstetrics of the University of Cape Town. This survey includes, therefore, only a few cases where the foetus was not viable. The foetal heart was heard in all cases at the time treatment was commenced. These latter two points were emphasised for two main reasons:- (i) it was intended that there should be no correction of foetal figures, and (ii) it was intended that a critical analysis of the effects of avertin on the individual symptoms and signs of imminent eclampsia should be made. Following upon intrauterine death of the foetus, these symptoms and signs usually improve and if such cases had been included in the survey, the assessment of the effects of avertin would have been prejudiced. Apart from the foetus being alive when the patient was first seen, the survey was conducted on an unselected series of cases of imminent eclampsia.

The survey was conducted over a period of 17 months and lasted from April 1960 to August 1961. The majority of the patients were treated in the Peninsula Maternity Hospital, Cape Town. There were 3 exceptions, all of whom were initially treated in their own homes by the "Flying Squad" of the Peninsula Maternity Hospital. The hospital treatment of these three patients was conducted one each in St. Monica's Home, New Somerset Hospital and Karl Bremer Hospital. The reasons for the inclusion of these three patients will be discussed in a later chapter.

Decisions which influenced the selection of avertin for the management of these cases were:-

(i) that it would be most satisfactory to have a single therapeutic regime for both hospital and initial domiciliary treatment,

(ii) that the treatment should be simple and sufficiently easy for one person to administer,

(iii) that it should be safe for both mother and foetus, and

(iv) that it should effectively relieve angiospasm and so lower the blood pressure.

Personal experience and the experiences of others[40,27,36,58,119], with avertin in the treatment of eclampsia, had shown that this drug fulfilled many of these requirements; particularly that it was safe to use in the patient's own home.

It is the practice of the Peninsula Maternity Hospital to send the "Flying Squad" out to supervise the initial treatment and transportation to hospital of cases of "imminent eclampsia". Many of the calls are to homes where washing and sanitary facilities do not exist, where candles supply illumination and where the whole structure is made up of galvanized iron strips wired together. The patient, if not lying on the floor amid a pile of blankets, lies almost buried in an old tumbledown bed. This description has been inserted to indicate that conditions for the domiciliary treatment of very ill patients are anything but ideal, and so of necessity influence the choice of therapy.

The actual treatment of the individual patients was carried out by a number of different people, but with the exception of five cases, all were seen by the author at some stage during their stay in hospital; and in the majority, prior to delivery.

The co-operation of the following persons made this survey and thesis possible and to all of them go my grateful thanks.

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IMMINENT ECLAMPSIA.

Pre-eclamptic toxaemia is a disease of unknown aetiology, characterized by the appearance of hypertension (140/90 mm of Hg or more), albuminuria and oedema, usually occurring after mid-pregnancy. It is generally accepted that any two of these signs is sufficient to make the diagnosis.

Essential hypertension can be diagnosed in a pregnant woman seen before the twentieth week of gestation who has a blood pressure of 140/90 mm of Hg. or more. In those patients seen after the twentieth week of gestation, the problem is more difficult and a post partum follow up of at least six months is usually necessary before a definite diagnosis can be made.

Unless a patient is seen in the early months of pregnancy, it is on clinical grounds, often impossible to place into a specific category of diagnosis a patient seen for the first time with hypertension and proteinuria in the third trimester of pregnancy. Throughout this thesis, therefore, the terms "imminent eclampsia" and "severe toxaemia of late pregnancy" will be used as including any one, or combination of, the following conditions:-

Pre-eclamptic toxaemia
Essential hypertension or hypertensive vascular disease.
Essential hypertension with superimposed pre-eclamptic toxaemia.
Chronic nephritis.

The Clinical State of Imminent Eclampsia.

No definition watertight to exception is possible, as the convulsions of eclampsia may occur without any warning symptoms and with the minimal of warning signs. Such cases are, however, rare.[22] In a consecutive series of 49 cases of eclampsia seen at the same time as this survey, Craig[36] found evidence of the impending fit in the known pre-convulsive history and findings in all cases. Oosthuizen[125] who studied the toxaemias of late pregnancy in the City of Cape Town, wrote as follows:- "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". Clayton and Oram[30] state that every case of eclampsia personally known to them, had some warning sign the previous day. Salerno[140] notes that only rarely does a patient manifest an eclamptic fit without preceeding signs of developing pre-eclamptic toxaemia.

It is to be expected, therefore, that the majority, if not all, cases of eclampsia will have a common pre-convulsive clinical picture. It is this state which is known as "imminent eclampsia" or "severe toxaemia of late pregnancy."

Symptoms.

The symptoms include all or any of the following:-

Severe headache, usually frontal in type.
Visual disturbances, including blurred or double vision and spots or flashes before the eyes.
Vomiting.
Epigastric pain.
Oliguria.
Muscular twitching.
Irritability.
Occasionally jaundice.

The majority of these symptoms are the sequelae of a generalised arterial hypertonus and the effects of the latter upon the kidneys, liver and other organs. The occurrence of a generalized oedema may also cause some of the symptoms.

Symptoms may or may not be present in every case; but when present they are universally accepted as specifically indicating imminent eclampsia.[82,39,45,97,3.]

Signs.

There is less uniformity concerning the signs that should be accepted as signifying imminent eclampsia or severe toxaemia.

Dieckmann[45] defines a case of severe pre-eclampsia as one in which -

(a) two or more of the following signs are present: repeated systolic blood pressures of 160 or more and diastolic pressures of 100 mm of mercury or more, proteinuria of more than 3.0 Gm. per 24 hours (3 plus), or marked oedema,

(b) at least one of the following signs is present: repeated blood pressures of 180/115 mm of mercury or more, proteinuria of 5.0 Gm. per 24 hours (solid), or generalized oedema, or

(c) one of the signs listed in (a) occurs together with the development of marked cerebral, visual, gastro-intestinal or renal symptoms.

The above definition, except for (c), is exactly the same as that given by the American Committees on Maternal Welfare as quoted by Pankamaa et al.[127] Kellar[82] considers eclampsia to be imminent where

(a) the blood pressure is greater than 160/110 mm of mercury,
(b) oedema is widespread,
(c) albuminuria, often of a severe degree, is present,
(c) symptoms of oliguria, headache, visual disturbance, vomiting and epigastric pain, perhaps jaundice and occasionally muscular twitching, may also be present.

The definition of Kellar is the one stated in the Clinical Reports of the Simpson Memorial Pavilion of the Royal Infirmary, Edinburgh.[151]

Townsend of Melbourne[162] like Dieckmann and Kellar, has made a special study of hypertension in pregnancy. He believes eclampsia to be likely where the systolic blood pressure is greater than 160 mm of mercury and the urine, after standing for one hour, is half solid with protein.

de Soldenhoff[39] classifies as severe toxaemia those patients who have a maximum blood pressure of 160/100 mm of mercury or more, along with one or more of the following symptoms if at all marked - headache, epigastric pain, oedema, albuminuria or vomiting. O'Sullivan[126] accepts the same blood pressure together with an albuminuria of two parts, while Hamilton, Jeffcoate and Lister[68] also using the same blood pressure, add that the urine must contain 2 mgm or more of albumin per litre.

Molumphy and Garcia[115] have a nearly similar definition of severe toxaemia with (1) blood pressure of 160/100 or above, and (2) albuminuria - two plus or more, and (3) oedema.

Gibson[62] of Belfast set an even more strict grading for severe toxaemia, i.e. a blood pressure of 170/105mm of mercury and/or urine containing three plus of albumen.

The Helsinki University Women's Clinic[127] has the same definition as the Royal Infirmary, Edinburgh.

Employing the prognosis of the child as a means of defining severe pre-eclampsia, Pankamaa et al[127] concluded that proteinuria of over 5 Gms in 24 hours and a blood pressure of over 180 mm of Hg. systolic, were significant.

Morris[117] emphasises that it is not possible to assess (a) cerebral arteriolar vaso-spasm, (b) increased irritability of the motor cortex, or (c) cerebral oedema, which are the underlying causes of the convulsions of eclampsia. He feels that no true definition of imminent eclampsia can be stated, but for practical purposes believes that any case in which the diastolic pressure rises to 100 mm of mercury or above, should be treated as such. He shows that the higher the diastolic pressure (which reflects vaso-constriction) the greater the incidence of eclampsia.

The views of Morris give the lead to possible assessment of the factors he quotes as being beyond assessment. McCall et al[107] have demonstrated that in all types of toxaemia of late pregnancy, the cerebral vascular resistance is elevated. They have measured this resistance and have found that it is elevated 38% above normal in pre-eclampsia, 56% in eclampsia and 63% in hypertension with superimposed pre-eclampsia. Despite the increased vascular resistance, the cerebral blood flow remains normal in all types of toxaemia. Although of great theoretical interest, these investigations play no part in the practical management of or defining of cases of imminent eclampsia.

In attempts to give a practical guide as to which cases may develop eclampsia, many electro-encephalogram studies have been made on eclamptic patients. Maltby and Rosenbaum[104] were the first to attempt such a study and detected a cerebral dysrhythmia in 13 out of 20 patients with eclampsia compared to 2 out of 20 controls. Gibbs and Reid[61] took tracings from pre-eclamptic and normal pregnant women: of the former, 4 out of 8 showed abnormal high voltage fast activity, while in the latter group this was absent. Jost[81] was able to get records of 9 eclamptic patients during and after convulsions. He found that the E.E.G. patterns may become normal when the blood pressure is lowered. In one of his cases, an E.E.G. taken three days before the onset of the convulsions was normal. Parvianinen et al[129] reported upon two cases of severe pre-eclampsia with marked cerebral dysrhythmia, who showed normal E.E.G. patterns a few days after treatment with ammonium chloride had commenced. Roubillard and Villavicencio[139] quoted by Kolstad[93] believe that toxaemia of pregnancy precipitates convulsions in pre-disposed women, and that such a pre-disposition can be demonstrated by E.E.G. McIntosh[112] observed a posteclamptic cerebral dysrhythmia in 5 of 6 patients and holds the opinion that persons with dysrhythmia are more prone to eclampsia.

James[79] in 1955 and Kolstad[93] in 1961 reviewed most of the above and other relevant literature on the electro-encephalogram in eclampsia and found that the idea that eclampsia occurs on a predisposition of an inherited cerebral dysrhythmia, was generally accepted. This concept would mean that a definite place existed for the use of E.E.G. studies

in patients suffering from severe toxaemia of pregnancy, and that all those with a dysrhythmia "should be dealt with radically and promptly". Neither James nor Kolstad, however, could support this view from their own figures. Kolstad was unable to detect a correlation between blood pressure elevation and E.E.G. patterns; nor between the degree of oedema, proteinuria or cerebral symptoms and E.E.G. tracings. In one of his patients an E.E.G. study done 38 hours before the onset of eclamptic convulsions was within normal limits.

It is possible that the previous conclusions on the value of the E.E.G. in eclampsia were based falsely on the post-convulsive tracings which, if followed up, can revert to normal. The work of Jost, James, Kolstad and Poidevin[132] show that the E.E.G. has no practical value in the selection of patients likely to develop eclampsia from a group who are suffering from severe toxaemia of pregnancy.

Criteria for defining imminent eclampsia - Cape Town 1960/61.

As I was unable to find a universally accepted standard for defining imminent eclampsia and accepting that E.E.G. studies would be of little clinical value in helping to arrive at such a standard, I decided to make my own standards, and these follow, together with the reasons for their selection -

1. A blood pressure of 160/110 mm of mercury or more, and urine containing two plus of albumen or more; or

2. Either of the above two signs with symptoms of severe headache, visual disturbances, vomiting or epegastric pain

Of the 100 patients in this survey, 82 fall into the first category and 18 into the second.

Blood Pressure.

The choice of a blood pressure of 160/110 mm of mercury or more, was influenced by the following factors -

(i) Age. Among the non-white population of Cape Town, particularly the Malays[125] and to a lesser extent the Bantu, it is customary to marry at an early age. Pre-marital pregnancies are also common. Many teenagers who in fact are severe cases of toxaemia, would be excluded from the survey if a systolic pressure of over 160 mm of mercury was used as a standard.

On the other hand, the same racial group do not usually practise contraception or family planning. Grande-multiparae and elderly (40 years) pregnant patients are relatively frequently seen. A systolic blood pressure lower than 160 mm of mercury, would have included many with early signs of hypertensive vascular disease who, in fact, would be most unlikely to have a convulsion.

From personal experience[36] the statement of Morris[117] "that the higher the diastolic blood pressure the greater the incidence of eclampsia" was accepted. The level of 110 mm of mercury as against 100 mm of mercury was chosen as it was thought that by using the former figure, mildly hypertensive elderly patients whose condition had not truly deteriorated because of a superadded pre-eclamptic toxaemia, would be excluded. From a study of previous clinical reports any lower figure would have included many elderly women suffering from relatively mild toxaemia of pregnancy.[164-169]

(ii) Height of blood pressure in relation to the onset of convulsions. It is well known that the onset of convulsions bears a relationship to the actual rise in a particular patient's blood pressure and that therefore they may occur at a comparatively low level. This occurrence is most often seen amongst young primigravidae. Nevertheless, such cases are the exception and not the rule.[140]

In the author's series[36] of 42 cases of eclampsia, there were 5 patients with a blood pressure lower than 160/110 mm of mercury when first seen after the onset of convulsions. Details follow:

(a) A primigravida aged 23 who was seen two hours after having four antepartum convulsions. B.P. 155/100. Albuminuria - Solid.

(b) A gravida 2, aged 19, seen one and a half hours after having one intrapartum convulsion. B.P. 150/110. Albuminuria - one plus.

(c) A primigravida, aged 22, had one antepartum convulsion one hour after receiving avertin for imminent eclampsia. B.P. 130/100 Albuminuria - 3 plus. This patient is one of the survey on imminent eclampsia and will be discussed more fully in a subsequent chapter.

(d) A para 4, aged 40, was seen half an hour after having one post-partum convulsion; the convulsion occurred half an hour after delivery. B.P. 150/100. Albuminuria - one plus

(e) A primigravida aged 17, was seen half an hour after having four postpartum convulsions. The convulsions occurred 4 hours after delivery. B.P. 120/90. Albuminuria - 2 plus.

Prior to the onset of the convulsions, all these patients suffered from one or more symptoms of imminent eclampsia. On the definition I have given for imminent eclampsia, only cases (b) and (d) would not have been so classified. As both patients were admissions via the Flying Squad, their immediate pre- and postconvulsion blood pressures were unknown, and therefore one cannot be too dogmatic on this point. An additional factor in case (b) was anaemia - the haemoglobin was 5 Gms per cent.

For the reasons stated above, a blood pressure of 160/110 mm of mercury or more, although an arbitary figure, is in my opinion the most satisfactory for partly defining imminent eclampsia.

Albuminuria.

In selecting two plus of albumen in a clean specimen of urine as the minimum to suggest imminent eclampsia, the following factors were considered:

(i) Time.

As a specific method of treatment was to be used on all patients in this survey, it was a sine qua non that an immediate diagnosis be made in each case. Any estimation of albumen in the urine involving a delay of half an hour or more, would have involved a similar delay in the commencement of the avertin therapy. From the maternal and foetal prognostic viewpoints, such a delay in the majority of patients would not be justified.

Therefore I accepted that for practical purposes a urine examination giving an estimation of the amount of albumen in a matter of minutes, would be the ideal.

(ii) Place.

As it was expected that many patients would be seen for the first time in their own homes, a test for albuminuria which could be simply and easily performed away from a laboratory or clinic room, was required.

(iii) Quantitative or Qualitative ?

From what has been written already, it is plain that an exact quantitative test was not needed. A sufficient guide to severity would be obtained where the test revealed the presence of albumen

in the urine, and at the same time gave a non-measurable quantitative estimate.

For the above reasons, I elected to test all specimens of urine for albumen by either the boiling test, the use of salicyl sulphonic acid or the use of "albustix." A catheter specimen of urine was obtained for the test in the majority of cases. Occasionally with an apparently less severe grade of toxaemia in a co-operative patient, the test was performed on a clean specimen of urine. In patients with any of the aforementioned symptoms of imminent eclampsia and blood pressures of 160/110 mm of Hg or more, treatment with avertin was started immediately. Only when the risk of a convulsion occurring appeared less likely, was an attempt made to obtain a catheter specimen of urine.

Where albumen was detected in the urine, the amount was classified as follows:-

(a) Trace - a portion of the tested specimen developed a slight opacity.

(b) One plus - the whole of the tested specimen developed a moderate opacity.

(c) 2 Plus - the whole of the tested specimen developed a deep white opacity.

(d) 3 Plus - the whole of the tested specimen was opaque with clumping of particles easily visible as small masses.

(e) Solid - the specimen formed a solid lump.

Where albuminuria was present, a spun deposit of a catheter specimen was always examined at a later stage. In no patient in this survey was it thought that the albuminuria resulted in part or in toto from a urinary tract infection.

(iv) <u>Amount of albuminuria in relation to the onset of convulsions.</u>

2 plus of albuminuria or more is found in the majority of patients with eclampsia. In 42 cases of eclampsia[36] I found only 6 patients to have less than this amount in the first urine specimen tested after the onset of the convulsions.

(a) and (b) are cases (b) and (d) mentioned under hypertension on page 12.

(c) A primigravida aged 16 who had a single convulsion while regaining consciousness from a general anaesthetic administered for a forceps delivery. B.P. 190/120. Albumen - one plus.

(d) A primigravida aged 28 who had one intrapartum convulsion. B.P. 160/110. Albumen - trace.

(e) A primigravida aged 15 who had three intrapartum convulsions. B.P. 190/120. Albumen - trace.

(f) A primigravida aged 14 who had five intrapartum convulsions. B.P. 170/140. Albumen - nil one hour before the first convulsion and two plus two hours after the first convulsion.

All these patients, including (c), had symptoms preceeding the occurrence of the fits.

Of the nine, cases of eclampsia which have been detailed as being exceptions to either the blood pressure or albuminuria levels of my definition of imminent eclampsia, 5 were in their teens and another three were in their twenties. It would appear important to view very seriously the occurrence of symptoms in primigravidae and teenagers suffering from toxaemia of late pregnancy. The results of the survey as will be seen in a later chapter, underline and re-emphasise this statement.

The definitions of imminent eclampsia given by Hamilton et al,[68] Sutton[157] and to a lesser extent Townsend,[162] all involve a time lag for a quantitative estimation of the albuminuria to be made. As imminent eclampsia is a state requiring emergency therapeutic measures, I feel these definitions, although of prognostic value (of Pankamaa et al[127]), are impractical for determining the management of such cases.

An albuminuria of 2 plus or more is easily estimated, is the minimum amount usually present in cases of eclampsia, and was therefore selected as being a practical guide as to the probability of convulsions occurring in cases of severe toxaemia.

Symptoms.

The importance of symptoms such as headache, visual distrubance, epigastric pain and vomiting as an indication of impending convulsions in a pregnant woman, has been previously stressed.

By emphasising these symptoms, young primigravidae with either a raised blood pressure or an albuminuria of 2 plus or more, would very correctly be included in this survey. In reviewing the exceptions to the blood pressure and proteinuria standards in known cases of eclampsia, I have shown that this is so. Similarly, it was expected that patients with hypertension and only a mild superimposed pre-eclamptic toxaemia, would not develop any symptoms and so not be included as cases of imminent eclampsia. (It will be seen later that these assumptions were not entirely incorrect).

Oliguria as a symptom was never volunteered by the patient, and the answers to direct questioning were as far as could be assessed, given so as to satisfy the questioner. In those cases of toxaemia who were observed to deteriorate while in hospital, a rise in blood pressure and/or an increase in the albuminuria, preceeded the diminishing urinary output. I have, therefore, not included oliguria as a symptom in my definition of imminent eclampsia, but I readily admit that it nearly always occurs in such cases.

Oedema.

It is difficult to give more than a very rough clinical quantitative estimation of the extent of oedema in an individual case, particularly when the patient is being seen for the first time. In those patients who attended antenatal clinics, the degree could also be assessed by the known first appearance of the oedema and by increases in body weight during pregnancy.

Oedema is an early, if not the first, sign of pre-eclamptic toxaemia[130,69,75], and was present in many, but not in all, the patients in this series.

Oedema was judged on purely clinical grounds and so the degree varied from observer to observer. In order to provide some sort of standard, the following terms are used -

(i) Slight - pitting after finger pressure over the lower third of tibia.

(ii) Moderate - deep pitting as above and also swelling of the fingers and hands assessed by ring tightness and pitting over the metacarpals.

(iii) Gross - as with (ii) plus eyelid and face oedema assessed on appearance and also pitting of the anterior abdominal wall.

The possible effect on the degree of oedema by stature, obesity, a pendulous abdomen or varicose veins, was considered in each case.

Generalised irritability.

This sign is not often stressed by those who write about imminent eclampsia; yet it was not infrequently seen by me.

Jaundice.

Kellar[82] states that jaundice occasionally occurs in imminent eclampsia. This must be a very rare finding. Samuels[141] found that jaundice occurred in .04% of pregnancies. In none of the cases he reported upon was the jaundice due to toxaemia of pregnancy.

Blood investigations.

Similar reasons to those already stated in connection with a time lag in albuminuria estimations, precluded any laboratary blood investigations from being of practical use in defining imminent eclampsia. Greenhill[66] has stressed the inconsistency of urea and uric acid levels in this type of case, and only where repeated estimations are available, do they have any real, although slight, therapeutic value.

SUMMARY:

The Clinical State of Imminent Eclampsia.

A condition seen in pregnant women in which symptoms of severe headache, visual disturbance, vomiting or epigastric pain are associated with a blood pressure of 160/110 mm of Hg or more and an albuminuria of 2 plus or more. Any two of these three features appearing in one patient are sufficient for the diagnosis of imminent eclampsia to be made.

Incidence of Imminent Eclampsia.

The varying incidences reported are mainly a result of the different standards of definition used. Retrospective surveys culled from hospital clinical reports appear to give higher incidences than prospective surveys.

O'Sullivan[126] found the incidence of imminent eclampsia to be 6.3 per cent of 2,062 cases of pre-eclamptic toxaemia. Kellar[82] from Edinburgh reported only 70 cases in 7 years. The medical and clinical report of the Simpson Memorial Pavilion, Royal Infirmary,[150]

Edinburgh, for the year 1960 notes 12 per cent of severe cases in 337 patients suffering from pre-eclampsia. Molumphy and Garcia[115] reported 61 cases in 2 years at the Baltimore City Hospital. de Soldenhoff[39](Scotland) found 352 cases among 477 with toxaemia. Townsend[162](Melbourne) made the incidence 40.1 per cent of 425 cases of pre-eclamptic toxaemia. The incidence for this survey, which lasted 17 months, was 13.6 per cent among 711 patients with toxaemia of late pregnancy.

The Pathology of Imminent Eclampsia.

Although for practical purposes the diagnosis of imminent eclampsia is always made on the clinical findings, an understanding of the underlying pathology is fundamental to the establishment of a sound concept of management. For years the spearhead of the therapeutic armamenterium has been sedation, i.e. an attempt to depress the unknown trigger which sets off the convulsions. The E.E.G. findings already referred to in part, support the rationale of this method; notwithstanding whether one believes the cerebral dysrythmia seen in some cases of eclampsia to be a temporary or permanent phenomenon. In Cape Town, treatment on these lines was only reasonably effective in presenting eclampsia as shown by the figures in Table 1 (page 2). However, as neither the underlying cause of severe toxaemia nor the resultant pathological changes therefrom were attacked sedative regimes could not be expected to be wholly effective. As yet the aetiology of pre-eclamptic toxaemia is unknown, so therapy is directed firstly towards correcting certain pathological changes and secondly towards depressing and/or eliminating any stimulus which might provoke a convulsion.

The pathology of severe toxaemia is difficult to study for a number of reasons. Very few of these patients die and so few autopsy examinations are performed. It is thus difficult for one morbid anatomist to have the opportunity of regularly examining such cases. Clinically many of the patients are so ill that there is rarely a justification for the performance of procedures such as liver and renal biopsies. It is unlikely that such procedures would in themselves jeopardize the mother's life, but they may well worsen the foetal prognosis by possibly precipitating a convulsion in the mother. Studies estimating vascular resistance in the different organs carry similar hazards. To perform any of these procedures after the commencement of therapy, immediately limits their value as some of the pathological changes are very rapidly reversed.

Much, therefore, of what is "known" has not been universally accepted.

Arteriolar vasoconstriction.

The fundamental change in acute toxaemia of pregnancy appears to be a generalised arteriolar vasoconstriction or hypertonus.[82,3,5,107,140] This causes an increased vascular resistance but does not affect the blood supply to an individual organ until a very late stage of the disease in most instances.[82,107]. The abnormality is widespread and involves both the peripheral circulation and the circulation to vital organs such as the brain, the kidneys and the liver.

The search for the cause or causes of toxaemia has led many workers to a possible humoral basis for the arteriolar vasoconstriction. Keller[82] stated that "the basic cause for the hypertension in pre-eclamptic toxaemia is humoral in origin", but noted that the hypertension can be modified by neurogenic activity. Gardiner[60] demonstrated that in the blood of toxaemia patients there is a pressor substance similar to nor-adrenaline. This substance was blocked by dibenyline and therefore the latter drug was used in the treatment of five cases of severe pre-eclamptic toxaemia. Paterson[130] in presenting the 1960 William Blair-Bell Memorial Lecture said that "there seems general agreement that hormonal influence plays a considerable part in the aetiology, but there is no agreement whatsoever as to which endocrine gland far less as to which hormone is involved." In patients suffering from pre-eclampsia or eclampsia, he found that there existed in the blood or urine, an antidiuretic substance which was not present in the vast majority of cases of uncomplicated pregnancy. He maintains that this antidiuretic substance is "in fact the antidiuretic hormone of the posterior pituitary gland." Jeffcoate and Scott[80] noted that in some types of pregnancy toxaemia, an associated hormone disturbance is present, but that this is not necessarily the agent causing the toxaemia. They found an increased gonadotrophin production in patients with coexisting toxaemia and erythroblastosis. More recently, Hunter and Howard[77,78] observed that decidual extracts from hypertensive pregnant women caused contraction in an aortic strip. These extracts, if injected intravenously into a cat, raised the blood pressure. The effects, they claim, are due to a peptide formed by a decidual enzyme in hypertensive cases acting on the proteins of the plasma or amniotic fluid. This peptide they have named "hysterotonin". By removing the decidual remnants in the immediate postpartum phase of hypertensive patients, a permanent fall in the blood pressure occurs.

The study of arteriolar vasoconstriction.

Vasoconstriction may be studied in 3 ways - (i) Direct vision - usually of the vessels of the optic fundi and less commonly of the nail-bed. (ii) Microscopy study of tissues from toxaemic patients, and (iii) Blood flow measurement to individual organs and to the limbs. This measurement may be direct or indirect.

(i) - Direct Vision.

Retinal vessels - The changes in the retinal vessels in the toxaemias of pregnancy have been studied by many workers. The more enthusiastic reports feel that these changes may be of inestimable value in the management of patients, while the less enthusiastic reports emanating mainly from practising obstetricians, indicate that ophthalmoscopic findings are of little more than academic interest.

To standardise the grades of retinopathy, the American Ophthalmological Society formulated the following classification - Wagener et al.[173]

Grade 0. - Normal retinal findings.

Grades 1 & 11 - Changes in the retinal arterioles - generalized narrowing, sclerosis (thickening) and focal spasm. Grade 1, mild. Grade 11, more advanced changes.

Grade 111 - Grades 1 and 11 plus abrupt development of serous and haemorrhagic extravasations into and under the retina. The serous oedema may be described as diffuse oedema or "cotton wool" patches.

Grade 1V - Grade 111 plus papilloedema or neuroretinopathy.

Landesman et al[95] did ophthalmoscopic examinations upon 205 cases of severe pre-eclampsia. (They do not state what the criteria for severity were). The findings and the foetal mortality may be summarised as follows -

Grade 0.	retinopathy	-	75	cases.	11%	foetal	loss.
Grade 1	"	-	80	"	15%	"	"
Grade 11 & 111	"	-	50	"	28%	"	"

Thus over 80% of all foetal deaths were associated with some retinal vascular alteration. They conclude that the examination of the retina reveals important objective information concerning the toxaemias peculiar to pregnancy, furthers the accurate diagnosis and refines the management provided that patients are seen from an early stage and followed through the pregnancy. Where the latter proviso has been fulfilled, the development of arteriolar spasm on retinal examination indicates an increased possibility of foetal death and in general, premature termination of pregnancy should be seriously considered.

Massey and Mundell[122] found retinal changes of diagnostic value in 8% of cases of pregnancy toxaemia, but these changes were never the sole diagnostic factors. They write that "the pressure and degree of spasm of the retinal arteries has paralleled so closely clinical evidence of the severity of toxaemia that we have increasingly depended on the examination." They emphasise that retinal examinations must be repeated and performed by "those skilled in the use of the ophthalmoscope" to determine whether acute vascular changes are advancing, receding or stationary.

Sodowsky et al[152] promoted a study to see if frequent examinations of the ocular fundi in addition to other routine investigations, would be helpful not only in the evaluation of the mother's condition, but also of the foetal progress. The results of this investigation showed a correlation between the vascular changes in the retina and the severity of the toxaemia, and also a close correlation between the retinal changes and the foetal mortality rate. They conclude that termination of pregnancy should be considered in all cases of Grade II to Grade IV retinopathy. Klien[92] in an editorial comment on this paper wrote that repeated fundus examinations by the same examiner in cases of mild toxaemia and in the more severe ones which respond to therapy "should prove most fruitful in reducing maternal and foetal complications "because the retinopathy is an assessment of the arteriolar spasticity and its complications which is equi-existent throughout the body."

Finnerty[55,56] has made extensive studies of the optic fundi in cases of pregnancy toxaemia. He found that in true pre-eclamptic toxaemia, apart from segmental vasospasm, the retinal vessels are entirely normal. In particularly severe and fulminating toxaemia, flame shaped haemorrhages and cotton wool exudates may occur and are a grave sign. Though the vessels themselves are normal the retina has a wet, glistening appearance - the retinal "sheen". This sheen is more pronounced in severe toxaemia and decreases promptly following diuretic therapy. It probably represents a superficial retinal oedema. Finnerty considers that the development of the retinal sheen necessitates prompt treatment. This sheen is not seen in hypertensive vascular disease complicating pregnancy.

In the second paper, Finnerty and his associates[55] appear to have revised his initial views concerning the retinal arteries. In toxaemia they describe the arteries as having more commonly a generalised reduction in calibre rather than segmental spasm as Finnerty had previously reported.

Finnerty maintains that an ophthalmoscopic examination and a complete urinanalysis allow a prompt differentiation of the various toxaemic states. He produces a table showing how the differentiation is made. The retinal sheen which as far as I can determine has only been reported by Finnerty and his co-workers, is an important differentiating feature. Salerno[140] reported that in toxaemic patients with apparently low blood pressures, marked vasospasm could be present. The vasospasm shows as retinal arteriolar constriction. Pollak and Nettles[133] detected spasm of the retinal arterioles in 27 out of 35 cases of true pre-eclampsia, but in only 2 out of 10 cases of hypertensive vascular disease. They consider retinal arteriolar spasm to be a valuable diagnostic sign.

SUMMARY: Direct vision of the retinal vessels has revealed that in pre-eclamptic toxaemia arteriolar narrowing is often present. Early retinal oedema is probably also present. These changes, including the arteriolar narrowing, are reversible[55] and therefore the latter is undoubtedly a reflection of vasospasm. The retinal changes of hypertensive vascular disease in pregnancy are similar to the changes in the non pregnant and are not completely reversible.

An isolated ophthalmoscopic examination in an emergency admission, particularly if done by an unpractised examiner, is of little clinical value.

Vessels of the nail bed. - The vessels in the nail bed have been directly studied in cases of severe pregnancy toxaemia.[107] The elongation of and the ischaemia of the capillary loops which occurs, is thought to be due to spasm of the terminal arterioles.

(ii) - Microscopy Study of Tissues.

Until the advent of biopsy techniques for investigating renal and hepatic disease, histological examinations of these organs in cases of toxaemia of pregnancy had been almost entirely confined to autopsy specimens. Such examinations could give only a limited view of the pathology as the progression and regression of any abnormalities that were detected could not be studied.

Kidney - Sheehan[146a] found that 50% of maternal deaths in toxaemia were due to obstetric or incidental conditions, 30% due to true convulsive eclampsia, 10% due to toxaemic collapse, 5% due to toxaemic coma and 5% due to primary cerebral harmorrhage. He states that the characteristic changes in the kidney of eclampsia, viz. enlarged and swollen glomeruli are also present in toxaemic collapse and in toxaemic coma, except that in the latter condition cortical petechiae are usually absent. In eclampsia, certainly, these changes are transitory and the majority are healed within a week if the patient survives the actual eclampsia.

Pollak and Nettles[133] obtained specimens for histological examinations from renal biopsies. In pre-eclamptic toxaemia they noted the following changes:-

(a) Glomeruli were enlarged and swollen.

(b) Capillary walls were widened due to oedema of the endothelial and epithelial cells.

(c) In severe cases (criteria of severity were not mentioned) the whole glomerular tuft appeared to be vacuolated.

(d) In some of the severe cases there was thickening of the capillary basement membrane.

(e) Ischaemia of the tuft was a marked feature.

(f) Oedema of the walls of small arteries and arterioles was present.

In hypertensive vascular disease in pregnancy they observed sclerosis of the small arteries and arterioles. The glomeruli were normal.

In primary renal disease in pregnancy they noted variable pictures with similar criteria as for the non-pregnant case of renal disease.

Pollak and Nettles found a correlation between the histologically severe renal lesions and the severe pre-eclampsia and eclampsia states. In the milder cases the lesions were reversible, but serial biopsies of the more severe renal lesions suggested that many of these patients develop permanent vascular and glomerular damage.

Dieckmann[47] and his co-workers also studied renal biopsies in the toxaemias of pregnancy. Renal lesions were found to occur in any variety of pregnancy toxaemia, but are more constantly present in primigravidae with a diagnosis of pre-eclampsia. They did not find

find histological study of kidney structure helpful in differentiating the various types of toxaemia, nor that glomerular lesions persisted to be responsible for permanent kidney damage. Glomerular changes were classified as follows:-

Severe - marked reduction in capillary lumina associated with thickening of the basement membrane and large amounts of fibrillar material in the cytoplasm.

Moderate - similar changes but with slightly less reduction in the capillary lumina.

Mild - the basement membrane is only slightly thickened and very few fibrils are present in the cytoplasm.

They make no mention of any parallel between the severity of the renal lesions and the severity of the toxaemic condition.

Liver - Sheehan[145,146,146a] has made extensive studies of the livers in postmortem specimens obtained from eclampsia and severe toxaemia cases. He observed that periportal necrosis was present in about 75% of patients who die of eclampsia in the first 24 to 48 hours after the onset of convulsions. In 20% of these "early" deaths the lesion extends to involve about the entire liver in a diffuse haemorrhagic process. The convulsions themselves do not precipitate these changes as they have been found at postmortem examination in cases of severe toxaemia who have died without having convulsions - the so-called "eclampsia sine eclampsia" syndrome.[43,144,155,136,90] Sheehan believes that the hepatic lesions are due to a predominantly vascular derangement and not due to a toxin, and therefore can be and are found in the absence of fits.

Antia and his associates[2] reported upon the liver changes detected by clinical, biochemical and pathological examination in (i) 15 patients suffering from eclampsia, (ii) 16 patients suffering from pre-eclampsia, and (iii) 10 apparently normal pregnant women. The histopathological examinations were made upon specimens obtained by liver biopsy. They concluded that there is no constant histopathological picture of the liver associated with pre-eclampsia or eclampsia. In only 5 of the 31 patients suffering from either eclampsia or pre-eclampsia were severe changes detected in the liver. Relevant to this may be Kellar's[83] observation that in liver biopsy from non-fatal cases it is often difficult to find a lesion.

Greenhill[67] agrees with Sheehan that the characteristic lesions of periportal haemorrhage and necrosis may be numerous or few and focal

or diffuse. It is not difficult, therefore, to understand why a classical histopathological picture of the pre-eclamptic liver has not been consistently found in specimens obtained by needle biopsy.

Placenta - Marais[105] performed colposcopic and histological examinations of more than 800 placentae. He detected varying mild to severe changes in some of the spiral arterioles. His study included 25 cases from this survey. These 25 cases as a group had the most severe spiral arteriolar changes of any group of patients throughout his survey, including the group of eclamptic patients. He postulates that arteriolar spasm may be a factor producing these changes.

N.B. The spinal arterioles of the decidual plate do not have any muscle in the vessel wall and therefore cannot themselves go into spasm. The arteriolar spasm referred to occurs in the uterine wall proximal to the spinal arterioles.

(iii) - Blood Flow Measurements.

Blood flow measurements to individual organs and in the limbs offer a further method for the assessment of arteriolar spasm. The inaccessability of organs such as the liver and kidneys, severely restricts the scope of these investigations.

McCall and his co-workers[107-111] have made numerous studies of the cerebral blood flow and cerebral oxygen metabolism in cases of pregnancy toxaemia, and have assessed through these methods the effects of some forms of treatment. Their results can be summarised as follows:-

Cerebral blood flow is not affected by pregnancy toxaemia.

Cerebral oxygen metabolism is unaltered in non-convulsive toxaemia, but is significantly depressed during the coma of eclampsia.

Cerebral vascular resistance is significantly raised in both convulsive and non-convulsive toxaemia.

Apresoline and unitensin (veratrum alkaloids), apresoline alone, veratrum viride alone and papaverine hydrochloride all caused a significant decrease in the cerebral vascular resistance. Apresoline and papaverine hydrochloride also caused an increased cerebral blood flow and an increased oxygen utilization by the brain. Heavy sedation (especially intravenous barbiturates) depresses the oxygen metabolism of the brain by about the same amount as does eclampsia itself. Because

of the experimental and clinical results he has obtained, McCall advocates the use of hypotensive drugs to counteract the arteriolar spasm present in cases of severe toxaemia.

I have been unable to find any reports of a similar kind concerning the renal and hepatic blood flow in pregnancy toxaemia. In other ways the renal haemodynamics and function have been extensively studied[163,38,48,158,24,25,84] and can be stated as follows:-

The glomerular filtration rate is reduced. This occurs on the basis of a reversible constriction of the affervent glomerular arterioles, particularly in eclampsia and severe pre-eclampsia.

The renal plasma flow is reduced in 50% or more of toxaemic patients.[82,38,48] Others have been unable to confirm this.[163,158]

The filtration fraction is normal or slightly reduced and this again suggests the possibility of afferent arteriolar constriction.

The blood flow through the liver in pre-eclampsia is the same as in normal pregnancy or even sometimes increased. (Kellar 1950[86])

Browne and Veall (1953)[23] attempted after injection of radio-active sodium into the placenta to observe clearance rates and so indirectly the placental blood flow. Although not definite, their results suggest a decreased placental blood flow. Morris et al[118] assessed clearance rates of radioactive sodium from the uterine wall and found a prolonged time in cases of severe pre-eclampsia as compared to normals for the radioactivity to be reduced to half.

Burt[25] observed the peripheral circulation in pregnancy and used the forearm at rest for her investigations. A greater increase in forearm blood flow was found in normal pregnant patients as compared with non-pregnant subjects and a greater increase was found in pregnant patients with pre-eclamptic toxaemia or with hypertension in whom the average resting forearm blood flow was twice that of the control group.

SUMMARY: The available evidence suggests that the hypertension of pregnancy toxaemia is due to a generalised arteriolar spasm resulting in an increased peripheral resistance. This latter may vary in degree from organ to organ, but if present in any one organ will also be present in others. Kellar[84] succintly put it as follows - "the hypertension of pre-eclampsia has probably a basic humoral background. The nature of the humoral agent is at present entirely unknown. Superimposed on

the humoral mechanism is a neurogenic agency, the extent of which will vary from case to case. The two mechanisms are not mutually exclusive." Since the above was written the humoral barrier appears to have been partially breeched by the work of Hunter and Howard[77,78] to which reference has already been made.

The Treatment of Imminent Eclampsia.

As with so much in obstetrics, preventitive treatment is the ideal for imminent eclampsia. The work of Hamlin[69] and Hughes[75] in Sydney has shown that the incidence of severe toxaemia and eclampsia can be considerably reduced by careful antenatal care in which special attention is paid to weight increases and relative increases of the blood pressure. These workers emphasise that the rules of attendance at antenatal clinics should be governed by only one factor, viz: "as often as the condition of an individual patient warrants it." Hughes gives in regard to the blood pressure the following standards for antenatal care -

(i) A rise of 5 mm of mercury in the diastolic pressure means that the patient must be observed within 7 days after the 20th week of pregnancy.

(ii) If the diastolic pressure has again risen the patient must be examined within 2-3 days or admitted to hospital if any other sign of toxaemia has developed.

(iii) If weight increase is associated with a relative rise in the diastolic pressure irrespective of successful weight control, the patient must be examined weekly.

(iv) Albumen in a catheter specimen of urine indicates immediate admission to hospital.

Eastman[51] in an editorial comment upon these two papers wrote:- "the attention which this group is giving to the earliest incipient signs of pre-eclamptic toxaemia - pre-hypertensive pre-eclampsia as they call the condition - impresses me as one of the few really practical developments in the toxaemias in the last decade." Browne[21] has also stressed the importance of the early diagnosis and treatment of raised blood pressure and oedema in preventing eclampsia and severe toxaemia. There are probably no antenatal clinics in the world where this preventitive aspect of obstetrics is not adhered to in principle. Unfortunately in practice the standard of care often falls short of the basic requirements.

Once the state of imminent eclampsia has developed, the first essential is the prevention of convulsions and the second is to achieve delivery of a living infant. Often the two objectives are opposed to each other, as for example when the severity of the maternal condition does not allow any delay in the hope of achieving a more mature foetus. Eastman[52] has stated the position very concisely - "We are still in grievous need, nevertheless, of some agent, or combination of agents which will so arrest the signs and symptoms of pre-eclamptic toxaemia as to make possible the carrying of severe pre-eclamptics not for a few days but for a month or two ------- This long term coverage is really the great need in the therapy of pre-eclampsia."

The methods which have been described for the prevention of convulsions in these cases are numerous and varied, but fundamentally are either sedative or hypotensive or a combination of both. Sedative regimes have been used for many years and closely follow the principles Strogonoff laid down for the management of eclampsia. The Mount Sinae Hospital[97] use 4 to 6 hourly injections of morphine and magnesium sulphate and claim that convulsive episodes are rare on this regime. At the Peninsula Maternity Hospital until 1960 a four hourly cycle of treatment with paraldehyde, sodium amytal and morphine was standard. More recently the trend has been to implicate directly the hypertension as a cause for the convulsions. Drugs that lower the blood pressure - which Assali[4] feels should be reduced by 20% to 25% from the initial control - have been widely used in cases of imminent eclampsia.[7,8,28,60, 111,115,117,123,137,157,162] All these reports emphasise the effectiveness of hypotensive agents in preventing convulsions and in improving the foetal prognosis. In some cases the initial treatment returned the patient from a state of severe toxaemia to one of mild toxaemia, thereby allowing the pregnancy to continue uninterrupted for a few more weeks. Bryce-Smith[179] amongst others, has through conduction analgesia produced a controlled fall in the blood pressure. The combined use of sedation and hypotension has many protagonists and amongst those whose work was quoted under hypotensive drugs are some who include reduced doses of sedative in their therapeutic regimes. Avertin although basically a sedative, has the capacity of producing a temporary fall in blood pressure and has found favour amongst some clinicians for use in severe toxaemia.[39,40,82,58,27]

Another school of treatment advocates immediate termination of pregnancy in these patients. They maintain that the pregnancy is the cause of the toxaemia and that logically the pregnancy must be removed before the risk of convulsions occurring can be eliminated. In the interim between diagnosis and delivery, sedation is usually given although in smaller doses than those used by the proposers of sedation

as a primary form of treatment. There is little doubt among those who have written about imminent eclampsia that pregnancy should be terminated, but the majority feel that the maternal state must be well controlled before this is undertaken. Except in a small minority of cases, termination is never delayed for more than a few days.

Greater controversy exists as to whether labour should be induced[82,162,39,8,50,172] or immediate caesarean section performed, especially if the period of gestation is less than 35 weeks?[41,57,68] On the whole induction of labour and vaginal delivery is preferred to caesarean section as it offers a better prognosis to the foetus. Huber[73] has shown that the premature infant has less chance of survival following caesarean section than following vaginal delivery, and Donald[49] states that hyaline membrane disease is much commoner in premature infants born by caesarean section. Varga and Fields[172] recommend vaginal delivery for maternal rather than foetal indications.

In regard to treatment, I feel the following factors must be considered -

1. The majority of patients are non-booked. The risk of convulsions occurring is increased if such patients are transported to hospital before receiving treatment.

2. The hypertension is a reflection of the underlying arteriolar constriction which in turn is due chiefly to humoral, but also neurogenic, factors.

3. A cerebral dysrhythmia may be present.

4. Prematurity is a factor in the majority of perinatal deaths.

The requisites are therefore -

1. A system that will prevent convulsions and which is safe to use in domiciliary work by an Obstetric Flying Squad.

2. A hypotensive agent that will effectively reduce arteriolar constriction and so lower the blood pressure.

3. A sedative that will reduce the impact of stimuli to the cerebrum where a dysrhythmia may be present.

4. An agent or agents which will reverse the toxaemic process to an extent justifying prolongation of pregnancy in order to obtain a more mature infant.

TRIBROMO-ETHYL ALCOHOL.

AVERTIN.

Tribromo-ethyl alcohol is more commonly known by the trade names of Avertin or Bromethol, the former being used more frequently. For this reason Avertin will be the term used throughout this commentary.

Avertin was first synthesized by Willstatter in 1923 and was employed clinically first by Butzengeiger[26] in 1926. The first series of cases anaesthetised outside of Germany were recorded in a publication by Morrin[116] in 1929. In South African Medical Literature, Hochschild[71] in 1931 was the first to report on the results of Avertin anaesthesia. In his paper he stated that "in the practice of obstetrics avertin is a useful accessory. In this case a smaller dosage is employed, namely 0.06 Gms per kilo of body weight and is usually administered towards the end of the first stage of labour. It replaces efficiently the use of twilight sleep, whilst having the added advantage of being safer and less toxic. It does not retard the uterine contractions, nor has it any effect on the child." Apart from what has been quoted above, and a recent publication by Craig[36] detailing the value of avertin in the management of eclampsia, there has been no other reference to the use of avertin in obstetrics in South African Medical Literature.[154,174,34,171,143,121,178] Discussing drugs that pass across the placenta Sapeika[142] mentions avertin and adds that as depression of the foetal respiration sometimes occurs, avertin is not advised in obstetrics.

In 1947 Dewar and Morris[40] reported a series of eclamptic patients managed by means of avertin. In an exhaustive search of the literature they were unable to find previous publication of a series of cases sufficiently large to warrant the drawing of statistically significant conclusions. Most of the eleven references to avertin used in eclampsia they were able to trace quoted "descriptions of comparatively few cases with favourable results, without any attempts to produce comprehensive surveys of all cases treated in the clinics concerned." Subsequent papers[27,36,58,119] on the same subject have confirmed both the safety and efficacy of this form of treatment and have stressed its value for domiciliary use by the Flying Squad.[58,27,99,36]

Mention has been made by Dewar and Morris,[40] Kellar,[82] Campbell and Burton,[27] Frew[58] and de Soldenhoff[39] about the place of avertin in the management of imminent eclampsia. I have, however, been unable to find any published series of results of such treatment sufficient in number to justify critical analysis.

Chemistry.

Avertin was available first as a crystalline substance soluble in water. Prior to administration it was necessary to dissolve the crystals and this was often time-consuming. Avertin is now supplied in a stock solution containing 100 G. of tribromoethyl-alcohol and 50 G. of amylene hydrate per 100 ml. This latter solution readily mixes with water.

$CBr_3 . CH_2OH$	Tribromoethanol
$(CH_3)_2 . C(OH)C_2H_5$	Amylene hydrate.

It is volatile and inflammable but not explosive and so should be kept tightly stoppered and not exposed to an open flame. At temperatures above 40° Centigrade, avertin breaks down into hychrobromic acid and dibromacetaldehyde. The main product of its metabolism is tribromoethyl-glucuronic acid (urobromalic acid) first described by Endeh in 1924. Urobromalic acid is the main excretary product in man.[175,64,94,153] The bromine remains in the organic molecule and is not excreted as the ion.[175,64,94,153] Sollman[153] mentions, however, that a case of bromide rash has been reported.

Dosage and Dispensing.

The basal anaesthesia dose is 0.1 ml. of the stock solution per kg of body weight. In order to achieve deeper anaesthesia, doses of up to 0.125 ml per kg[11] and occasionally as high as 0.15 ml per kg have been given. In order to achieve a state of "twilight sleep" 0.075 ml per kg is administered.

The dose for use in eclampsia[40] and throughout this series falls between the basal anaesthesia and twilight sleep doses and is 0.09 ml per kg.

The avertin is mixed as a 2.5% solution in ordinary tap water at a temperature of 104°F (40°C) or slightly less. In order to simplify dispensing it has been found convenient to keep a chart available with the equipment.[36] (Table III, page 32).

TABLE 111.

Weight of patient (lb.)	Amount of avertin (ml.)	Amount of water (ml.)
112	4.5	172
126	5.0	194
140	5.5	220
154	6.0	240
168	6.5	260
182	7.0	280
196	7.5	300
210 or more	8.0	320

From the above a simple calculation will show that the dosage is approximately 0.09 ml. avertin per kg. body weight made up into a 2.5% solution. Where the patient's weight is unknown, a rough estimate is made and the dose administered accordingly, or alternatively the dose for a 140 lb woman may be given. Accuracy is not essential. If an obstetric case is seen who has previously received a sedative, the calculated dose is only altered if the patient is (i) an unusually small person, or (ii) deeply sedated. In the former circumstances a smaller dose is administered, while in the latter 3-4 hours are allowed to elapse before avertin is given, unless restlessness suggesting imminent eclampsia occurs first, in which case a routine dose is administered immediately.

Prior to administration, 5 ml. of the dispensed solution are tested with 2 drops of 1:1000 Congo-red solution. The solution should remain red - if it turns purple or blue it is discarded. A purple or blue discolouration develops at a pH below 5 and indicates that a breakdown into hydrobromic acid and dibromacetaldehyde has occurred. These substances are extremely irritant to the rectal mucosa. Excessive heat or exposure to light can cause this breakdown.

A potential disadvantage[14] often overemphasised, particularly in obstetric cases, is the time consuming preparation of the solution. To avoid any delays the equipment used at the Peninsula Maternity Hospital has been specifically assembled to be time-saving.[36] The "avertin set" contains all the necessary apparatus for dispensing and administration in a padded box of many compartments. A selection of premeasured doses is available. When the Flying Squad is summoned a thermos flask is filled with water at a temperature of 104°F. Thus

within 2 or 3 minutes of arrival at a patient's home, administration of avertin is practical.

Administration (Obstetric cases).

A medium sized bladder catheter, attached by rubber tubing to a well fitting funnel, is lubricated, filled with the solution to expel all air and then passed 4-6 inches up the rectum. The shorter insertion is used in patients not in labour while the longer insertion is necessary when the presenting foetal part is low down in the pelvis. By means of finger or clamp compression of the tubing, the solution is run slowly into the rectum over a period of 3-5 minutes. The insertion of the catheter and the instillation of the fluid cause very little discomfort to the patient and are easily performed with the patient in the left lateral or dorsal position.

Repeat doses are indicated by a lessening of the sedative effect and a rise in the blood pressure. A second dose is never given until 2 hours have elapsed from the first, nor a third until 4 hours have elapsed from the second.

The possibility of the solution causing rectal necrosis has already been mentioned. Andersen[1] writes that "rectal necrosis a not uncommon complication in the early history of the drug's employment, has not been encountered since the concentration of the solution has been reduced, the heat of the solution kept near body temperature and the drug tested routinely for free hydrobromic acid." Certainly all those who have used avertin in the management of eclampsia have seen no evidence of rectal irritation. Maddox,[102] Shipway,[147] Wood,[176] Balsam[6] and Coghlan[32] all specifically note the complete absence of bowel symptoms. Sollman,[153] however, states that tenesmus and blood stools sufficient to be mentioned occur in 1% of clinical anaesthetics; about a fourth of these are fairly severe.

Lundy[100] has reported on a single intravenous administration of avertin. Anaesthesia appeared quickly and also disappeared within a matter of minutes.

Absorption, Detoxication and Excretion.

Avertin is rapidly absorbed by the rectal mucosa; average figures[64] are that 50% is absorbed within 10 minutes, 75% within 20 minutes, 85% within 25 minutes and 90-95% within 2 hours. The individual variations in response to avertin depend more on the rapidity of absorption than on the final amount absorbed. These variations constitute for many a definite disadvantage and contraindication[99] to the use of avertin.

Detoxication occurs in the liver by conjugation with glucuronic acid.

Excretion, which is rapid, is via the kidneys. Excretion lags only slightly behind the rate of absorption and 95% is excreted in the first 2 hours.

Tissue concentration is maximal after 20-30 minutes and decreases in the order liver, heart, brain, kidneys, lungs, spleen and blood. (Sollman[153] quoting Fischer and Huppmann, 1934).

Indications.

The withdrawal of avertin from the British Pharmacopoeia in 1958 implies that in present day therapeutics no indication for its use exists. Certainly there is no place for using avertin in general anaesthesia, obstetric analgesia, the management of tetanus and the management of ureteric calculi in all of which conditions avertin has been used. Avertin used as a basal anaesthetic may occasionally be justified.

The success of avertin in the management of eclampsia, especially in domiciliary initial treatment, appears to justify its use under these conditions.

Contraindications.

Even in the early 1930s when avertin was a favoured anaesthetic agent, there existed a formidable list of contraindications including toxaemia, sepsis, acidosis, shock, dehydration, hepatic or renal disease, chronic pulmonary disease, hypothyroidism, colitis, diabetes, neoplastic disease, old age hypertension and hypotension.

Williams[175] thinks the high toxcity is probably due to rapid reaction with sulphydryl groups or enzymes.

Great emphasis has been laid on the fact that avertin should at all costs be avoided where there is renal or hepatic disease. Thus eclampsia and imminent eclampsia are certainly theoretical and possibly practical contraindications to the use of avertin. This point will be fully elaborated in a later section.

Actions of Avertin.

The site of action for avertin has not been exactly determined. Sollman[153] quotes Cushing as saying it acts by depressing the diencephalon, but also quotes Chauchard and Monod as saying that the depressive effect extends also to the cerebral cortex. A definite depressive action on the heart and vasomotor centre occurs and there is also a direct action on the blood vessels.

The clinical effects include the following -

(i) - Loss of consciousness.

Dewar and Morris[40] noted that in eclamptic patients loss of consciousness occurred within 20 minutes. Beckman,[9] Goodman and Gilman[64] and Parsons[128] give an approximately similar time. Personal experience[36] with eclamptic patients showed that loss of consciousness usually occurred 5-8 minutes after the commencement of the administration. Lawrence and Mouton,[96] Balsam,[6] Hughes,[74] Young,[177] Bernheim et al[13] Shipway,[147] Benthin[11] and Kennedy[88] have all found that consciousness is lost in a few minutes. Bollinger and Maddox[17] experimenting with dogs, observed that loss of consciousness occurred in 2 minutes.

The maximal effect on the state of consciousness is observed after 20-30 minutes[64,94,9,177,147,11] when the concentration of avertin in the blood is about 6-10 mgm %. The corneal reflex is lost relatively early on and so is no indication of the depth of consciousness. The eyeballs are fixed and the pupil although small, reacts to light. Consciousness is regained in from 1½-3 hours[64,9,147,121,33,15] at which time the concentration of avertin in the blood has fallen to below 3 mgms.%.[64] Return of consciousness is usually followed by a long sleep which may last for many hours. Complete amnesia exists for the entire period.[40,64 121,113,128,171] Neither induction nor recovery are associated with coughing or vomiting.

Featherstone[54] quoting Wall claims that the duration of action appears increased if avertin is dissolved in milk. Coghlan[31] maintained that the sedative effect could be prolonged for 4-6 hours if the administration of avertin was preceded by the giving of nembutal gr. 3.

(ii) - Effect on the circulation.

Blood pressure - a fall in the blood pressure invariably occurs when avertin is used, whether for anaesthesia or obstetric analgesia. This hypotensive effect results from the direct action of the drug upon the vasomotor centre, heart and blood vessels.

Dewar and Morris[40] and Frew[58] noted sharp and welcome falls in the blood pressures of eclamptic patients. Campbell and Burton[27] in their series of eclamptics recorded the fall in systolic pressure as being up to 50 mm of mercury. Craig[36] emphasised that irrespective of the initial blood pressure in cases of eclampsia, a fall to below 140/100 mm of mercury in the first hour was recorded in 85% of patients.

Beckman[9] states that avertin lowers the blood pressure by 15 to 40 mm of mercury and that this effect begins in a few minutes and lasts usually for no longer than 15 minutes. These levels and times, with slight variations, are also mentioned by Goodman and Gilman[64] Coghlan[32] who writes "I have not recorded a drop of more than 15 mm of mercury" in a series of 175 cases including 36 obstetrical patients, Balsam,[6] Blomfield and Shipway,[16] Shipway,[148] Bernheim et al[13] in 63% of cases, Wood,[176] Connell,[33] Hornung,[72] Norton,[124] Taylor and Hunt,[159] Gorham,[113] Parsons[128] and Raginsky et al.[130] It is perhaps significant that not one of the above references indicates when or how often the blood pressure was recorded.

Benthin[11] published one of the earliest clinical reports about the effects of avertin anaesthesia. His findings as regards the blood pressure were as follows -

A rise - one case.
A 10-20 mm of mercury fall - 25%
A 30-40 mm of mercury fall - 25%
A 60-100mm of mercury fall - 19 cases
A 135-150 mm of mercury fall - 2 cases

Many others, including James Young,[177] Morrin,[116] Llewellyn Jones,[99] Kennedy[88] and Craig[36] have observed in a relatively high percentage of cases considerable falls in both the systolic and diastolic blood pressures. Despite these large falls in blood pressure, only Llewellyn-Jones and Morrin have reported in all three cases who required special resuscitative measures. Madon[101] routinely administered by intramuscular injection ephedrine grs.$\frac{3}{4}$ to counter any possible hypotension; others[116,64,13,159] have noted that ephedrine rapidly corrects hypotension occurring after avertin administration.

I have found no report stating that the hypotensive effect of avertin is a real danger. Young[177] wrote that "we are coming to regard the fall in blood pressure with increasing equanimity."

The fall in blood pressure commences within 10 minutes of the administration of avertin and is maximal about 10-15 minutes later.

Thereafter there is a rapid rise to the previous level. Personal study[36] of avertin used in cases of eclampsia indicated that the blood pressure seldom returned to its initial level and that the hypotensive effects commonly lasted for 2-3 hours.

The fall in systolic pressure is usually more than the fall in diastolic pressure.

Heart - Avertin has a direct action on the heart which is so slight that clinical and electrocardiographic examinations usually reveal no change[64,153,176] Meyler[114] states that ventricular fibrillation and bradycardia may occur.

Pulse - A slight rise in the pulse rate is the only change, if any, that occurs with Avertin.[6,13,176,33,147,72,11,65,128] Young[177] noted an association between the pulse rate and the fall in systolic blood pressure. Benthin[11] observed occasional marked increases in the pulse rate and cited as an example a rise from 80 to 160.

(iii) - Effects on the Respiratory System.

Edwards[53] writes that avertin has no effect on the respiratory system. On the other hand, Beckman[9] states that respiratory failure leading to immediate death can occur.

Respiratory depression bears a direct relationship to the dose of avertin administered and is rarely seen where avertin is used as either a basal anaesthetic[64,16,11,72,124] or for obstetric analgesia[72] or in cases of eclampsia.[27,36] When avertin was first available, attempts to achieve prolonged or deep anaesthesia with large doese often caused severe respiratory depression. The depression was accentuated in those patients to whom both avertin and morphine were administered.[174,153,128] The administration of 5% carbon dioxide brings quick relief in cases of respiratory depression.[177,88]

Minute ventilation and oxygen consumption are reduced.[64]

Relaxation of both the jaw and pharyngeal muscles causing stridor and cyanosis commonly follows the use of avertin. To prevent the latter complication, a metal or rubber airway should be inserted in all cases.[64,74,13,176,121,88]

Llewellyn-Jones[99] observed that much mucus accumulated in the pharynx.

Young,[177] Balsam,[6] and Mueller [121] state that postoperative pulmonary complications are minimal. This in part is accounted for by the fact that the cough reflex is only slightly diminished and that the laryngeal reflex is not abolished.[149]

(iv) - Action on the liver.

Used in basal anaesthesia doses, avertin rarely has a serious effect on a normal liver but may cause further damage in a previously diseased liver. Van Zyl[171] made a particular study of the effects of avertin when used in the presence of hepatic disease. He concluded that (a) the surgeon need not fear if the liver is normal; (b) the danger in a case of hepatic slight hypofunction is small and avertin is not contraindicated; and (c) avertin is contraindicated where marked liver deficiency exists.

Raginsky and Bourne[181] agree that avertin can safely be used in individuals with moderate liver damage.

Avertin is detoxicated in the liver by conjugation with glucuronic acid. Hepatic disease will delay this process and therefore in such cases avertin may result in unusually deep or prolonged anaesthesia. Paradoxically, it was observed in alcoholics that only a stupefying effect could be achieved.[6,16] There exists a quite considerable literature on the hepatotoxic effect of avertin. Beecher[10] reviewed a number of fatal toxic reactions to avertin anaesthesia and placed first as a cause of death, central necrosis of the liver. In this oft-quoted paper he claims that avertin may break down in the body to hydrobromic acid. This particular action is not known to occur and I cannot agree with either this statement or all his conclusions about the seven fatal cases he reports. Bourne et al[18] in experimental work on dogs found that there was a slight and transient alteration in liver function with avertin anaesthesia, but that no delayed liver damage was caused. Krantz and Carr [94] observed a diminished functional activity by the liver when assessing with the bromsulphalein excretion test. Hill [70] mentions that a hypersusceptibility to avertin may show as a liability to necrosis of the central cells of the liver lobule. The increased susceptibility may be due to a lack of sodium xanthine. The liver damage presents clinically as "delayed chloroform poisoning." Andersen[1] uses the same description in reporting one personal and 16 other fatal cases associated with avertin anaesthesia. Autopsies showed acute yellow atrophy and lower nephron nephrosis. Beckman[9] writes that autopsies in fatal cases revealed extensive damage to liver and kidney, while Meyler[114] reports hepatitis and acute yellow atrophy following the use of avertin.

Sellman[153] in A Manual of Pharmacology writes that impaired liver function is reported in 1 or 2% of clinical administrations. He, however, quotes Kaczinder 1930 and Bruger et al 1930 as maintaining that avertin has little effect on the normal liver. Shipway[149] concluded that the toxicity of avertin even to a damaged liver has been exaggerated.

In the published series where avertin has been used in eclampsia[27,40,36,58,119] particular stress has been laid on the complete absence of liver damage.

It would appear that a schism exists between on the one hand pharmacologists and reviewers of fatal cases of avertin anaesthesia, all of whom emphasise the hepatotoxic effects, and on the other hand clinical workers who have never observed liver damage due to avertin. Great consideration has been paid to these opposing views, particularly by those who favour the use of avertin in eclampsia. As previously stated, overdosage was more commonly seen when the drug was first introduced, and undoubtedly it was this factor that caused many deaths and much of the liver damage. Goldschmidt et al[63] investigated the causes of liver damage by potentially hepatoxic anaesthetic agents, not including avertin. They found that liver damage occurred most frequently in dogs who had been on poor carbohydrate diets and who suffered a relative anoxia during anaesthesia. A relative anoxia occurs when the open drop method of anaesthesia is employed. In the late 1920s and early 1930s, basal anaesthesia by means of avertin was often supplemented by either open drop ether or chloroform. It is not difficult to follow how this combination might reproduce the conditions of the above experimental work. Probably relevant too is the fact that cyanosis readily occurs if an airway is not inserted.

The standard procedure with avertin in the management of eclampsia is to insert an airway in all cases and to administer oxygen should cyanosis or any respiratory difficulty occur. The routine administration of intravenous glucose for nutrition is also practised. It is probable that these practices all play a definite, even if small, part in preventing immediate or delayed liver damage.

(v) - Action on the kidneys.

The kidney excretes the detoxicated conjugated product urobromalic acid and probably also excretes that small fraction of avertin which is not conjugated in the liver and which still possesses anaesthetic potency. Thus where pre-existing renal insufficiency exists, the margin of safety with avertin is considerably lowered and abnormally long and deep anaesthesia may result from standard doses. It is

possible that the enhanced sedative and hypotensive effects noted by those who have used avertin in eclampsia could be explained by the above mechanism. However, the increased urinary output seen after the use of avertin in eclampsia[119,58,36] contradicts this possible explanation. In many cases the amount of albuminuria decreased dramatically; this too points to other reasons for the observed good effects. Brown et alia[19] showed that in normal pregnant women avertin causes an increased renal plasma flow and a slight decrease in the reabsorption fraction. These two results tend to produce a slight diuretic response. Beckman,[9] Krantz and Carr,[94] Sellman,[153] Norton,[124] and Bourne et al[18] all maintain that during avertin anaesthesia the excretion of urine is suppressed and that this supression may last for up to 22 hours.[94] Shipway,[149] however, states that the renal depression lasts less than an hour and that there is no contraindication to the use of avertin in cases of renal disease.

Van Zyl[171] writes that in practice and experimentally, the use of avertin causes no poisoning symptoms in cases of very obvious renal damage. There is merely a moderate extension of the excretion time. Ballinger and Maddox[17] used avertin in dogs suffering from experimental nephritis and found no apparent worsening of the condition. The American Council of Pharmacy and Chemistry 1930[35] reported that in avertin anaesthesia there was an absence of direct injurious action on the kidney. Pitt[182] wrote specifically about the effects of avertin upon renal function. Slight renal damage shown by a fleeting albuminuria and an occasional transient postoperative nephritis were never serious and cleared up spontaneously in about 2 days. He concluded that of itself the influence of avertin upon the kidneys forms no contraindication to its use. Krantz & Carr[94] observed a transient proteinuria in 20% of cases after avertin anaesthesia.

Goodman and Gilman[64] on the other hand state that albuminuria and even frank renal damage, can occur if avertin is used in patients with renal disease. Hornung[72] write that avertin in obstetric cases is inclined to cause a haemorrhagic nephritis. Meyler[114] notes that avertin can cause a toxic nephrosis, and Beecher[10] reported tubular necrosis at autopsy in fatal cases.

(VI)- Temperature.

The body temperature falls slightly with avertin anaesthesia.[64,18,153]

(VII) - Basal metabolic rate.

The basal metabolic rate is reduced by an average of 15%.[64]

(VIII) - Blood Sugar.

There is a slight but transient rise in the blood sugar level.[64,153,17,124,76,114]

(IX) - Alkali reserve.

The carbon dioxide combining power of the blood is slightly decreased.[64,153,17,114]

(X) - Cerebro-spinal fluid pressure.

The cerebro-spinal fluid pressure is reduced.[27,64,153,9] It is said to occur in 15-20 minutes[153] and has been offered as an explanation for the effectiveness of avertin in preventing further eclamptic convulsions.[27] Stephen et alia[156] maintain that avertin causes a rise in the C.S.F. pressure.

(XI) - Bile acids.

The secretion of bile acids is decreased.[76]

General note on the actions of avertin.

I have elaborated at length and quoted freely on the circulatory, respiratory, hepatic and renal effects of avertin because the drug has its greatest potential toxicity in these areas. Early publications on avertin anaesthesia and recent textbooks of pharmacology stress the dangers inherant in the use of avertin. Reading the reports of some fatal cases thirty years after they were written, and in the light of present day knowledge, factors other than the drug per se are apparent as the actual cause of death. Overdosage in attempts to obtain full surgical anaesthesia caused many deaths[1] as did failure to maintain a clear airway.

It is probably significant that those who have written on the uses of avertin (particularly in eclampsia) during the last 15 years, have emphasised how safe it is to use. The absence of immediate toxic effects has made avertin the first choice for the initial domiciliary treatment of eclampsia. Remote toxic effects upon the liver or kidneys have not been reported in cases of eclampsia treated with avertin.

AVERTIN IN OBSTETRICS.

Not long after 1926, when avertin was first introduced for clinical anaesthesia, obstetricians were evaluating its capacity for the relief of pain in labour. An extensive but predominantly German literature was soon available on the subject.[31,32,11,72,89,106,87,120,33] However, the absolute necessity for the constant supervision of patients under avertin limited its clinical application in this field and from about 1935 onwards its use in midwifery was virtually abandoned. In 1947 Dewar and Morris[40] published a paper detailing the use of avertin in eclampsia and the excellence of their results has given the drug a new lease of life. The effectiveness of avertin in preventing a recurrence of convulsions in cases of eclampsia makes it a logical step to extend the use to the prevention of convulsions in cases of severe toxaemia of pregnancy.

In obstetrics the actions of avertin are assessed in three ways, viz: (i) on the mother; (ii) on the child; and (iii) on the labour.

(i) - <u>On the Mother</u> - The effects of avertin upon the mother remain exactly as discussed under the general properties of the drug. Probably because smaller doses are used respiratory, renal and hepatic complications have rarely been seen in obstetrics - this despite the fact that eclamptic patients have in most instances renal and hepatic dysfunction.

(ii) - <u>On the child</u> - Beckman[9] maintains that the use of avertin in obstetrics is undesirable because its presence in the foetal circulation in full concentration can have a long lasting depressant action on the baby. These views are shared by Goodman and Gilman[64] and Sapeika.[142] Coghlan[32] in 36 obstetric cases found 3 infants slightly cyanosed at birth and 4 who were sleepy for a day or two.

Morrison[120] states that the child is born "in a lively condition" as compared to morphine-scopolamine narcosis. Connell[33] noted that the condition of the child is "generally better than after an ordinary unassisted labour". Featherstone[54] quotes Wall as saying that where avertin was administered for operations upon the gravid uterus, there was no action upon the foetus. Benthin[11] in 16 cases detected no depression in the infant. Hornung[72] found the babies unaffected. Killian, quoting from the relevant German literature, states that the foetal heart remains unchanged.

Where cases of eclampsia have been treated with avertin, severe apnoea has rarely been observed.[40,27,36] Many infants were undoubtedly depressed at birth but they soon attained a normal circulation and respiration. It is difficult in these cases to apportion the respective contributions to the depression of the disease process and of the drug.

(iii) - On the labour. First and Second Stages. - The effects of avertin upon the first and second stages of labour are not agreed upon in the literature on the subject. There appear to be two diametrically opposite views.

Dewar and Morris[40] claim that in most of their patients, labour was not interfered with in any way apart from a poor use of the voluntary muscles in the second stage. Campbell and Burton[27] observed the same in their patients but emphasise that in eclampsia it is an aim to save the patient from the stress and strain of the second stage. The absence of voluntary bearing down efforts are therefore not relevant to the management. Coghlan[32] noted no interruption of or delay in labour in patients receiving avertin. The average duration of labour in his series for primagravidae was 15 hours 45 minutes and for multigravidae it was 8 hours. Craig[36] observed neither hypotonic inertia nor incoordinate uterine action attributable to the administration of avertin.

On the other hand, Beckman[9] emphasises that avertin has a depressant action on the uterus causing a prolongation of labour and a consequent increase in the numbers of instrumental deliveries. Goodman and Gilman[64] share this view and note that uterine atony can occur with even small doses such as 60 mgm per kg. body weight while Sollman[153] mentions a dose as low as 50 mgm per kg. body weight. Morrison[120] writes that avertin tends to prolong and slightly diminish the pains of labour. Connell[33] in more than 50 cases found labour to be prolonged, but that this was not of such a degree as to affect the child. Featherstone[54] quoting Wall, says that the rate of contractions is slowed down to about half but that the intensity is only slightly reduced. Hornung[72] observed less effective contractions and therefore a slightly longer labour. Killian[89] writes that (i) "greater pauses and a weakening of travail have been observed", that (ii) obstetric forceps deliveries were difficult, and apparently contradicting his first statement, that (iii) "the times of labour were remarkably short."

Third stage of labour - Connell[33] found no lengthening of the third stage of labour in patients under avertin, but noticed that in primigravidae the uterus tended to contract less well and that third

stage blood loss "may be rather more free." Hornung[72] in 100 cases had 27 instances of atonic post-partum haemorrhage. 22 of the 27 patients had had a good analgesic response following the administration of avertin. In 3 of his patients a manual removal of the placenta was necessary. Morrison[120] observed no delay in the delivery of the placenta and quotes Martin as saying that avertin was not a cause of postpartum haemorrhage.

Puerperium and Lactation - As avertin is rapidly excreted, any observed changes in the puerperium or in the establishment of lactation can hardly be attributed to a direct action of the drug. Despite this, Coghlan[32] reports that lactation, if anything, was quicker and freer than otherwise and Martin is reported[120] as stating that no deleterious effect on the puerperium occurs. Connell[33] found no delay in the onset of lactation and that involution of the uterus proceded normally.

A SURVEY OF 100 CASES OF IMMINENT ECLAMPSIA.

SELECTION OF PATIENTS.

In April 1960, avertin was introduced at the Peninsula Maternity Hospital, Cape Town, for the management of eclampsia. It was known at that time that in previous years many of the cases of eclampsia had had their first convulsions whilst in hospital (Table 1, page 2). A need existed for a more intensive management of patients suffering from severe toxaemia. As avertin had been singularly successful in preventing recurrences of convulsions[40,119,85] it was thought that it might be equally successful in preventing an initial convulsion. Therefore, in April 1960 avertin was introduced into the regime for the management of cases of severe toxaemia of late pregnancy seen either at the Peninsula Maternity Hospital or by the Flying Squad in domiciliary work. After treatment by the Flying Squad, patients are usually transferred to the Peninsula Maternity Hospital; but when the bed shortage is critical, they are admitted to other maternity units. The present survey covers the first 100 patients of severe toxaemia treated with avertin by the staff of the Peninsula Maternity Hospital. 3 of these patients after treatment with avertin by the Flying Squad were admitted to other institutions. As their further management did not differ from the routine at the Peninsula Maternity Hospital, they have been included in this survey so as to obtain a consecutive series.

The criteria for deciding that a particular patient was in a state of imminent eclampsia have already been discussed. They were strictly adhered to at all times. In each latient the blood pressure reading was confirmed at least once and usually by a second observer. No contraindication to the use of avertin on the grounds of severity occurred. (Dewar and Morris[40] accepted one case of eclampsia as having a contraindication to avertin. The eclampsia was complicated by concealed accidental haemorrhage with marked shock). In all antepartum and intrapartum cases the foetal heart was heard before the commencement of treatment.

Very occasionally patients who fulfilled the criteria for a diagnosis of imminent eclampsia were already in the second stage of labour. Such patients were not given avertin but were submitted to general anaesthesia and labour was completed by means of a forceps delivery.

As far as is possible, I believe that no bias existed in the selection of these 100 cases of imminent eclampsia.

An addendum contains the folder numbers of the 100 cases. They were seen over a 17 month period from April 1960 to August 1961. The incidence of imminent eclampsia for that period amongst cases of toxaemia of pregnancy at the Peninsula Maternity Hospital was 13.6 per cent.

The Routine Management.

Avertin regime. The dosage of avertin was 0.09 ml. per kg. of body weight and was calculated according to the dosage chart as shown in Table III. Where the patient's weight was unknown, a rough estimate was made and the dose calculated accordingly. Precision accuracy was not practised; nor was it found to be necessary. Even if the patient had previously received some form of treatment, the usual dose of avertin was administered provided that at that time the patient fulfilled the criteria for diagnosing imminent eclampsia.

Prior to administration 5 ml. of the dispensed solution were tested with 2 drops of Congo-red solution. On no occasion was the avertin solution discarded because of the development of a purple or blue discolouration. The administration of avertin has been described on page 33.

Repeat doses of avertin were given when there was a lessening of the sedative effect and a rise in the blood pressure. A second administration was never given until 2 hours had elapsed from the first+ nor a third until 4 hours had elapsed from the second.

Avertin therapy was continued portpartum depending on the patient's condition. Usually not more than one postpartum administration was necessary.

From the moment that avertin was first given until 24 hours after delivery (occasionally longer) each patient was constantly observed by either a doctor, midwife, medical student or pupil midwife. Throughout this time records, of the maternal pulse, respiration, blood pressure and degree of sedation, of the foetal hearts sounds and of the uterine contractions, were made every 15 minutes. Immediately after the first and every subsequent administration of avertin, such records were made every 5 minutes for 30 minutes. The sedative effect was correlated against the standards which follow so that any observer bias was eliminated.

+One exception - this patient had a convulsion within two hours of the first dose and was immediately given a second dose.

Sedation - (a) Deep - airway tolerated. No response to ordinary stimuli nor to uterine contractions.

(b) Moderate - mostly asleep. Response to uterine contractions.

(c) Light - restless more than asleep. Response to calling of name and light stimuli such as the taking of a blood pressure.

(d) No effect.

Obstetric management. Patients who were already in labour received no special management during the first stage. Those who were not in labour but who were more than 32-34 weeks pregnant had a surgical induction of labour performed as soon as sedation had been achieved or as soon as possible after admission to hospital in the case of admissions via the Flying Squad. Following upon the surgical induction, patients were given 'pitocin' by drip infusion. In a minority of cases where conditions for allowing a surgical induction were not favourable or where a specific indication (other than the severe toxaemia) existed, an elective caesarean section was performed.

A conservative approach was adopted in a few patients who were less than 32-34 weeks pregnant and who had small infants on clinical examination. Such patients were administered repeat doses of avertin for 24 hours when a careful reassessment was made. If the blood pressure and the degree of albuminuria had decreased and if the patient was free from symptoms, other sedative and/or hypotensive therapy was commenced and the avertin gradually discontinued over the next 12-24 hours. The supplementary sedative was invariably sodium amytal and the hypotensive agents were mecamylamine or guanethidine.

In all patients, once the cervix was fully dilated, delivery as far as possible was completed by means of forceps with the patient under general anaesthesia. If labour was unduly prolonged, i.e. longer than 24 hours, or if attempts at induction of labour failed, caesarean section was performed.

Additional therapy. In fully established labour the contractions occasionally caused considerable discomfort to a patient who otherwise remained well sedated under avertin.[33] In such cases morphine grs.$\frac{1}{4}$ was given by intramuscular injection. Despite what has been written we observed no severe respiratory or other depression when patients were given both avertin and morphine.

In an occasional patient marked restlessness was observed where the blood pressure was still very low following the avertin; such patients received supplementary sedation in the form of intramuscular injections of paraldehyde.

No oral feeding was permitted. Nutrition was maintained by intravenous injections of 50 ml. of 50% dextrose, or infusions of 10% dextrose in water.

An initial catheter specimen of urine was taken in all patients and thereafter catheterisation was only performed if the patient was unable to void urine or if an assessment of urinary output was required to assist the further management.

Observed Data Concerning Patients.

Race.

There were 10 White and 90 non-White patients.

White: 4 of 10 were non-booked admissions. There was no admission via the Flying Squad. The general practioners serving the white population drained by the Peninsula Maternity Hospital tend to send their patients direct to the out-patient department should they develop toxaemia. Such patients occasionally attend days, or even weeks, after seeing their practioner. It is not a policy we condone, but it has as yet proved difficult to eliminate. It explains in part the manner of admission of the four non-booked cases.

Non-White: 51 of the 90 were non-booked admissions. 17 were admitted via the Flying Squad. As with the white patients, many were referred direct to the out-patient department. In about 5 cases the services of the Flying Squad were refused when offered.

The failure to appreciate the severity of toxaemia of late pregnancy, as revealed above, will be fugue-like in its repetition throughout this analysis.

The racial distribution of patients has no further relevancy to this analysis and will not be discussed further.

Age.

The age distribution of the patients in this survey is shown in Table IV (page 49).

TABLE IV.

Age in Years.	Primigravidae No.	%	Multigravidae No.	%	All Patients No. & %
15 - 20	14	34	3	5	17
20 - 24	18	44	9	15	27
25 - 29	6	14.5	11	19.3	17
30 - 34	2	5.0	16	27	18
35 - 39	1	2.5	13	22	14
40 - 44	-	-	6	10	6
45 - 49	-	-	1	1.7	1
50 - 54	-	-	-	-	-
Total	41	100%	59	100%	100

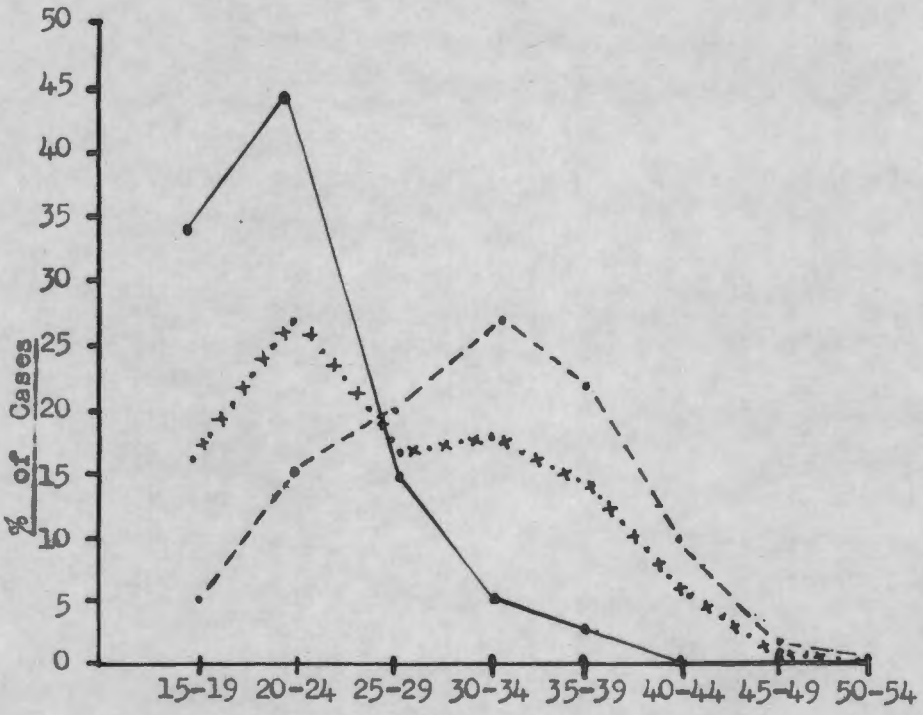
The mean age for all patients was 26.3 years.
The mean age for primigravidae was 21.7 years.
The mean age for multigravidae was 31.0 years.

The youngest patient was aged 15 years and the oldest patient was aged 47 years.

The differences in the age distributions of primigravidae, multigravidae and all patients is illustrated graphically. (Graph 1, page 50)

Although no attempt was made to diagnose in individual patients the underlying type of toxaemia of late pregnancy, it was suspected that many of the multigravidae would be patients with hypertensive vascular disease and superimposed pre-eclamptic toxaemia. Graph 1 suggests that this is so. The expected graphs for a comparison of age with parity with other factors being equal, would show two similar curves with a shift to the right of the curve for multigravidae. In the illustrated graph, the curve distribution and the actual numbers are disproportionately shifted to the right which suggests an underlying factor amongst the multigravidae which is associated with increasing age. It is reasonable to assume that this additional factor is hypertensive vascular disease. The alternative assumption would be that imminent eclampsia arises de novo more frequently in multigravidae over the age of 30 years than in those under the age of 30 years. This latter view is not tenable with the known facts concerning pre-eclamptic toxaemia culled from series where the patients were regularly examined from the earliest months of their pregnancies until at least six months postpartum.[42]

G R A P H 1.



——— Primigravidae

- - - - Multigravidae

·x·x·x All Patients

RELATIVE DIFFERENCES IN AGE DISTRIBUTION OF PRIMIGRAVIDAE, MULTIGRAVIDAE AND ALL PATEINTS WITH IMMINENT ECLAMPSIA.

A scattergraph (Graph 11, page 52) was designed which related foetal mortality in both primigravidae and multigravidae to maternal age. The graph reveals that the foetal prognosis in cases of imminent eclampsia worsens with increasing maternal age in both groups. The actual figures are as follows -

Primigravidae: Mean age 21.7 years.
Mean age of patients suffering foetal loss 26.5 years.
Only one of the 6 infants lost was born to a mother younger than the mean age.

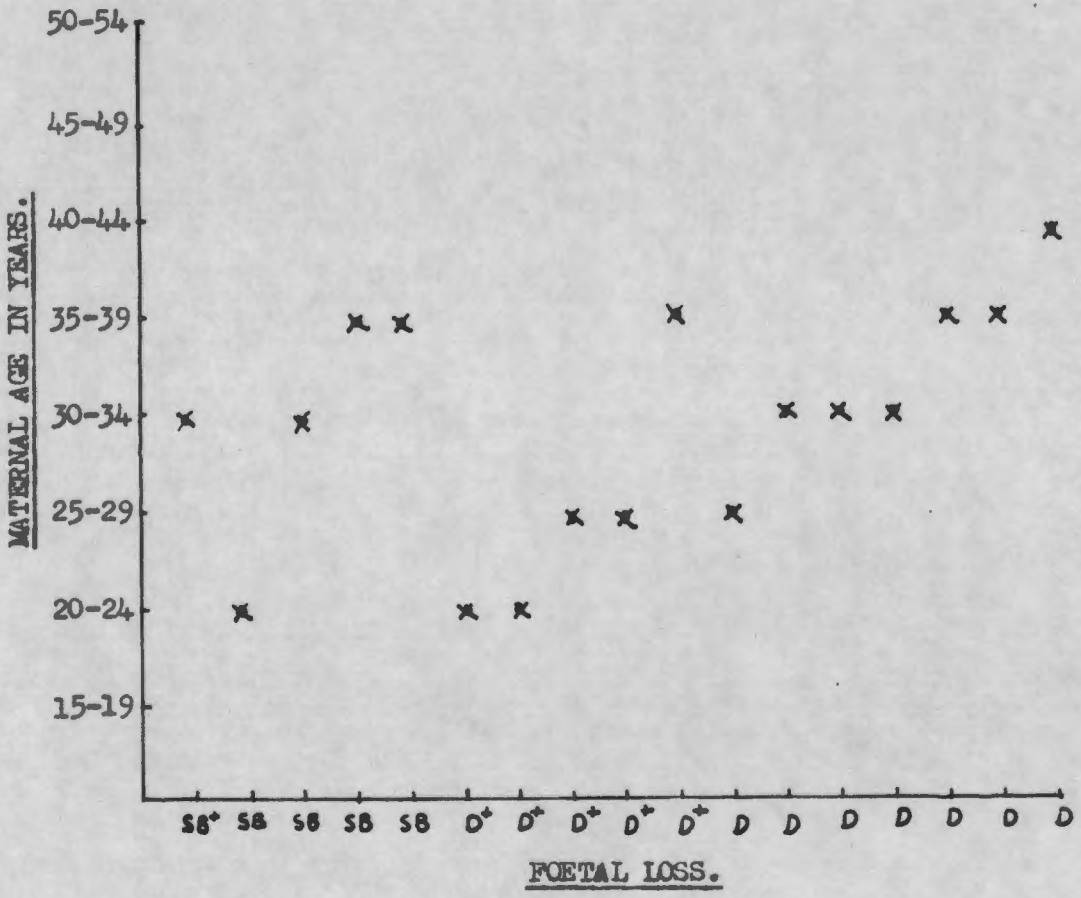
Multigravidae: Mean age 31.0 years
Mean age of patients suffering foetal loss 33.0 years.
4 of the 11 infants lost were born to mothers younger than the mean age

It is tempting to read too much from these figures, but increasing age in cases of imminent eclampsia undoubtedly worsens the foetal prognosis. It is unlikely that age per se carries the poor prognosis but rather that the prognosis is dependent on a disease seen more frequently amongst the elderly or a factor (possibly occult) associated with age. As the signs and symptoms of imminent eclampsia differed little at the time of treatment between primigravidae (younger) and multigravidae (older) (see later tables), the presumed disease or unknown factor was probably operative throughout the pregnancies of the more elderly patients. I believe that this factor is hypertensive vascular disease. Some support is given to this belief by the slightly higher mean age of the mothers delivered of stillborn infants - 31.6 years, as compared to the mean age of the mothers whose infants died within a month of birth - 30.3 years, as compared to the mean age of the mothers whose infants survived - 25.4 years. The figures of the infants who failed to survive are, however, too small to be statistically significant.

Gravidity.

Table V (page 53) classifies certain basic facts concerning primigravidae and multigravidae.

GRAPH 11.



+ = Primigravida. SB = Stillbirth. D = Neonatal death.

N.B. Mean age for all patients 26.3 years.

RELATIONSHIP OF FOETAL LOSS TO MATERNAL AGE.

TABLE V.

	Primigravidae	Multigravidae.
Number	41	59
Booked	27	18
Non-booked	14	41
Mean age	21.7 years	31.0 years
Infants delivered	41	60
Stillbirths	1	4
Neonatal deaths	5	7

Table VI (page 56) shows the numbers of previous pregnancies amongst the multigravidae; the mean is 4.7 previous pregnancies.

The reversed non-booked/booked ratio between primigravidae and multigravidae was not an unexpected finding as at the Peninsula Maternity Hospital multigravidae are only booked if they have (i) an associated disease or abnormality, (ii) a previous history of a complicated pregnancy, labour or puerperium, or (iii) a current complication of pregnancy. It was decided to assess amongst the 41 non-booked multigravidae to see if any should have been booked on the basis of their previous obstetric history. Some of the patients had never received antenatal care while others remembered little about any care they had received with previous pregnancies. Details about previous confinements were remembered more often on the whole. None-the-less, from amongst the 41 patients a clearly abnormal previous obstetric history was obtained from 19. 11 of these 19 cases had received antenatal care during their current pregnancies for at least two weeks before being admitted to hospital as emergency cases of imminent eclampsia. For easy assimilation, the facts concerning these 19 patients have been tabulated - Table VII (page 57).

A study of Table VII reveals that more than one third of the total foetal loss is found amongst these 19 patients. The 8 patients who received no antenatal care cannot be lightly dismissed. It is the duty of medical practioners who do obstetrics, to impress upon patients when discharging them postpartum, (i) the need for early and adequate antenatal care in subsequent pregnancies, and (ii) the need for hospital confinement in certain circumstances. Approximately 4 of the above 8 patients assured me that they were given no such directives, while the remainder could not remember.

More distressing are the 11 patients who attended for and received antenatal care. Whatever the reasons for not immediately referring these patients for bookings for hospital confinement, they constitute grave errors of judgement. The foetal loss amongst this group was 36.4%. More distressing still is that a few of these 11 patients were informed that a hospital confinement would not be necessary.

To create a balanced picture the 8 booked multigravidae, who had previous abnormal obstetric histories, have been tabulated in the same way - Table VIII (page 58). The table reveals that the foetal mortality is only a third of that in Table VII (page 57). Careful antenatal care and admission to hospital when the early symptoms and signs of toxaemia are detected are vitally important where there is a history of toxaemia in a previous pregnancy.

A scattergraph (Graph III, page 59) was designed which related foetal mortality to increasing gravidity in the multigravidae. The graph shows that only 3 of 11 patients whose infants did not survive are of less gravidity than the mean for all multigravidae, viz: 4.7 previous pregnancies. Increasing gravidity implies increasing maternal age and so the above is not an unexpected finding.

Mode of Admission.

There were 27 booked primigravidae. One of these patients was admitted via the Flying Squad. She developed a severe headache when 31 weeks pregnant and was seen by her general practitioner who found her in a state of imminent eclampsia.

There were 14 non-booked primigravidae of whom one was a Flying Squad admission. This patient was fetched 75 miles from a rural hospital.

There were 18 booked multigravidae of whom one was a Flying Squad admission. This patient had failed, despite letters, to attend the antenatal clinic for 2 months.

There were 41 non-booked multigravidae of whom 15 were admitted via the Flying Squad.

The total admissions via the Flying Squad numbered 17.

It has been previously stated that the majority of the non-booked admissions are referred direct to a hospital clinic irrespective of the severity of the disease. During the period of this survey two such patients developed ecalmptic convulsions while en route to hospital. I am satisfied that the Flying Squad is an essential to the management of imminent eclampsia and that avertin is both safe and effective for initial domiciliary use. Barry,[7] Dewar and Morris[40] and Campbell and Burton[27] have all emphasised the need for the Flying Squad in the management of cases of severe toxaemia of pregnancy.

TABLE VI.

Number of Previous Pregnancies in Multigravidae with Imminent Eclampsia.

Number of Previous Pregnancies	Number of Patients.
1	15
2	7
3	3
4	7
5	6
6	6
7	1
8	2
9	3
10	6
11	1
12	1

Average number of previous pregnancies = 4.7.

TABLE V11.

Non-Booked Multigravidae with a Previous Abnormal Obstetric History.

Number	Nature of Previous Abnormality.	Current Antenatal Care.	Infant Result
1	Accidental antepartum haemorrhage - stillborn infant	Private Midwife	N.N.D.
2	Toxaemia of late pregnancy	General practitioner	A
3	Hysterotomy for toxaemia	General practitioner	A
4	Toxaemia - stillbirth	Municipal Clinic	A
5	Toxaemia - stillbirth	Municipal clinic	N.N.D.
6	Toxaemia plus accidental antepartum haemorrhage	General practitioner	A
7	Toxaemia of late pregnancy	Divisional Council Clinic	A
8	Essential hypertension with superimposed pre-eclamptic toxaemia	General practitioner	S.B.
9	Toxaemia of late pregnancy	Municipal Clinic	A
10	Toxaemia of late pregnancy	Municipal Clinic	N.N.D.
11	Toxaemia of late pregnancy	General practitioner	A
12	Toxaemia of late pregnancy	Nil	A
13	Eclampsia	Nil	N.N.D.
14	3 previous stillbirths	Nil	A
15	Caesarean section for toxaemia	Nil	A
16	Toxaemia of late pregnancy	Nil	A
17	Toxaemia of late pregnancy on two occasions	Nil	A
18	Toxaemia of late pregnancy	Nil	N.N.D.
19	Toxaemia of late pregnancy	Nil	A

A = Alive. S.B. = Stillbirth N.N.D. = Neonatal death.

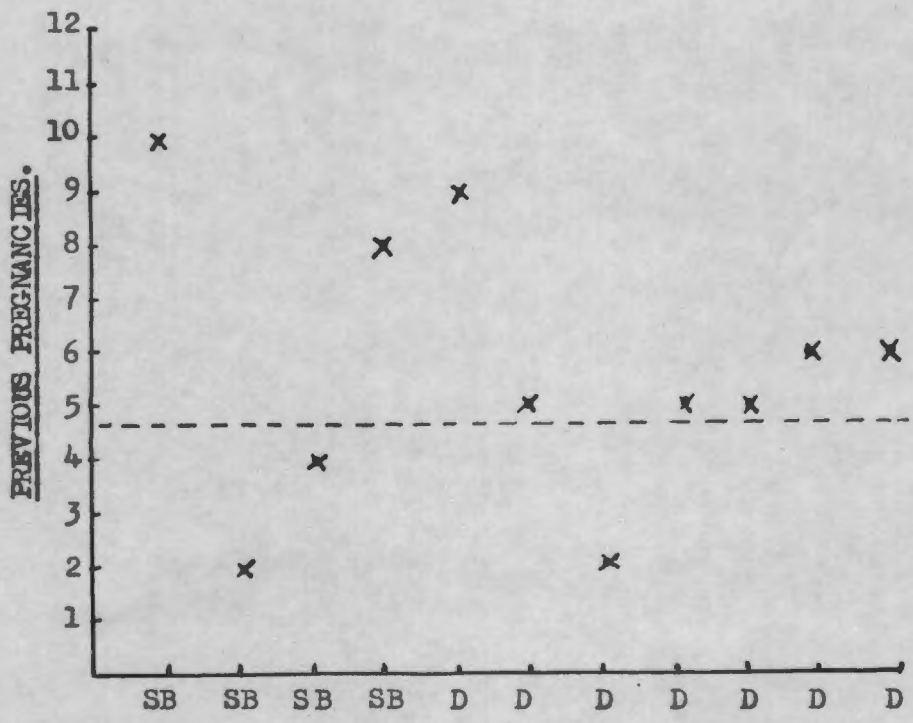
TABLE V111.

Booked Multigravidae with a Previous Abnormal Obstetric History.

Number.	Nature of Previous Abnormality.	Clinic Attended+	Infant Result.
1	Two premature infants	Routine antenatal	S.B.
2	Toxaemia of late pregnancy	Toxaemia clinic	A
3	Hysterotomy for toxaemia of late pregnancy	Toxaemia clinic	A
4	Toxaemia of late pregnancy	Toxaemia clinic	A
5	Diabetes. Toxaemia of late pregnancy	Routine antenatal	A
6	A stillbirth. A neonatal death. Toxaemia of pregnancy.	Routine antenatal	A
7	Toxaemia of late pregnancy on 3 occasions	Toxaemia Clinic	A
8	Toxaemia of late pregnancy	Toxaemia Clinic	A

+At the Peninsula Maternity Hospital a special toxaemia clinic is conducted for patients with (i) a past history of toxaemia of late pregnancy, (ii) a known history of hypertension preceding the pregnancy, and (iii) a labile or elevated blood pressure detected in the first two trimesters of pregnancy. Patients are seen more frequently and antihypertensive and diuretic drug therapy is used in certain cases. Where improvement does not occur or where there is regression after improvement, the patients are admitted to hospital.

GRAPH 111



FOETAL LOSS.

SB = Stillborn. D = Neonatal death.

– – – – – = Line of mean Gravidity.

RELATIONSHIP OF FOETAL LOSS TO NUMBER OF PREVIOUS PREGNANCIES IN MULTIGRAVIDAE.

Observations in Patients who had received Antenatal Care on at least Two Occasions.

Apart from the 45 booked admissions, 28 of the non-booked admissions had received antenatal care on at least two occasions - a total of 73 patients. An analysis was made of the obstetric care to assess whether any of the above 73 patients had shown signs of toxaemia prior to admission. Tables IX, X, XI, and XII (pages

Table IX shows that amongst 27 booked primigravidae 14 presented with one or other sign of toxaemia during their period of antenatal care. Of these 14 patients special observation and/or treatment was accorded to only 6 - no foetal loss. The remaining 8 patients were presumably accepted as being obstetrically normal and received no special management - two neonatal deaths occurred.

Table X shows that amongst 18 booked multigravidae 14 presented with one or other sign of toxaemia during their period of antenatal care. Special observation and/or treatment was accorded to 11 of the 14 patients - there was one stillbirth. The remaining 3 patients were presumably accepted as being normal and received no special management - there was one stillbirth.

From both tables there was a total of 17 patients who during their period of antenatal care presented with neither hypertension nor albuminuria until the day of admission. There was one neonatal death in this group.

In all amongst the 45 booked cases there was a total foetal loss of 5.

A study of Tables IX and X indicates that 8 patients attending the special toxaemia clinic were admitted in a state of imminent eclampsia. There was no foetal loss in this group, a finding which may be due to the special treatment administered antenatally. However, these 8 patients must be accepted as cases of failed management. I feel that a clinic of this nature, to justify its policy of treating toxaemic patients on an out-patient basis, would function better if patients were seen twice weekly. In this way the sudden development of pre-eclamptic toxaemia upon an existing hypertension would be detected at an earlier stage than at present happens.

Table XI shows that amongst 8 non-booked primigravidae receiving antenatal care, 7 presented with one or other sign of toxaemia. There was one stillbirth and 2 neonatal deaths amongst these 7 of whom only 3 received special observation and/or treatment.

Table XII shows that amongst 20 non-booked multigravidae receiving antenatal care, 18 presented with one or other sign of toxaemia. The antenatal findings of the remaining 2 patients are unknown. Special observation and/or treatment was accorded to 8 of these 18 cases. Among these 18 cases there was one stillbirth and 3 neonatal deaths - a known history of toxaemia in a previous pregnancy was present in all four

In all amongst the 28 non-booked admissions who had received antenatal care, there was a total foetal loss of 7.

These tables reveal many deficiencies in the standard of antenatal care in Cape Town. The tables, however, do not indicate all the imperfections. Two cases from municipal clinics and two from general practitioners did not have their urines examined at every antenatal visit - this despite having elevated blood pressures. The blood pressure was not recorded in a fifth patient who presented with albuminuria at a municipal clinic.

Some of the apparent neglect in admitting patients for treatment is due to a permanent shortage of antenatal maternity beds. This shortage of beds becomes the cloak for disguising inefficiency, but on the whole the poor standard of antenatal care bears little relationship to the bed shortage. Carelessness and ignorance are the main factors as tables IX, X, XI and XII clearly show. Of 28 booked admissions who presented antenatally with a sign of toxaemia, only 17 received special observation and/or treatment; of 25 non-booked admissions who presented antenatally, at a clinic or privately, with a sign of toxaemia, only 11 received special observation and/or treatment. These figures indicate that if there was no bed shortage whatsoever, only 53% of patients with an antenatal sign of toxaemia would be admitted to hospital. In the other 47% of such patients, no apparent notice would be taken of the warning signs.

From the tables it appears that the standard of antenatal care in Cape Town often falls short of even basic requirements, and certainly does not approach the meticulous but rewarding methods practised in Sydney, Australia and elsewhere. The possible non-avoidable cases of imminent eclampsia in this survey number 48 - the 27 patients who received no antenatal care and the 21 patients who revealed no fore-warning signs of toxaemia while receiving antenatal care.

TABLE IX.

Antenatal Care of Booked Primigravidae.

Number	Clinic	Hpt.	Alb.	Observed before admission.		Treatment.	Foetal Result.
1-13	Antenatal	-	-	-	-	-	A 12 NND 1
14	Antenatal	+	-	4 weeks	-	Nil	NND
15	Toxaemia	+	-	7 weeks	-	Hypotensives	A
16	Antenatal	+	+	8 weeks	1 week	Nil	A
17	Antenatal	+	-	3 weeks	-	Nil	A
18	Antenatal	+	-	8 weeks	-	Sedatives	A
19	Antenatal	-	+	1 week	-	Nil	A
20	Antenatal	+(once only)	-	3 weeks	-	Seen after 3 days.	A
21	Antenatal	+	-	8 weeks	-	Nil	NND
22	Antenatal	+(once only)	-	2 weeks	-	Seen after 3 days	A
23	Antenatal	+	+	1 week	1 week	Nil	A
24	Antenatal	-	+(once only)	-	6 weeks	Nil	A
25	Antenatal	+	-	2 weeks	-	Sedatives	A
26	Antenatal	+(once only)	-	9 weeks	-	Nil	Postpartum
27	Antenatal	+	+	11 weeks	1 week	Admitted & discharged.	A

Hpt = A blood pressure of 140/90 mm of mercury or more.
Alb = The presence of albumen in a clean specimen of urine.
A = Alive.
SB = Stillbirth
NND = Neonatal death.
Treatment = Indicates treatment before being admitted in a state of imminent eclampsia.

TABLE X.

Antenatal Care of Booked Multigravidae.

Number	Clinic	Hpt.	Alb.	Observed before admission		Treatment	Foetal Result.
1- 4	Antenatal	-	-	-	-	-	A 4
5	Antenatal	+	-	7 weeks	-	Admitted	SB
6	Antenatal	+	-	1 week	-	Admitted	A
7	Toxaemia	+	-	5 weeks	-	Hypotensives	A
8	Toxaemia	+	-	2 weeks	-	Hypotensives	A
9	Antenatal	+	+	16 weeks	1 week	Admitted & discharged.	A
10	Antenatal	+	+	1½ weeks	1½ weeks	Nil	A
11*	Antenatal	-	+(once only)	-	7 weeks	Nil	SB
12*	Toxaemia	+	+	4 weeks	1 week	Hypotensives	A
13*	Toxaemia	+	+	12 weeks	1 week	Admitted & discharged.	A
14*	Toxaemia	+	-	12 weeks	-	Hypotensives Admitted & discharged	A
15*	Antenatal	+	-	2 weeks	-	Hypotensives. Nil	A
16*	Toxaemia	+	-	20 weeks	-	Hypotensives	Postpartum.
17*	Toxaemia	+	-	13 weeks	-	Sedatives	A
18*	Antenatal	+	-	6 weeks	-	Sedatives	A

*Known previous history of toxaemia.

TABLE XI.

Non-Booked Primigravidae who had received antenatal care.

Number	Antenatal Care.	Hpt.	Alb.	Observed before admission.	Treatment.	Foetal Result.
1.	General Practitioner	+	-	8 weeks	Nil	A
2.	Rural Hospital	+	+	3 weeks	Sedation	A
3.	Municipal Clinic	-	-	-	-	A
4.	General Practitioner	+	+	1 week	Sedation	NND
5.	Municipal Clinic	+	+	2 weeks	Nil	NND
6.	Specialist Obstetrician	+	+	2 weeks	Hypotensives	SB
7.	Municipal Clinic	+	-	2 weeks	Nil	A
8.	Municipal Clinic	+	+	4 weeks-1 week	Nil	A

TABLE XII.

Non-Booked Multigravidae who had received antenatal care.

Number	Antenatal Care.	Hpt.	Alb.	Observed before admission.	Treatment	Foetal Result.
1	Municipal Clinic	+	+	4 weeks - 1 week	Nil	A
2	General Practitioner	+	+	1 week or more	Sedation	A
3	Divisional Council Clinic	Unknown		-	Nil	A
4	Rural Hospital	+	+	3 weeks	Sedation	A
5	General Practitioner	+	-	4 weeks	Nil	A
6	General Practitioner	Unknown		-	Nil	A
7	Rural Hospital	+	+	1 week	Sedation	A
8	Municipal Clinic	+	-	1 week or more	Nil	A
9	Municipal Clinic	+	-	1 week or more	Nil	A
10 *	Private Midwife	+	?	2 weeks or more	Nil	NND
11 *	General Practitioner	+	+	2 weeks	Nil	A
12 *	General Practitioner	+	-	Many weeks	Sedation	A
13 *	Municipal Clinic	+	+	8 weeks - 1 week	Advised rest	A
14 *	Municipal Clinic	+	-	8 weeks	Nil	NND
15 *	Rural Hospital	+	+	1 week	Sedation	A
16 *	Divisional Council Clinic	+	-	1 week or more	Nil	A
17 *	General Practitioner	+	+	2 weeks	Sedation	SB
18 *	Municipal Clinic	+	-	1 week or more	Nil	A
19 *	Municipal Clinic	-	+	1 week	Nil	NND
20 *	General Practitioner	+	-	1 week	Rest	A

*Previous history of toxaemia of pregnancy.

Days in hospital prior to the administration of Avertin.

Tables IX and X indicate that very few of the booked cases were admitted to hospital with mild toxaemia which progressed to severe toxaemia. The majority of patients were extremely ill when admitted and required immediate avertin therapy. Tables XIII, XIV & XV (pages 67 and 68). There were three patients only who developed imminent eclampsia after being in hospital for more than a week. Details follow -

(i) J.F., a primigravida aged 25, was admitted to hospital with a diagnosis of pre-eclampsia. When 39 weeks pregnant and after being in hospital 18 days, a surgical induction of labour was performed. Labour progressed satisfactorily and delivery was by means of forceps. Immediately postpartum the blood pressure was 215/130 mm of mercury and the urine was solid with albumen. Avertin was administered.

(ii) M.R., a primigravida aged 21, was admitted to hospital with a diagnosis of pre-eclampsia. When 39 weeks pregnant and after being in hospital 21 days, she developed a severe headache and a rise in blood pressure to 170/130 mm of mercury and the albuminuria increased from one plus to solid. Avertin was administered and six hours later a caesarean section was done because of the severe toxaemia and a breech presentation in a primigravida.

(iii) S.I., a gravida 6 aged 47, was admitted to hospital with a diagnosis of hypertension and was treated with mecamylamine. After being in hospital 18 days there was an increase in the albuminuria from one plus to solid and the patient reported symptoms of severe headache and visual disturbance. Avertin was administered and repeated once after $5\frac{1}{2}$ hours. Surgical induction of labour was performed. Foetal distress followed the second administration of avertin which also lowered the maternal blood pressure to 50/30 mm of mercury. Although the blood pressure quickly rose to a level of ± 110/50 mm of mercury, the foetal heart remained slow and irregular and for this reason a caesarean section was done. This is the only case in the survey where avertin was recorded as causing foetal distress.

During the 17 month period of the survey, 711 patients with toxaemia of pregnancy were admitted to the Peninsula Maternity Hospital. This figure includes 97 patients from this series. Considering that only 3 of these 600 odd patients developed imminent eclampsia while being

treated as in-patients; hospitalization with the benefits of controlled rest and treatment, and the advantage of early detection of deterioration, is an effective means of preventing imminent eclampsia from developing in cases of toxaemia of pregnancy.

TABLE XIII.

Number of Days in Hospital Prior to the Administration of Avertin.

Primigravidae.

Days in Hospital.	Number of Patients.
0	30
1	5
2	2
4	1
5	1
18	1
21	1
	41

TABLE XIV.

Number of Days in Hospital Prior to the Administration of Avertin.

Multigravidae.

Days in Hospital.	Number of Patients.
0	53
1	4
2	1
18	1
	59

TABLE XV.

Number of Days in Hospital Prior to the Administration of Avertin.

Primigravidae and Multigravidae

Days in Hospital.	Number of patients.
0	83
1	9
2	3
4	1
5	1
18	2
21	1
	100

The Duration of Pregnancy in relation to the Development of Imminent Eclampsia.

Table XV shows that at least 95% of patients are admitted with a diagnosis, or near diagnosis of "imminent eclampsia". The period of gestation at the time of the first avertin administration, therefore, probably reflects the duration of pregnancy at which imminent eclampsia is most likely to develop. It was not always possible to obtain an accurate date for the last menstrual period from each patient. By perusal of antenatal records where available, and by considering other factors such as quickening and foetal size, a reasonably true estimate of the period of gestation was obtained for all cases. Table XVI (page 69).

This table shows that there is little difference in the stages of pregnancy when imminent eclampsia develops in primigravidae and multigravidae. 34% of primigravidae and 39% of multigravidae were less than 36 weeks pregnant. Among the 45 booked cases, only 18% were less than 36 weeks pregnant, while 67% of the 55 non-booked admissions were less than 36 weeks pregnant. It was felt that these facts indicating prematurity would affect the foetal loss and this is the purpose of Table XVII (page 70).

TABLE XVI.

Duration of Pregnancy and the Development of Imminent Eclampsia.

Duration of Pregnancy in weeks.	Primigravidae	Multigravidae	All Patients.	Booked Cases.
26	-	1	1	-
27	-	-	-	-
28	-	-	-	-
29	1	2	3	-
30	1	4	5	-
31	2	1	3	1
32	3	2	5	1
33	2	7	9	2
34	4	4	8	2
35	1	2	3	2
36	3	5	8	3
37	6	11	17	9
38	5	8	13	6
39	6	2	8	7
40	4	5	9	8
41	2	4	6	3
42	1	1	2	1
Total	41	59	100	45

TABLE XVII.

Foetal Loss in Relation to the Duration of Pregnancy at which Imminent Eclampsia Develops.

	Foetal Loss.	Duration of pregnancy in weeks.	Booked or Non-Booked.
1	NND	26	NB
2	*SB	29	NB
3	SB	29	NB
4	NND	29	NB
5	NND	30	NB
6	*NND	31	B
7	*NND	32	NB
8	SB	33	NB
9	*NND	33	NB
10	NND	33	NB
11	NND	34	NB
12	SB	35	B
13	*NND	36	B
14	*NND	40	B
15	SB	40	B
16	NND	41	NB
17	NND	41	NB

*Primigravidae.

Table XVll shows that 70.6% of the total foetal loss occurred in cases where the diagnosis of imminent eclampsia was made before the 36th week of pregnancy. A 100% foetal loss occurred in the 4 cases diagnosed before the 30th week of gestation.

Imminent eclampsia was not diagnosed in a booked patient less than 31 weeks pregnant. Two factors account for this - the majority of booked cases were primigravidae with less likelihood of underlying hypertension,and a higher standard of preventative antenatal care was accorded to booked patients (Tables lX, X, Xl and Xll).

Tables XVl and XVll show that there was a 33.4% foetal loss amongst 37 patients diagnosed before the 36th week of pregnancy, but only a 7.9% foetal loss amongst 63 patients where the diagnosis was made when the patient was 36 or more weeks pregnant. Prematurity is undoubtedly the major factor causing foetal loss in patients with imminent eclampsia. The standard of antenatal care is an important factor in allowing the development of imminent eclampsia - especially the early development before the 36th week of pregnancy.

The Symptoms and Physical Signs Present in 100 cases of Imminent Eclampsia.

Symptoms.

Symptoms were present in 86% of patients. Table XVlll (page 73) indicates the variety and frequency of the presenting symptoms.

Severe persistent headache was the most frequent complaint and was present in 81 patients. Usually frontal in type, it was often not relieved by common household analgesics. Of the 19 patients who were headache free, 14 were completely symptom free. The remaining 5 patients complained respectively of (i) antepartum haemorrhage - 2 cases; (ii) extreme irritability - 3 cases, associated with fainting and epigastric pain in one case each

Many patients had more than one symptom - Table XlX (page 73). The maximum number of presenting symptoms in any one patient was 4, although no less than 11 different symptoms were recorded.

In discussing the selection of criteria for diagnosing imminent eclampsia, I stated that I expected that symptoms would be more prevalent amongst the primigravidae and so ensure their rightful

inclusion for special treatment. I reasoned that primigravidae developing a raised blood pressure for the first time would be more sensitive to the effects thereof than multigravidae who, in many cases, would have underlying hypertensive vascular disease and so would be accustomed to the effects of hypertension. To determine whether this was in fact true, the 14 patients in whom there were no presenting symptoms of imminent eclampsia were carefully assessed. Table XX (page 74).

The findings in table XX were to me totally unexpected. No less than 11 of the 41 primigravidae were asymptomatic cases of imminent eclampsia, whereas only 3 of the 59 multigravidae were asymptomatic. The mean age of these 14 patients was 24.4 years as compared to a mean age of 26.3 years for the whole series. The mean blood pressure of these 14 patients was 187/124 mm of mercury as compared to a mean of 195/126 mm of mercury for the whole series.

It is obvious that symptoms in cases of imminent eclampsia are much less frequently seen in primigravidae. Asymptomatic primigravidae do not differ from those with symptoms of imminent eclampsia as regards age or presenting blood pressure.

In this series of 100 cases of imminent eclampsia, 3 patients developed convulsions. All had presented with symptoms and 2 were primigravidae. Thus of the 30 primigravidae with presenting symptoms 2, or 1 in 15, developed eclampsia.

Although the numbers are few (it is difficult to obtain large numbers in this type of work) I believe that the appearance of symptoms in primigravidae with the other criteria of imminent eclampsia present, indicates an even greater likelihood of convulsions occurring. Put in another way - to delay treatment in severe cases of toxaemia in primigravidae because they are asymptomatic is not justified, because the onset of symptoms increases the likelihood of convulsions.

Foetal loss was assessed against the presenting maternal symptoms, Table XXI (page 75). Among the 41 primigravidae in this series there was a foetal loss of 6. Four of these 6 infants were born to mothers who were asymptomatic. The previous paragraph dealt with the maternal viewpoint in relation to symptoms of imminent eclampsia. The views expressed there are underlined by the foetal prognosis as shown in Table XXI. From the foetal viewpoint it appears unwise to delay delivery in an asymptomatic primigravidae with imminent eclampsia.

TABLE XVIII.

The Nature and Frequency of the Symptoms seen in 100 Cases of Imminent Eclampsia.

Symptom.	Number of patients.
Severe headache	81
Visual disturbance	18
Extreme irritability	15
Epigastric pain	10
Antepartum haemorrhage	10
Vomiting	8
Dyspnoea	5
Vertigo	2
Fainting	2
Congestive cardiac failure	2
Oliguria	1

TABLE XIX.

The Number of Presenting Symptoms per Patient.

Number of symptoms.	Number of patients.
0	14
1	37
2	31
3	16
4	2
	100

TABLE XX.

Data Concerning Patients with Asymptomatic Imminent Eclampsia.

	Patient	Age	Blood Pressure	Albuminuria	Oedema.
Primigravidae	1	20	230/130	Solid	Gross
	2	19	180/140	++	Moderate
	3	20	170/120	++	Moderate
	4	17	170/130	++	Gross
	5	27	180/130	+++	Gross
	6	17	160/110	Solid	Gross
	7	18	160/115	+++	Nil
	8	21	160/110	Solid	Gross
	9	25	165/110	+++	Nil
	10	25	215/130	Solid	Slight
	11	25	185/135	Solid	Moderate
Multigravidae	1	41	230/130	+++	Slight
	2	40	200/130	+++	Slight
	3	27	210/120	Solid	Moderate

Mean age = 24.4 years. Primigravidae = 21.3 years. Multigravidae = 36 years.
Mean blood pressure = 187/124 mm of mercury.

TABLE XXI.

Foetal Loss in relation to the Presenting Maternal Symptoms.

	Foetal Loss.	Maternal Symptoms.
Primigravidae.	SB	Headache. Visual disturbance. Epigastric pain.
	NND	Headache.
	NND	Nil
	NND	Nil
	NND	Nil
	NND	Nil
Multigravidae.	SB	Headache. Dyspnoea, Antepartum haemorrhage. Congestive cardiac failure.
	SB	Headache. Epigastric pain.
	SB	Headache. Visual disturbance. Epigastric pain.
	SB	Headache.
	NND	Headache. Small antepartum haemorrhage.
	NND	Antepartum haemorrhage
	NND	Headache. Epigastric pain. Vomiting.
	NND	Headache.
	NND	Headache.
	NND	Headache.
	NND	Headache.

Symptoms were present in all multigravidae who suffered foetal loss. As only 3 out of 59 were asymptomatic this is a not unexpected finding.

The absence of symptoms in cases of imminent eclampsia, particularly in primigravidae (? young patients) does not justify a less immediate or a less intensive form of management.

Blood Pressure.

The overall mean presenting blood pressure in this survey was 195/126 mm of mercury. For primigravidae the mean was 182/123 mm of mercury and for multigravidae the mean was 204/128 mm of mercury. Apart from Molumphy and Garcia [115] who in their series found the mean blood pressure for primigravidae 170/115 mm of mercury and for multigravidae 190/120 mm of mercury, comparative blood pressures were not available. The Cape Town survey figures show that the minimal blood pressure for diagnosing imminent eclampsia as defined by me, was clearly surpassed in the vast majority of cases. Only 2 patients had a blood pressure lower than the standard of 160/110 mm of mercury. The lowest blood pressure of any primigravidae in this series was 150/105 mm of mercury, while the highest was 230/130 or 205/155 mm of mercury. These latter two patients were aged 20 and 18 years respectively. The corresponding figures for multigravidae were 160/100 and either 290/160 or 260/190 mm of mercury.

The foetal loss in relation to the presenting maternal blood pressure is shown in Table XXII(page 77). The mean diastolic blood pressure in both primigravidae and multigravidae who suffered foetal loss was slightly higher than for the whole series. From amongst the 6 primigravidae with systolic blood pressures of 210 mm of mercury or more, 2 infants were lost. From amongst the 5 multigravidae with systolic blood pressures of 260 mm of mercury or more, 3 infants were lost. 6 multigravidae had diastolic blood pressures of 160 mm of mercury or more, and there was a foetal loss of 3 from this group.

Although the mean maternal blood pressure associated with infant loss differs little from the overall mean maternal blood pressure in this series there is definitely an increased foetal loss in patients with exceptionally high systolic blood pressures and in multigravid patients with exceptionally high diastolic blood pressures.

The presenting blood pressures of the 3 patients who subsequently developed convulsions were 200/140 and 170/125 in primigravidae, and 160/120 mm of mercury in a multigravida.

TABLE XX11.

Foetal Loss related to the Presenting Maternal Blood Pressure.

	Foetal Loss	Maternal blood pressure.
Primigravidae.		
	SB	210/130
	NND	185/135
	NND	170/120
	NND	220/110
	NND	180/130
	NND	160/110

Mean = 187/122 mm of mercury.

Multigravidae.		
	SB	190/120
	SB	175/105
	SB	210/160
	SB	180/130
	NND	260/190
	NND	260/130
	NND	160/125
	NND	180/120
	NND	170/120
	NND	260/160
	NND	185/115

Mean = 203/134 mm of mercury.

Albuminuria.

Table XXIII (page 79) indicates that only 17 of the 100 patients in the survey had less than a 2 plus albuminuria when first treated with Avertin. At the opposite end of the scale, 44% of patients presented with a solid albuminuria.

As it is commonly believed that the duration of the albuminuria affects the foetal prognosis, Table XXIV (page 80) was drawn up to show the foetal loss in relation to both the amount of and the known duration of the albuminuria. 82.3% of the total foetal loss occurred in patients with a 3 plus or solid albuminuria, whereas only 64% of the total patients had this degree of albuminuria. In primigravidae especially the foetal prognosis bears a direct relationship to the degree of albuminuria present. The duration of the albuminuria also probably affects the foetal prognosis, although the available figures are too small to be significant. Albuminuria was known to have been present in one patient delivered of a stillborn infant for 7 weeks. Apart from the 7 cases in Table XXIV, there were another 16 patients - Tables IX, X, XI and XII - with an albuminuria present at an antenatal examination. In 4 of these 16 patients the albuminuria was present for more than one week as was the case with 4 of the 7 cases in Table XXIV. Among these 8 cases of albuminuria of more than one week's standing there was a foetal loss of 4.

Table XXIII reveals that there were 17.2% of the primigravidae and 17.0% of the multigravidae with less than a 2 plus albuminuria. Table XXV (page 81) shows the age group of patients with solid albuminuria compared to the overall age groups, and that these ages correspond. It was expected that some older multigravid patients with underlying hypertensive vascular disease and very mild superimposed pre-eclampsia would be included in this survey, but in fact such cases if included did not present as a group, an indication that the standards set for definition are satisfactory.

Oedema.

The extent of the oedema detected in each patient is shown in Table XXVI (page 82). As stated on page the oedema was assessed on an entirely clinical basis. 74% of the patients had moderate or gross oedema, while only 6% did not have any at all. There was no obvious difference in the extent of oedema detected in primigravidae and multigravidae. Table XXVII (page 83) shows that the mothers, whose infants died, all had some degree of oedema - 88% having moderate or gross oedema.

TABLE XXIII.

The Presenting Albuminuria in Imminent Eclampsia.

Amount of Albuminuria.	Primigravidae.		Multigravidae.		All Patients.
	No.	%	No.	%	No. & %.
Nil	2	4.9	-		2
Trace	1	2.5	2	3.4	3
+	4	9.8	8	13.6	12
++	8	19.6	11	18.7	19
+++	10	24.7	10	17.0	20
Solid	16	38.5	28	47.3	44
	41	100%	59	100%	100

TABLE XXIV.

Foetal Loss in relation to the Presenting Maternal Albuminuria.

	Foetal Loss.	Presenting Albuminuria.	Known duration of Albuminuria.
Primigravidae.			
	SB	+++	2 weeks.
	NND	Solid	Nil prior to admission.
	NND	Solid	1 week.
	NND	+++	4 days.
	NND	Solid	Nil prior to admission.
	NND	Solid	2 weeks.
Multigravidae.			
	SB	Solid	Unknown.
	SB	Solid	7 weeks.
	SB	Solid	Nil prior to admission.
	SB	+	2 weeks.
	NND	Solid	Unknown.
	NND	+++	Unknown.
	NND	Solid	Unknown.
	NND	Solid	Unknown.
	NND	Solid	1 week.
	NND	Trace	Unknown.
	NND	++	Unknown.

TABLE XXV.

Ages of Patients with Solid Albuminuria Compared to Overall Ages.

Age.	Solid albuminuria group.		Total Patients.
	No.	%	No. & %
15-19	5	11.3	17
20-24	13	29.7	27
25-29	10	22.7	17
30-34	8	18.2	18
35-39	5	11.3	14
40-44	2	4.5	6
45-49	1	2.3	1
	44	100%	100

TABLE XXVI.

Degree of Presenting Oedema.

Degree of Oedema.	Primigravidae.		Multigravidae.		All Patients.
	No.	%	No.	%	No. & %.
Nil	3	7.4	3	5.1	6
Slight	9	22.2	11	18.8	20
Moderate	14	33.9	21	35.6	35
Gross	15	36.5	24	40.5	39
	41		59		100

TABLE XXVII.

Foetal Loss in relation to the Presenting Maternal Oedema.

	Foetal Loss.	Presenting oedema.
Primigravidae.		
	SB	Moderate.
	NND	Moderate.
	NND	Gross.
	NND	Gross.
	NND	Gross.
	NND	Gross.
Multigravidae.		
	SB	Moderate.*
	SB	Moderate.
	SB	Moderate.
	SB	Gross.
	NND	Slight.
	NND	Slight.
	NND	Moderate.
	NND	Gross.
	NND	Gross.
	NND	Gross.
	NND	Gross.

*Received diuretics before admission.

Haemoglobin on admission.

Table XXVIII given below reveals that only 80 of the 100 patients had haemoglobin estimations recorded on admission to hospital. It is surprising that no less than 14 (25%) of the emergency admissions did not have this important examination. (Booked patients all have at least one haemoglobin estimation antenatally). The lowest recorded haemoglobin was 3.9 Gms%. As bone marrow examinations were not performed on any of these patients, the aetiology of the detected anaemias is unknown.

Patients with low haemoglobin levels created many problems in management. Avertin was administered in the usual manner, but induction of labour or caesarean section delivery had to be delayed until a slow transfusion of packed cells had been completed. During the period of the transfusion, avertin administrations were repeated when indicated. Despite the prolongation of foetal risk in such cases, all the infants survived.

The antenatal clinics at the Peninsula Maternity Hospital supply tablets of ferrous sulphate routinely to all patients. Table XXVIII suggests that iron supplements in pregnancy prevent the development of anaemia. Table XVI which showed greater maturity amongst booked patients with imminent eclampsia, lends indirect support to the assumption for it is known that the greater part of the demand for iron in pregnancy is exerted in the latter months.[37]

TABLE XXVIII.

Presenting Maternal Haemoglobin.

Haemoglobin in Gms.%	Booked patients.		Non-booked patients.	
	No.	%	No.	%
Less than 6	-	-	1	2.4
6 - 7.9	-	-	1	2.4
8 - 9.9	1	2.6	6	14.6
10 - 11.9	18	46.1	17	41.5
12 - 13.9	17	43.6	15	36.6
More than 14	3	7.7	1	2.4
	39		41	

Blood Groups.

The blood groups were available in 56 of the 100 patients. Table XXIX

A random sample of blood groups from a a similar racial distribution was extracted from the records of the Blood Transfusion Laboratory at the Medical School, Cape Town. The percentages differed only slightly from those of the survey group.

TABLE XXIX.

Maternal Blood Group.

Blood Group.	Numbers.	%
A Rh +ve	15	26.6
A Rh -ve	1	1.8
B Rh +ve	7	12.4
B Rh -ve	1	1.8
AB Rh +ve	4	7.1
AB Rh -ve	-	-
O Rh +ve	26	46.7
O Rh -ve	2	3.6
	56	100%

The Management of 100 Cases of Imminent Eclampsia.

The Administration of Avertin.

Avertin was administered to every patient in this survey and formed the basis of the medical - as opposed to obstetrical - management. The dosage for each case was calculated according to the chart shown in Table 111(page 32). Table XXX (page 87) indicates the individual doses administered. The mean doses were, (a) for all patients 5.9 ml, (b) for primigravidae 5.7 ml, and (c) for multigravidae 6.0 ml. As doses are calculated according to weight, it is apparent that the multigravidae are more obese than the primigravidae. This table confirms the selection by Campbell and Burton[27] which was later endorsed by Morris[119] that 5.5 ml is a safe and satisfactory amount to use when the patient's weight is unknown.

Table XXXl (page 88) reveals the number of occasions upon which avertin was administered to individual patients. Factors that influence the number include:-

(i) - Duration of pregnancy. A conservative attitude towards terminating pregnancy was adopted in a few patients less than 32-34 weeks pregnant.

(ii) - Stage of pregnancy or labour. Antepartum patients required a longer period of medical management.

(iii) - Method of delivery. The period of medical management was usually reduced in patients submitted to an elective caesarean section.

(iv) - Gravidity. Primigravidae have longer labours than multigravidae and so need avertin more often.

(v) - Unknown factor, i.e. the response of the patient to the initial dose.

The finding that primigravidae on the average required 2.1 doses as against the 1.8 doses of the multigravidae is not unexpected.

An analysis of the first four factors which affect the number of doses of avertin needed suggests that the foetus has a poorer prognosis in such cases. Table XXXll (page 89) reveals that this is so. The mean number of doses and the mean total dose given to patients whose

infants did not survive was markedly in excess of the respective means for all patients. In these cases I do not believe that the foetal mortality stems from the administrations of avertin, but that the factors requiring the increased doses are the underlying cause of the poorer foetal prognosis.

TABLE XXX.

The Dose of Avertin Administered to 100 Cases of Imminent Eclampsia.

Avertin in ml.	Primigravidae.		Multigravidae.		All Cases.
	No.	%	No.	%	No. & %.
4.0	1	2.5	-	-	1
4.5	1	2.5	5	8.5	6
5.0	9	21.9	7	11.9	16
5.5	9	21.9	14	23.7	23
6.0	12	29.2	12	20.2	24
6.5	5	12.2	8	13.6	13
7.0	4	9.8	4	6.8	8
7.5	-	-	7	11.9	7
8.0	-	-	2	3.4	2
	41	100%	59	100%	100

Mean dose primigravidae = 5.7 ml.
Mean dose multigravidae = 6.0 ml.
Mean dose all patients = 5.9 ml.

TABLE XXXI.

The Number of Doses of Avertin Administered to Each Patient.

Doses of Avertin.	Primigravidae.	Multigravidae.	All Cases.
1	17	27	44
2	11	20	31
3	7	8	15
4	3	3	6
5	2	1	3
6	1	-	1
	41	59	100

Mean number of doses primigravidae = 2.1

Mean number of doses multigravidae = 1.8

Mean number of doses all cases = 1.96

TABLE XXXII.

Foetal Loss in Relation to the Dose and Number of Doses of Avertin Administered.

	Foetal Loss	Avertin in ml.	Number of Doses.	Total Avertin in ml.
Primigravidae.				
	SB	6.0	2	12.0
	NND	4.5	3	13.5
	NND	5.5	4	22.0
	NND	7.0	3	21.0
	NND	5.5	5	27.5
	NND	5.5	2	11.0
Multigravidae.				
	SB	7.5	3	22.5
	SB	7.0	3	21.0
	SB	6.5	1	6.5
	SB	5.0	2	10.0
	NND	6.0	3	18.0
	NND	7.5	2	15.0
	NND	5.0	3	15.0
	NND	7.0	2	14.0
	NND	5.5	3	16.5
	NND	7.0	1	7.0
	NND	5.5	2	11.0

Primigravidae.

Mean dose = 5.7 ml.
Mean number of doses = 3.2
Mean total dose = 17.8 ml.
Mean total dose all primigravidae = 12.0 ml.

Multigravidae.

Mean dose = 6.3 ml.
Mean number of doses = 2.3
Mean total dose = 14.0
Mean total dose all multigravidae = 10.8 ml.

The Effects which followed the Administration of Avertin.

Sedative effect.

On page 47 details were given of the criteria used for the estimation of the sedative effect of avertin. The results in the 100 cases in this survey are shown in Table XXXIII. below. The maximal depth of sedation achieved in the first hour after treatment has been used as the assessment standard. After 2-3 hours patients usually regained full consciousness, but soon lapsed into a tranquil sleep. It was the exceptional patient who was restless during the recovery phase. 82% of patients were deeply sedated, 15% were moderately sedated, 2% were only lightly sedated and in 1 multigravidae there was no apparent sedative effect at all. In 3 patients deep sedation, not previously present, followed the second administration of avertin. 6 patients in whom there was only moderate or light sedation, received avertin in the late first stage of labour. In all, avertin was administered to 9 patients in the late first stage of labour, and in only 3 was both deep sedation and a fall of blood pressure to a satisfactory level produced.

Unconsciousness invariably followed within 5 minutes of the administration of avertin. I found that the loss of the corneal reflex was not a reliable guide in assessing the depth of sedation. I noted that just prior to the loss of consciousness many patients gave a deep sigh. This observation, as far as I am aware, has not previously been recorded.

TABLE XXXIII.

The Sedative Effect of Avertin in Imminent Eclampsia.

Sedative Effect.	Primigravidae.	Multigravidae.	All Patients.
	Number.	Number.	No. & %
Deep	34	48	82
Moderate	6	9	15
Light	1	1	2
No effect	-	1	1

Blood Pressure.

The basic pathology in cases of imminent eclampsia is an arteriolar vasoconstriction. Avertin acts direct on the blood vessels, heart and vasomotor centre, and should therefore be capable of relieving any vasoconstriction present.

The effect of avertin upon the blood pressures of the 100 patients in this series is revealed in Table XXXIV (page 93). In every patient there was a fall in the systolic blood pressure and in only one patient - a primigravida - was there no fall in the diastolic blood pressure. In 3 patients the fall in the diastolic pressure was greater than the fall in the systolic pressure, while in 11 patients there were equal drops. A table of figures gives no indication of the clinical improvement which avertin exerts on the hypertension of toxaemia. In my paper detailing the value of avertin in the management of eclampsia [36] I assessed the falls in blood pressure in the following manner. The lowest blood pressure reading in the first hour after the administration of avertin was classified as -

(i) - Satisfactory - if below 140/100 mm of mercury.
(ii) - Moderate - if between 140/100 and 160/110 mm of mercury.
(iii) - Poor - if above 160/110 mm of mercury.

The classification was based on the probable diminishing risks of eclampsia occurring with blood pressures at lower levels.

This same clinical assessment was applied to the 100 cases of imminent eclampsia in the survey and the results are set out in Table XXXV (page 94). In 73% of patients there was a satisfactory response. Because many patients when first treated had presented with phenomenally high blood pressures, it was thought that some who were classified as poor responses may, in fact, have responded well to avertin. A more critical analysis was therefore made of the 27 patients whose falls in blood pressures were considered either moderate or poor, Tables XXXVI and XXXVII (pages 95 & 96).

It is plain that many of these patients showed considerable drops in their blood pressures; no less than 15 out of 27 having a fall in the systolic blood pressure of 40 mm of mercury or more. In 6 cases the hypotensive effect was considered satisfactory after a second administration of avertin. 16 patients were deeply sedated despite having comparatively poor blood pressure responses. On the whole I found that the administration of avertin in the late first stage of labour produced neither a satisfactory fall in the blood pressure nor a deep level of sedation. It is likely that there is poor absorption in such patients.

In only two patients was the fall in blood pressure considered to have produced a deleterious effect -

(1) The patient referred to on page 66 in whom the second dose of avertin caused a considerable fall in blood pressure and also foetal distress.

(2) A multigravid patient whose blood pressure dropped from 180/120 to 80/65 mm of mercury and who exhibited the signs of shock. A small dose of methidrine corrected the hypotension. Two subsequent administrations of avertin produced no ill effects.

In the majority of patients the blood pressure remained at a lower level for 2-3 hours after the first lot of avertin and for even longer periods after the second and subsequent doses. Graphs IV, V and VI, (pages 97, 98 and 99) are examples of the effect of avertin upon the hypertension associated with imminent eclampsia.

In an occasional patient avertin apparently restored the blood pressure to a basic level and so termination of pregnancy was delayed for days, and in one case, weeks. Table XLIV (Page 113).

In discussing the objectives for the management of imminent eclampsia I emphasised that it was necessary - (i) to achieve an effective degree of sedation, and (ii) to relieve the arteriolar vasoconstriction and so reduce the elevated blood pressure. The efficacy of avertin in these regards was that -

(a) A deep sedation and a fall in the blood pressure to a satisfactory level was obtained in 72 patients.

(b) A deep sedation but a less satisfactory fall in blood pressure occurred in 10 patients.

(c) A fall in the blood pressure to a satisfactory level but only a moderate or light sedation occurred in 7 patients.

(d) Mixed moderate and poor responses - 10 patients.

(e) No sedative effect and only a fall in blood pressure to a poor level - 1 patient.

Overall, avertin appears to be successful in sedating and in producing a reasonable hypotensive effect in 89% of patients diagnosed as being in a state of imminent eclampsia. No less than 6 of the 11 failures in treatment had avertin administered in the late first stage of labour. A failure of absorption due to the presenting part occupying the pelvis is the most likely explanation. It seems that in cases of this type intravenous therapy would be more predictable and so more effective than is avertin administered per rectum.

TABLE XXXIV.

The Effect of Avertin upon the Blood Pressure in Imminent Eclampsia.*

A. **Blood Pressure.** **Mean fall in m.m. of mercury.**

	Primigravidae.	Multigravidae.	All Patients.
Systolic	59	75	68
Diastolic	40	43	42

B. **Maximum fall in B.P.**

	Primigravidae.	Multigravidae.
Systolic	125 mm of Hg.	160 mm of Hg.
Diastolic	90 mm of Hg.	100 mm of Hg.

The maximum fall in an individual primigravid patient was from 205/130 mm of Hg to 80/40 mm of Hg, i.e. 125/90 mm of Hg.

The maximum fall in an individual multigravid patient was from 260/190 mm of Hg to 110/90 mm of Hg, i.e. 150/100 mm of Hg.

C. **Minimum fall in B.P.**

	Primigravidae.	Multigravidae.
Systolic	10	20
Diastolic	0	10

The minimum fall in an individual primigravid patient was 10/10 mm of mercury and in an individual multigravid patient, either 30/10 or 20/20 mm of mercury.

*The fall in blood pressure used for this table was the maximal that occurred in the first hour after the administration of avertin.

TABLE XXXV.

The Fall in Blood Pressure due to Avertin assessed as a clinical response in 100 cases of imminent eclampsia.

Clinical Response.	Primigravidae.	Multigravidae.	All Patients.
Satisfactory	35	38	73
Moderate	5	11	16
Poor	1	10	11
	41	59	100

TABLE XXXVI.

Clinical Data concerning 16 Patients Treated with Avertin whose Blood Pressures fell only to a Moderate Level.

Age.	Duration of Pregnancy.	Actual fall in Blood Pressure.	Sedative effect.	Post - Partum Time	Post - Partum B.P.	Remarks.
*20	34	200/140 - 145/115	Deep	32 days.	140/90	-
*19	40	170/110 - 150/110	Moderate	6 weeks	110/70	Late 1st stage.
*21	42	160/110 - 150/100	Moderate	10 days	140/120	Late 1st stage.
*27	36	180/130 - 140/100	Moderate	10 days	160/120	-
*23	41	170/100 - 145/80	Deep	9 days	120/80	-
37	33	190/120 - 140/100	Deep	18 days	160/120	-
26	37	170/110 - 150/90	Deep	10 days	150/90	-
38	38	170/130 - 120/110	Deep	4 days	180/120	-
40	30	230/150 - 150/90	Deep	10 days	180/110	-
39	41	210/110 - 150/80	Deep	-	-	-
33	37	200/140 - 150/115	Deep	7 weeks	130/95	-
39	33	290/160 - 150/100	Deep	10 days	200/120	-
40	40	170/110 - 145/80	Poor	6 days	130/90	Late 1st stage.
36	38	210/130 - 160/100	Moderate	17 days	140/100	-
33	41	170/120 - 140/100	Deep	6 days	150/110	-
35	29	260/160 - 160/100	Deep	7 days	180/110	-

*Primigravidae.

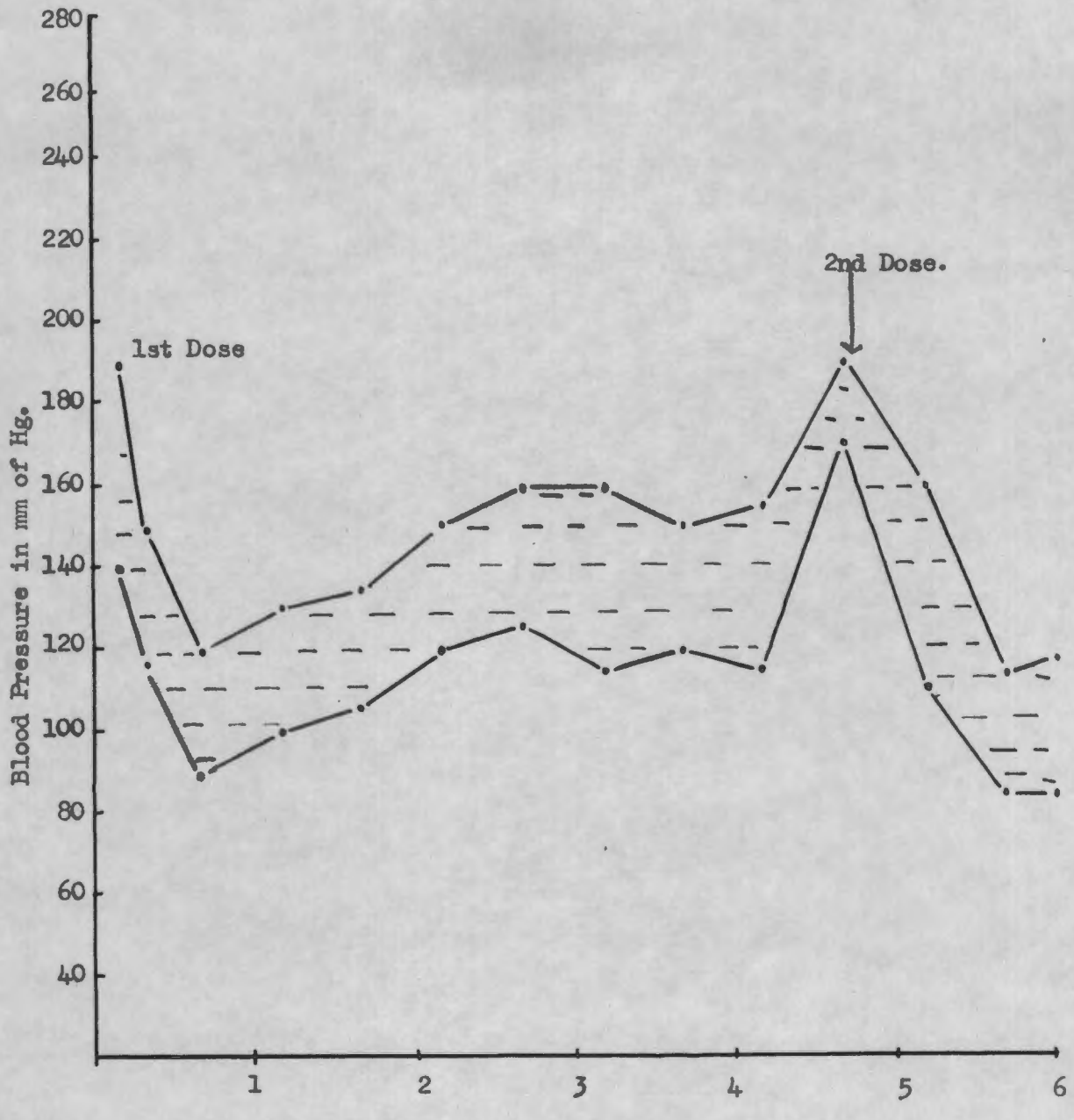
TABLE XXXVII.

Clinical Data Concerning 11 Patients Treated with Avertin whose Blood Pressures fell only to a Poor Level.

Age.	Duration of Pregnancy.	Actual fall in Blood Pressure.	Sedative effect.	Post Partum. Time	B.P.	Remarks.
*31	29	210/130 - 165/115	Moderate	12 months.	150/100	2nd dose response
31	32	250/160 - 165/115	Deep	22 days	190/120	
21	37	180/130 - 150/120	Moderate	6 weeks	130/100	
40	37	200/130 - 170/100	Moderate	10 days	130/90	
32	33	180/130 - 160/110	Deep	6 weeks	165/105	
19	39	230/150 - 170/110	Poor	10 days	130/90	2nd dose response
38	36	250/160 - 220/140	Moderate	11 days	170/120	2nd dose response
33	38	220/130 - 165/115	Moderate	21 days	140/100	2nd dose response
30	29	210/160 - 175/145	Deep	9 days	160/130	2nd dose response
38	40	180/130 - 160/110	Deep	14 months.	130/70	
32	41	225/145 - 175/125	Deep	1 month	130/90	2nd dose response

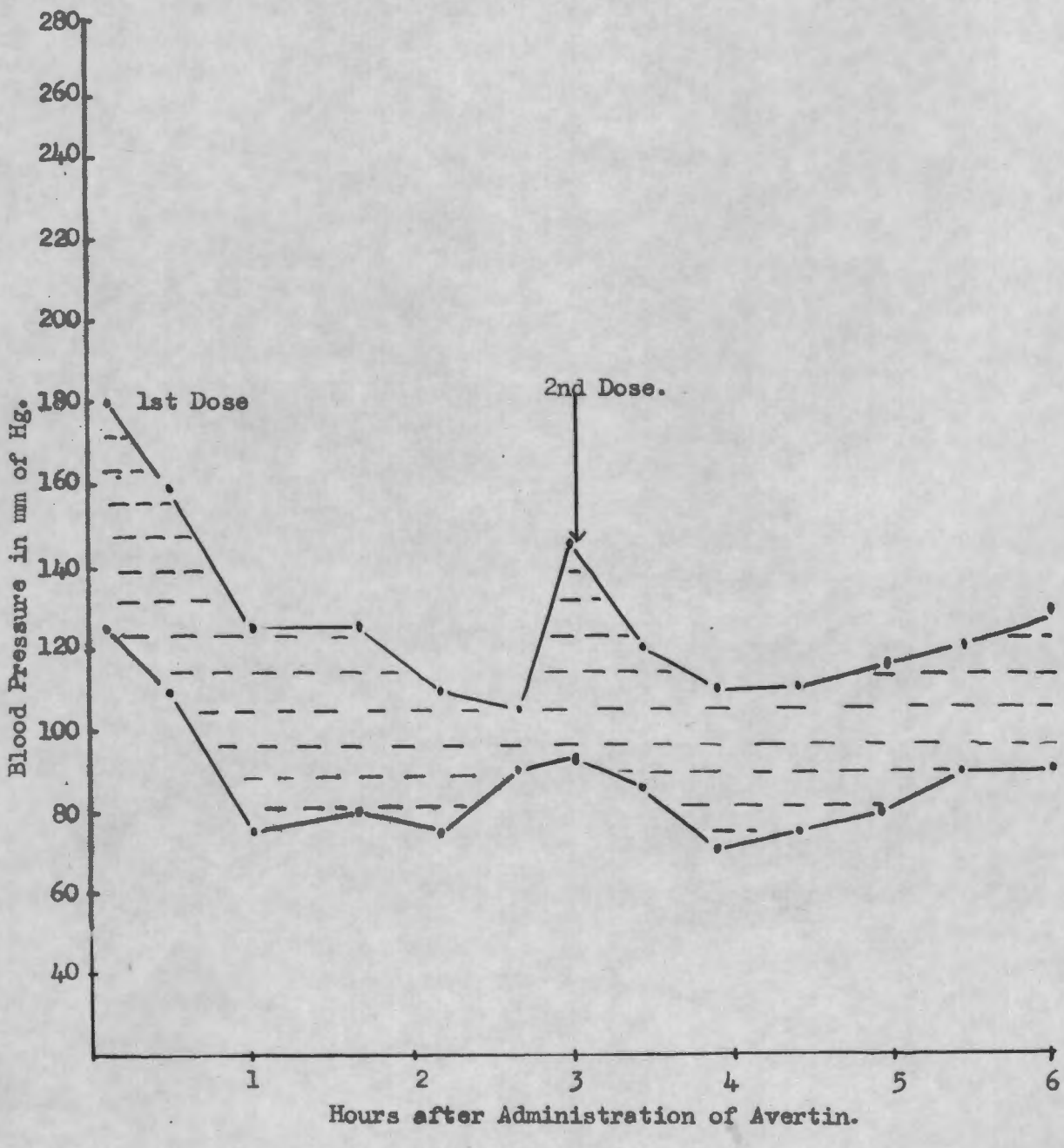
*Primigravida.

GRAPH. 1V.



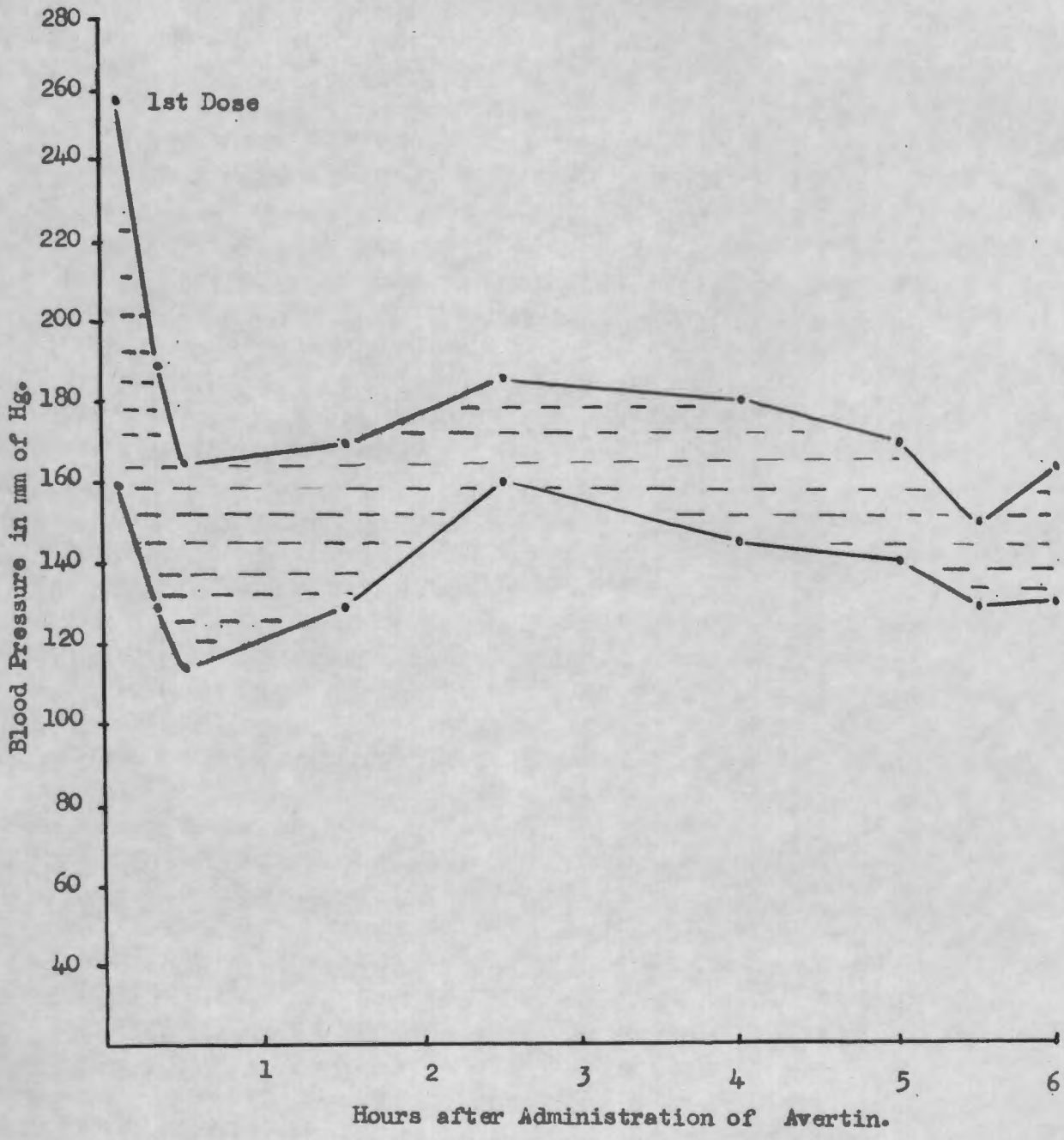
P.M.H. 1698 Age 26. Gravida 111.

GRAPH V.



P.M.H. 986/60 Age 31. Gravida 11.

GRAPH VI.



P.M.H. 1820/60. Age 31. Gravida V.

Albuminuria.

As previously stated, the amount of albumen in the urine was always assessed by a rough quantitative method only. In no patient did the albuminuria increase in degree after the administration of avertin. On the contrary, in many cases a solid albuminuria would become a two plus or one plus within a matter of hours. This effect was not predictable in an individual patient.

Maternal Pulse.

The majority of the patients presenting with imminent eclampsia have a tachycardia. The pulse rate is usually 100 or more beats per minute. Table XXXVIII below reveals the effect of avertin on the maternal pulse. In this table the average pulse rate during the hour following the first dose of avertin was compared to the pulse rate present at the commencement of therapy. In 38% of patients the pulse rate remained unchanged; in 5% it was decreased, and in 57% it was increased by an average of 10 to 20 beats per minute. An increased pulse rate was often associated with an effective drop in the blood pressure - an observation first made by James Young[177]

TABLE XXXVIII

The Effect of Avertin on the Maternal Pulse Rate.

Changes in Pulse Rate.	Numbers of patients.		
	Primigravidae.	Multigravidae.	All.
-20	-	2	2
-10	1	2	3
Nil	20	18	38
+10	11	18	29
+20	8	16	24
+21 and over	1	3	4
	41	59	100

Maternal Respiration.

A tachypnoea was a common presenting sign in cases of imminent eclampsia. Table XXXIX given below shows the changes in the maternal respiration which followed after the first administration of avertin. Respiratory depression was observed in only one case and followed after a third dose of avertin. The patient was given intermittent positive pressure respiration for 55 minutes. Details are given on page The undoubted cause of the respiratory depression was overdosage with avertin and morphine. This was the only patient in whom cyanosis occurred.

In 64% of patients the respiratory rate remained unchanged; in 29% the rate was decreased by usually less than 10 breaths per minute, and in 7% the rate was increased. There were 3 patients in whom the respiratory rate fell by more than 10 breaths per minute and in all three deep sedation had been achieved.

A well marked laxity of the jaw and pharyngeal muscles occurred very soon after the avertin administration. Airways were routinely inserted during the induction period and were well tolerated.

An obvious accumulation of secretions in the upper respiratory tract was rare, but nevertheless the patients were nursed on their sides with a change of position every hour, and aspiration of the pharynx was also a routine every hour. Prophylactic antibiotics were not administered. There was one case of postpartum respiratory infection.

TABLE XXXIX.

The Effect of Avertin on the Maternal Respiratory Rate.

Changes in Respiratory Rate.	Numbers of patients.		
	Primigravidae.	Multigravidae.	All.
-11 to -15	-	3	3
- 6 to -10	6	13	19
- 1 to - 5	2	5	7
Nil	28	36	64
+ 1 to + 5	1	-	1
+ 6 to +10	4	2	6
	41	59	100

Foetal Heart Rate.

All counting of the foetal heart rate was done with simple auscultation. As many of the patients were obese, and as all were nursed in a lateral position, auscultation was often difficult. The method was the only one available to us and clinically proved very reliable. A method of monitoring the foetal heart would be much less disturbing to the patient and would ease the task of those who 'special' these cases.

Table XL presents the effects of avertin on the foetal heart rate. The average rate during the first hour following the avertin administration was compared to the foetal heart rate present at the commencement of treatment. In 80% of cases the rate was unchanged, in 10% it was decreased and in 10% it was increased. In only one instance was foetal distress directly attributable to the administration of avertin. This patient was discussed on page 66.

There was no obvious parallel between the effects of avertin on the maternal and foetal systems.

TABLE XL.

The Effect of Avertin on the Foetal Heart Rate.

Changes in the Foetal Heart Rate.	Number of patients.		
	Primigravidae.	Multigravidae.	All.
-21 to -30	-	1	1
-11 to -20	1	1	2
- 1 to -10	3	4	7
Nil	35	45	80
+ 1 to +10	2	6	8
+11 to +20	-	-	-
+21 to +30	-	2	2
	41	59	100

Can Avertin Prevent Eclampsia?

Of the 100 patients in a state of imminent eclampsia, 3 developed convulsions after treatment with avertin had started. Details of the three patients follow -

1). J.T. (P.M.H. 2487/60) - a primigravida aged 22. This patient was a booked case who attended the routine antenatal clinics for 4½ months. The first seven antenatal visits revealed no abnormality. One week prior to admission the urine contained a trace of albumen and the blood pressure was 120/65 mm of mercury. The weight gain was 19 lbs spread over 18 weeks. She was admitted in labour when 38 weeks pregnant and was found to have a 3 plus albuminuria, a blood pressure of 170/125 mm of mercury and gross oedema. Avertin was immediately administered and she was soon deeply sedated. The blood pressure fell to 120/80 mm of mercury in 30 minutes. One hour and 10 minutes after receiving avertin while still deeply sedated and with a blood pressure of 130/100 mm of mercury, the patient had a convulsion. A generalised tonic stage was followed by a generalised clonic stage. A second dose of avertin was administered and the maximum fall of blood pressure occurred after 30 minutes. The level reached was 75/50 mm of mercury. Two hours later morphine grs.¼ was given to alleviate the discomfort caused by the uterine contractions. Due to an error, a second lot of morphine was given two hours after the first. One hour later, i.e. six hours after the first administration of avertin, a third dose of avertin was given because the blood pressure had risen to 150/105 mm of mercury. There was an immediate fall in the respiratory rate to less than 6 per minute and the respiratory movements were shallow. Cyanosis ensued and was not much improved by the administration of oxygen through a mask. Therefore intratracheal intubation was undertaken and intermittent positive pressure respiration was applied for 55 minutes. 3½ hours later the patient was delivered of a healthy infant. There were no further convulsions.

The convulsion was due to eclampsia.

2). H.W. (P.M.H. 1355/60) - a primigravida aged 22. This patient was a booked case who attended the routine antenatal clinics for 3½ months. All seven antenatal attendances revealed no abnormality, and the weight gain was 4½ lbs over 14 weeks. She was admitted in labour at term with a blood pressure of 130/90 mm of mercury and no abnormal constituents in her urine. 6 hours after admission a

sudden development of facial oedema was observed. The patient admitted that she had a severe headache. The blood pressure was 200/140 mm of mercury but the urine was free of albumen. Avertin was immediately administered. The blood pressure fell to 130/70 mm of mercury and thereafter never rose higher than 140/100 mm of mercury. 80 minutes later delivery was completed under general anaesthesia by means of forceps. While the patient was coming round from the anaesthetic with the anaesthetist still present, two clonic type convulsions occurred. A small dose of thiopentone was administered intravenously. There were no further convulsions. During the first 10 postpartum days a trace of albumen was present in the urine on 3 occasions.

The convulsions were accepted as being due to eclampsia. The anaesthetist noted that during the recovery phase from the anaesthetic prominent overbreathing occurred, and therefore tetany is also a possibility.

3). W.F. (P.M.H. 2337/61) - a gravida 2 aged 26. This patient was an emergency admission who had not received regular antenatal care. Her previous pregnancy, labour and puerperium were uncomplicated. She was admitted when 34 weeks by dates with a twin pregnancy, a solid albuminuria and a blood pressure of 160/120 mm of mercury. Avertin was immediately administered and a maximum fall in the blood pressure to 90/60 mm of mercury occurred. Thereafter the blood pressure remained at about 140/100 mm of mercury for the next 20 hours during which period of time two intramuscular injections of paraldehyde were administered. The degree of albuminuria remained unchanged and therefore induction of labour was performed. Five hours later twin boys weighing 3 lb 11 oz and 4 lb 1 ozs were delivered under general anaesthesia. Morphine grs.$\frac{1}{4}$ was administered once postpartum, and was followed by sodium amytal grs.3 six hourly for four days. On the first postpartum day the blood pressure was 180/110 mm on one occasion and a two plus albuminuria was present. On the second and subsequent days of the puerperium the urine was albumen free, although the blood pressure remained elevated. 82 hours after delivery the patient had a convulsion for which she received avertin therapy. The post convulsion blood pressure was 160/100 mm of mercury. There were no further convulsions and the blood pressure remained at about 140/90 mm of mercury until the patient was discharged 7 days later.

The convulsion was accepted as being due to eclampsia, although the presentation was unusual.

It is difficult to see how any of the convulsions in these three patients could have been prevented. In the first two cases effective sedation and hypotension was obtained. Neither the second nor third patient had an albuminuria at the times that they had their convulsions. It is possible that the convulsions in these patients were not due to eclampsia. Dieckmann[44] states that eclampsia does not occur later than 24 to 30 hours postpartum. He quotes Zangmeister as limiting eclampsia to fits in the first 3 postpartum days, but mentions that Simpson diagnosed eclampsia 8 weeks postpartum, Baudeloque 6 weeks postpartum and Bar 4 weeks postpartum. Jeffcoate and Scott[80] from their own work believe that fits beginning more than 24 hours after delivery are rarely, if ever, caused by eclampsia. Browne[20] on the other hand states that 10% of cases of eclampsia occur 2 to 3 days after delivery. Other causes of convulsions in obstetric patients are epilepsy, cerebral venous thrombosis, cerebral haemorrhage, phaeochromocytoma and tetany.

In addition to the above three patients who developed generalised convulsions, two patients (P.M.H. 1825/60 and P.M.H. 3204/60) were observed having localised muscular twitchings. In one patient the right hand only was affected, while in the other both the left hand and left leg were involved. These Jacksonian type movements lasted on and off for periods of about 5 minutes, while the patient herself remained well sedated. They undoubtedly reflect a motor disturbance of a lesser degree than occurs with the typical eclamptic fit.

Can avertin prevent accidental antepartum haemorrhage?

Severe accidental antepartum haemorrhage is usually preceded by the appearance of a raised blood pressure. Only one patient in the survey presented with an accidental antepartum haemorrhage after avertin had been administered. In this patient (P.M.H. 1140/60) it is possible that the haemorrhage was entirely concealed prior to treatment.

In addition there were 10 patients who gave a history of antepartum haemorrhage before admission. In not one of these patients was any further haemorrhage observed.

The excretion of urine in cases of imminent eclampsia following the administration of avertin.

In every case a record was kept of the amount of urine excreted in the first 24 hours after the administration of avertin and in the first 24 hours postpartum. In 96 of the 100 patients the records were accurately maintained and the data that follows was obtained from these records. Table XLl (page 107). The mean excretion figures as shown in this table do not suggest an oliguria, or even that the excretion of urine is depressed by the giving of avertin. On the contrary, it appears that avertin promotes a diuresis when administered to patients in a state of imminent eclampsia.

In the first 24 hours following the administration of avertin there were only two patients who failed to excrete more than 10 ounces of urine. The first patient was a primigravida with gross oedema who received in all four doses of avertin. 9 ounces of urine were excreted post-avertin and 36 ounces postpartum. The second patient was a multigravida with gross oedema who received 2 doses of avertin. The post-avertin and postpartum periods overlapped to a large extent and in this time only 3 ounces of urine were passed. (This patient was discussed more fully under foetal distress on page 66).

There were three other patients who excreted less than 10 ounces of urine postpartum - (i) A primigravida who twice received avertin and excreted 7 ounces of urine; (ii) a primigravida who received 5 doses of avertin and excreted 7 ounces of urine; and (iii) a multigravida who received a single dose of avertin and excreted only 4 ounces of urine. All four patients excreted large amounts of urine in the 24-36 hour postpartum period. There was no case of anuria.

The maximum outputs of urine are set out in Table XLl. There was no obvious correlation between the degree of oedema assessed clinically and the amount of urine passed in the first 24 hours postpartum. Although the information was not extracted in this analysis, it is my impression that there is a parallel between the clinical oedema and the amount of urine excreted in the first 4 days postpartum.

TABLE XLI.

The Excretion of Urine following the Administration of Avertin.

Patients*	1st 24 hours Post-avertin. Urine in Ounces.	1st 24 hours Postpartum. Urine in ounces.
Mean Primigravidae	39	52.6
Mean Multigravidae	37.5	50.3
Mean - All Patients	38.1	51.2
Minimal Primigravidae	9	7
Minimal Multigravidae	3	3
Maximal Primigravidae	101	140
Maximal Multigravidae	112	138

*38 Primigravidae
58 Multigravidae

Obstetric Management.

There were 73 antepartum diagnoses of imminent eclampsia, 25 intrapartum and 2 postpartum. The obstetric management of the latter two patients will not be discussed.

Antepartum Imminent Eclampsia.

The management of this group was roughly by three methods, viz:-

(i) a. Immediate induction of labour - 51.
b. Induced patients first treated when not in labour - 4.

(ii) Immediate elective caesarean section - 9.

(iii) Elective postponement of termination of pregnancy - 9.

(i) a. Immediate induction of labour was performed in 51 patients, i.e. induction of labour was commenced within 24 hours of the first administration of avertin. 42 patients were induced within the first 5 hours and 9 in the period 5-24 hours. These latter 9 included 2 very anaemic patients who were being transfused slowly, 1 patient in congestive cardiac failure who was treated initially with digitalis and diuretics, and 2 patients induced at 15 and 23 hours post-avertin respectively when conservative management was abandoned. The delay in the remaining four cases is accounted for by the time lag between domiciliary management by the Flying Squad and admission to hospital.

b. For purposes of analysis the 4 patients who received avertin after induction but before the onset of labour, are grouped with the above 51 patients. Induction of labour was always by artificial rupture of the membranes - forewater membranes if possible - followed by a 'pitocin' drip infusion if labour did not immediately ensue. 9 of these 55 patients were subsequently delivered by caesarean section and are tabulated in Table XLII (page 111). An absolute failure to induce labour was the indication for caesarean section in only 3 patients.

The foetal loss amongst the 55 patients was 10 - 4 stillbirths and 6 neonatal deaths. In only one patient suffering foetal loss was induction followed by caesarean section. 5 of the 10 perinatal deaths were in infants weighing less than 3 lbs.

There were two sets of twins delivered, giving a total of 57 viable infants. The foetal loss, therefore, is 17.5%. From among the 15 infants delivered who weighed less than 4 lbs, there was a loss of 5, i.e. 33.3%.

(ii) An immediate elective caesarean section was performed on 9 occasions. Table XLIII (page 112). There were no stillbirths but there were 5 neonatal deaths. Of the 5 infants who were delivered weighing less than 4 lbs, only 1 survived - an 80% foetal loss.

Dewhurst[41] concluded that the foetal mortality in imminent eclampsia would be likely to improve with more deliveries by caesarean section in the 30-35 week mature group. Hamilton et al[68] suggested that in cases of severe toxaemia the survival rate of babies under 4 lbs would be better when they were delivered by caesarean section. The figures I have stated do not support either of these views. Even when those patients who were induced but who subsequently were delivered by caesarean section are grouped with the elective caesarean section patients, the foetal mortality is still worse for the infants delivered by caesarean section as compared to those delivered vaginally.

The findings in this survey support the opinions of Kellar,[82] Barry[7] and Douglas[50] among others who advocate vaginal delivery in cases of imminent eclampsia.

(iii) Elective postponement of termination of pregnancy by either induction of labour or elective caesarean section, was the management selected for 9 patients. Table XLIV (page 113). This group includes all patients in whom no attempt was made to deliver the infant or induce labour within the first 48 hours after the administration of avertin for the first time.

At the start of this survey there was no plan for a group of patients as depicted in Table XLIV. However, early cases treated with avertin occasionally improved dramatically and gave the impression that the toxaemic process might be reversible. Subsequently, therefore, in patients who were by dates premature or who suffered from an additional complication such as severe anaemia or congestive cardiac failure, termination of pregnancy was deliberately withheld. These patients were very carefully

watched and created a heavy load for both the nursing and medical staff. The results are gratifying and suggest that with the right drug or drugs, delaying tactics are not only practical but safe and probably beneficial to the foetus. My experience was that the switch from avertin to other sedative and/or hypotensive therapy was difficult to achieve without the degree of albuminuria suddenly increasing to its pre-avertin level. It was only in 3 patients that termination of pregnancy could be justifiably postponed for 5 days or more. 2 of these patients were probably cases of hypertensive vascular disease with relatively mild superimposed pre-eclamptic toxaemia.

Although the numbers are small it seems that a policy of delay in terminating pregnancy offers to the foetus under 4 lbs in weight a better prognosis than does immediate elective caesarean section - a 50% as compared to a 20% chance of survival.

Intrapartum Imminent Eclampsia.

25 patients who were already in labour presented with the signs and symptoms of imminent eclampsia. Table XLV (page 114). There were 13 primigravidae and 12 multigravidae. With one exception, all patients were 36 or more weeks pregnant. The exception was a 29 weeks mature primigravida in labour who was transferred from a private maternity home to the Peninsula Maternity Hospital. There was a 7.7% foetal loss - an improvement on the antepartum foetal loss - probably reflecting the more mature infant delivered rather than any other factor.

If avertin causes less efficient uterine action this table would show an excess of prolonged labours. In actual fact 8 of the 25 patients had labours lasting longer than 18 hours and 4 patients (Nos. 3,5,15 & 24) were delivered by caesarean section. These findings suggest that avertin may retard the progress of labour. However, in these 4 patients the avertin was first administered late in labour and so could not possibly have had much effect on the duration. A clinical impression was that labour often progressed more satisfactorily after the administration of avertin.

TABLE XLII.

Caesarean Section following Induction of Labour.

Case	Maturity. Weeks.	Induction - Delivery Interval.	Duration in Labour.	Indication.
* 1	34	21 hrs. 40 mins.	6 hrs.10 mins.	Duration.
* 2	38	8 hrs. 14 mins.	6 hrs.24 mins.	Deterioration.
* 3	38	36 hrs. 50 mins.	32 hrs.30 mins	Inertia.
4	37	17 hrs. 44 mins	-	Previous Hysterotomy Failed Induction.
5	38	24 hrs. 1 min	-	Failed Induction
6	41	15 hrs. 55 mins.	-	Failed Induction
7	34	11 hrs. 43 mins.	9 hrs.23 mins.	Foetal Distress.
8	36	7 hrs. 26 mins.	7 hrs.26 mins.	Foetal Distress
9	33	18 hrs. 20 mins	14 hrs.50 mins.	Inertia

*Primigravidae.

Duration implies that although induction had not failed the time lapse until the onset of contractions was such as to reduce the time available for labour.

Deterioration implies a worsening of, or failure of improvement in the signs and symptoms.

Inertia implies inefficient uterine action of any type and not necessarily as a result of avertin. Any avertin effects would have been cancelled out by the routine use of pitocin.

Foetal distress in case 8 had no relation to avertin - in fact it followed 6 hours after the avertin administration.

TABLE XLIII.

Immediate Elective Caesarean Section.

Case.	Maturity.	Weight of Infant.	Infant Result.	Other Factors.
*1	33	2.14	NND	-
2	33	3.10	A	Diabetes.
*3	36	6.0	NND	Breech
*4	39	6.14	A	Breech
5	29	2.14	NND	-
6	33	3.15	NND	-
*7	36	5.6	A	-
8	26	3.1	NND	-
9	37	5.4	A	Previous Hysterotomy

*Primigravidae.

TABLE XLIV.

Delayed Delivery in Imminent Eclampsia.

Case.	Gravidity.	Maturity.	Presenting. Bld. Pressure.	Albuminuria.	No. Doses of Avertin.	From first Avertin to Delivery.	Method of Delivery.	Weight of Infant.	Infant Result.
1	0	31	220/110	Solid	4	4 days 18 hours.	Induction & Vaginal.	2.15	NND
2	2	32	175/130	++	5	2 days 16 hours.	Induction & Vaginal.	4.8	Alive.
3	4	32	250/160	+	1	11 days 4 hours.	Induction & Vaginal.	4.9	Alive.
4	10	30	230/150	Trace	1	55 days	Caesarean Section	5.4	Alive
5	9	30	230/130	Solid	1	4 days	Caesarean Section	2.14	Alive
6	12	38	210/130	Solid	1	4 days	Vaginal	7.15	Alive
7	0	30	205/130	Solid	4	4 days 10 hours	Induction & Vaginal	2.6	Alive
8	0	35	200/130	+++	3	9 days 13 hours	Induction & Vaginal	5.7	Alive
9	0	32	160/110	Solid	5	1 day 22 hours	Induction & Vaginal	2.6	NND

TABLE XLV.

Intrapartum Imminent Eclampsia.

Case.	Maturity.	Duration of Labour.	Weight of Infant.	Infant Result.
* 1	40	10 hours 10 mins.	6.10	A
* 2	41	22 hours 30 mins.	7.2	A
* 3	39	41 hours 22 mins.	4.13	A
* 4	42	9 hours 40 mins.	7.12	A
* 5	40	17 hours 40 mins.	7.7	NND
* 6	37	12 hours 27 mins.	4.7	A
* 7	37	25 hours 25 mins.	6.1	A
* 8	40	10 hours 15 mins.	7.12	A
* 9	29	10 hours 50 mins.	2.8	SB
*10	37	3 hours 58 mins.	7.1	A
*11	39	26 hours 5 mins.	7.4	A
*12	40	22 hours 15 mins.	7.12	A
*13	38	18 hours 35 mins.	5.6	A
14	36	8 hours 50 mins.	6.13	A
15	37	12 hours 45 mins.	5.1	A
16	37	3 hours 50 mins.	5.6	A
17	38	15 hours 45 mins.	5.9	A
18	39	9 hours 36 mins.	5.14	A
19	40	8 hours 15 mins.	7.4)	A
			9.0)	A
20	41	31 hours 15 mins.	7.14	A
21	37	5 hours 20 mins.	6.2	A
22	39	6 hours 25 mins.	6.9	A
23	40	13 hours 5 mins.	8.14	A
24	40	36 hours	7.11	A
25	38	4 hours 23 mins.	5.14	A

*Primigravidae.

The First Stage of Labour in Patients Delivered per Vaginam.

Tables XLVI and XLVII show that 31 primigravidae and 43 multigravidae were delivered per vaginam. The mean duration of the 1st stage of labour for the primigravidae was 16 hours 11 minutes and for the multigravidae was 10 hours 16 minutes. In only 3 patients did the first stage of labour last longer than 30 hours. The length of the 1st stage was affected by the fact that many of the patients had had labour induced by rupture of the membranes and pitocin drip infusion.

I am satisfied that avertin neither causes hypotonic uterine inertia nor inco-ordinate uterine action.

TABLE XLVI.

1st Stage of Labour in Primigravidae delivered per vaginam.

Classification	Result.
Mean duration of 1st stage.	16 hours 11 minutes.
Longest 1st stage	47 hours 35 minutes.
Shortest 1st stage	3 hours 45 minutes.
Number with 1st stage lasting more than 18 hours.	11 - i.e. 35.5 per cent.
Surgical inductions	22 - i.e. 71 per cent
Pitocin drips.	16 - i.e. 51.6 per cent.

TABLE XLVII.

1st Stage of Labour in Multigravidae delivered per vaginam.

Classification	Result.
Mean duration of 1st stage	10 hours 16 minutes.
Longest 1st stage	31 hours
Shortest 1st stage	1 hour 18 minutes.
Number with 1st stage lasting more than 18 hours	4 - i.e. 9.3 per cent.
Surgical inductions	35 - i.e. 81.4 per cent
Pitocin drips	30 - i.e. 69.8 per cent

The Second Stage of Labour in Patients Delivered per Vaginam.

Tables XLVIII & XLIX. The duration of the second stage of labour was in many patients shortened by the routine application of forceps to effect delivery. Although it was the policy to assist delivery routinely, a large number of patients, especially multigravidae, had very short second stages of labour ending in spontaneous deliveries. Multigravidae under the effects of avertin on the whole, gave few, if any, warning signs that delivery was imminent.

I agree with Hamilton et al[68] that a forceps delivery in a patient suffering from imminent eclampsia does not worsen the foetal prognosis.

TABLE XLVIII.

2nd Stage of Labour in Primigravidae delivered per Vaginam.

Classification	Result.
Mean duration of 2nd stage	22 Minutes.
Longest 2nd stage	1 Hour
Shortest 2nd stage	5 Minutes
Spontaneous vertex delivery	9
Forceps delivery	21
Breech delivery	2

There was one set of twins.

TABLE XLIX.

2nd Stage of Labour in Multigravidae delivered per Vaginam.

Classification	Result.
Mean duration of 2nd stage	14 Minutes
Longest 2nd stage	1 Hour 3 Minutes
Shortest 2nd stage	2 Minutes
Spontaneous vertex delivery	34
Forceps delivery	8
Breech delivery	3

There were two sets of twins.

Method of Delivery.

101 infants were delivered in the survey. There were 3 sets of twins. Two patients were treated postpartum. Tables XLVIII and XLIX indicated the manner of vaginal delivery for primigravidae and multigravidae. There were 24 caesarean sections - 9 in primigravidae and 15 in multigravidae.

In Table L foetal loss has been assessed against the method of delivery. Numerous factors influence the choice of method of delivery and prematurity is the major cause of foetal loss in imminent eclampsia. Nevertheless the figures of this survey suggest that caesarean section is not to be recommended as a form of treatment or a method of delivery, in patients suffering from imminent eclampsia.

TABLE L.

The Foetal Loss in Relation to the Method of Delivery.

Method of Delivery.	Number of Infants.	Foetal Loss No.	Foetal Loss %	Foetal Loss Infants under 4 lbs.
Spontaneous vaginal del.	43	6	14	4
Forceps del.	29	1	3.4	-
Breech del.	5	3	60	2
Caesarean Section	24	7	29.2	4
Total	101	17	16.8%	10

The Third Stage of Labour in Patients Delivered per Vaginam.

34 of the 74 patients were under a general anaesthetic when delivered. 38 patients received intravenous ergometrine with either the crowning of the foetal head or the birth of the anterior shoulder.

The average 3rd stage blood loss was 9.3 ounces. There were 6 cases of postpartum haemorrhage* one of which was due to bleeding from an episiotomy. The incidence of placental site postpartum haemorrhage was therefore 8.1%. This incidence of postpartum haemorrhage is slightly higher than the overall incidence for the hospital. As precautions to prevent postpartum haemorrhage had been taken in more than half of the patients, it was thought that the avertin might be a factor in producing this high incidence. Table Ll shows that 4 of the 5 patients were delivered soom after an administration of avertin, which strongly suggests that avertin predisposes to third stage haemorrhage. Only 1 of the 5 patients received prophylactic intravenous ergometrine.

Manual removal of the placenta was often performed, but always for a reason other than postpartum haemorrhage or a prolonged third stage of labour.

TABLE Ll.

The Relationship of Postpartum Haemorrhage to the interval from the last Administration of Avertin.

Amount of Postpartum haemorrhage.	Gravidity.	Intravenous Ergometrine.	Interval from last Avertin administration.
22 ozs.	6	-	2 hours.
21 ozs.	0	-	2 hours 10 minutes.
26 ozs.	1	-	1 hour 35 minutes.
22 ozs.	0	-	9 hours 35 minutes.
24 ozs.	1	+	1 hour 5 minutes

*20 ounce or greater blood loss.

THE MORTALITY OF IMMINENT ECLAMPSIA.

Maternal Mortality.

There was no maternal mortality.

Foetal Mortality.

There were 5 stillbirths and 12 neonatal deaths, i.e. deaths within the first 28 days from the time of delivery.

The foetal loss was 16.8 per cent.

As has been shown throughout this analysis, many factors influence the prognosis for the foetus and these have been discussed under the appropriate headings. The factors as found by me correspond closely to those stated by Peckham[131] 30 years ago.

Table Lll (page 121) indicates the possible effects avertin may have on the foetal mortality. If the accepted time for the excretion of avertin is 2-3 hours, it would appear that possibly 2 stillbirths, and even less likely, 2 neonatal deaths could be attributed to the administration of avertin. However, as none of these four infants weighed more than 2 lbs 14 ozs it is probable that prematurity was the cause of death.

The second part of Table Lll reveals that no less than 9 of the 12 neonatal deaths occurred in male infants. This figure was surprising as amongst live-born infants the ratio of male to female was 53:43. To test the significance of this difference the formula

$$\chi^2 = S\left\{\frac{(x_e - x_o)^2}{x_e}\right\}$$

was applied to the figures. The result was correlated with Fisher's Tables and gave $P \simeq .05$. This indicates that as a chance finding the above sex difference would only occur 1:20 or thereabouts, thus making it statistically significant. As no clinical impression had been gained that male infants born to imminent eclamptic mothers were less lively than female infants, Table Llll (page 122) was compiled to assess this facet of the problem. In this table the Apgar[183]

scores between the two sexes at various weights were compared. The mean Apgar score for all infants was 4.9; in males the mean score was 4.5 and in females it was 5.4. Applying the X^2 formula a result of $P \simeq .20$ was obtained which indicates that the difference is not statistically significant.

Thus at birth - if the Apgar scoring system truly reflects foetal well being - male and female infants born to mothers suffering from imminent eclampsia have an equal chance of survival. Soon after, however, in the early neonatal period, the outlook for the male is significantly worse than for the female. If this male weakness was an inherited one, not only would male infants predominate among the neonatal deaths, but they would be dominant among the still-born infants and among the infants born with low Apgar scores as well. Since this is not so, the explanation for this difference possibly lies in changes occurring after the infant has been separated from the maternal blood supply. The absence of statistical significance in the difference between male and female Apgar scores suggests that the maternal supply of oxygen up to and including the time of delivery is equal for both sexes. Table LIV (page 123) shows no sex difference in the weights of these infants - a rough indication that the nutritional supply is equal for both sexes as well. It seems, therefore, that it is the withdrawal of a maternal factor that leaves the infant, especially the male infant, liable to cardio-respiratory collapse. I think this factor may well be humoral in origin. There is increasing evidence that in imminent eclampsia the hypertension is due to a humoral induced vasoconstriction. Should this 'humoral agent' cross the placental barrier it would produce the same effects in the infant. These effects would be abruptly reversed after birth and in some infants a state of shock going on to death might possibly occur.

This assumption would not explain a sex difference unless in the male neonate there was a more marked depression of the adrenal cortex. This explanation, for proof or otherwise, would require, (i) the isolation in cord bloods of a humoral agent found also in the blood or urine of mothers with imminent eclampsia, (ii) evidence that the agent is not long present in the foetal blood stream after birth, and (iii) evidence that the activity of the adrenal cortex is less in male infants born to mothers with imminent eclampsia.

I personally, do not know of any published work in this particular field. A combined approach using hormonal assays and chromatography in both mother and new-born infant might throw some light on the subject.

TABLE LII.

The Foetal Loss related to the Administration of Avertin and to the Foetal Weight.

Stillbirths.

No.	Wt.	Administrations of Avertin.	Interval from last avertin administration to loss of foetal heart sounds.	Sex.
1	2.8	2	1 hour 10 minutes.	M
2	4.4	1	3 hours 15 minutes	F
3	2.12	2	4 hours	F
4	2.13	3	1 hour 5 minutes	F
5	7.4	3	3 hours	M

Neonatal Deaths.

No.	Wt.	Administrations of Avertin.	Interval from last Avertin administration until delivery.	Age at Death.	Certified Cause of Death.	Sex.
1	3.1	1	6 hrs.38 minutes	48 hrs.	Prematurity	M
2	5.1	2	14 hrs. 7 minutes	5 days	Pneumonia	M
3	7.7	2	8 hrs.45 minutes	25 hrs.	Hyaline Membrane disease	M
4	2.14	3	10 hrs.30 minutes	$3\frac{1}{2}$ days	Prematurity	M
5	2.15	4	6 hrs.10 minutes	2 days	Prematurity	M
6	4.8	2	6 hrs.53 minutes	8 days	Staphylococcal Enteritis	M
7	2.15	3	7 hrs.50 minutes	10 hrs.	Prematurity	M
8	6.0	3	12 hrs.18 minutes	3 days	Staphylococcal Pneumonia	F
9	2.6	5	2 hrs.10 minutes	25 mins.	Prematurity	F
10	5.13	3	4 hrs.57 minutes	5 hrs.	Cerebral Haemorrhage	M
11	2.14	2	2 hrs.29 minutes	8 hrs.	Premature	M
12	3.15	3	9 hrs.15 minutes	4 days	Staphylococcal Enteritis	F

TABLE L111.

Apgar Scores for Male and Female Infants of Various Birth Weights.

Weight in lbs & ozs.	Male		Female	
	Number	Mean Apgar	Number	Mean Apgar.
2 - 2.15	4	3.5	2	4.5
3 - 3.15	7	4.57	4	2.25
4 - 4.15	11	5.82	7	5.71
5 - 5.15	12	3.58	12	5.08
6 - 6.15	8	4.37	7	5.86
7 - 7.15	8	4.25	7	6.43
8 or more	3	5.66	1	10
Total*	53	4.5	40	5.4

*The above figures do not include the 5 stillborn infants nor the 3 infants born in institutions other than the Peninsula Maternity Hospital.

Mean Apgar all infants = 4.9

TABLE LIV.

Weights of Infants Born to Mothers in a State of Imminent Eclampsia.

Weight in lbs & ozs.	Male Number	Male Per cent.	Female Number	Female Per cent.
2 - 2.15	5	9.1	5	10.9
3 - 3.15	7	12.7	5	10.9
4 - 4.15	11	20.1	8	17.4
5 - 5.15	12	21.8	13	28.2
6 - 6.15	8	14.5	7	15.2
7 - 7.15	9	16.3	7	15.2
8 or more	3	5.5	1	2.2
Total	55		46	

Mean weight males	=	5 lbs 5 ozs.
Mean weight females	=	5 lbs 5 ozs.
Overall mean weight	=	5 lbs 5 ozs.
Smallest infant	=	2 lbs 6 ozs
Largest infant	=	9 lbs 0 ozs

POSTPARTUM FOLLOW-UP.

Although every effort was made to get these patients to attend a follow-up clinic at least once, less than half the patients in the survey were seen after the 30th postpartum day. The patients in the follow-up have been divided, therefore, according to how long after labour they were last seen. Table LV (page 125).

Of the 100 patients in the survey, 5 were discharged home or to another hospital before the 6th postpartum day and their records are incomplete. Up until the 30th postpartum day, more than 70% of patients still presented with either hypertension or albuminuria. After the 30th postpartum day, residual hypertension was found in 20 of 39 cases and albuminuria in 9. Among the latter 9, a confirmed diagnosis of neoplastic syndrome was made in one patient. Residual hypertension was more commonly seen in multigravidae than primigravidae and suggests that the former group included patients with underlying hypertensive vascular disease.

There was no obvious parallel between the height of the presenting blood pressure and the height of the final postpartum blood pressure recorded. There was a definite correlation between the fall of blood pressure obtained with avertin and the final postpartum blood pressure. Satisfactory hypotension was associated with normal or near normal follow-up blood pressures. The follow-up on the 3 patients who developed convulsions was -

(i) J.T. - seen at 9 months - 120/90 mm of mercury - no albumen.
(ii) H.W. - seen at 13 months - 100/70 mm of mercury - no albumen.
(iii) W.F. - seen at 10 days - 160/90 mm of mercury - no albumen.

It is my intention to perform a further long term follow-up on as many of these patients as possible. On the surface it seems that imminent eclampsia is quite often followed by hypertension, but as in the majority of my patients pre or early pregnancy blood pressures were not known, the hypertension may have been present before the pregnancy.

TABLE LV.

The Follow Up of 100* Cases of Imminent Eclampsia.

Duration Post-Partum.	Primigravidae. No.	Residual Hypertension.	Residual Albuminuria.	Multigravidae. No.	Residual Hypertension.	Residual Albumimuria.
6th-10th day	11	6	7	29	27	22
10th-30th day	7	4	4	9	9	6
1st-3rd mnth.	7	2	-	12	6	3
3rd-6th mnth.	4	1	2	2	2	2
6 or more months.	9	6	1	5	3	1
	38			57		

Residual hypertension: A diastolic blood pressure of 90 mm of mercury or more after resting.

Residual albumimuria: Albumen present in a catheter specimen of urine and not due to urinary tract infection.

*Excludes 5 cases discharged before the 6th postpartum day.

Residual hepatic or renal damage due to avertin.

Neither liver nor renal biopsies were taken.

Liver function tests were analysed in 29 patients seen 2 or more months postpartum. In each case the results were within normal limits. These tests do not exclude the possibility of liver damage due to avertin, but coupled with the absence of toxicity to the liver at the time of the administration, they suggest that only slight, if any, damage occurs.

In the same patients blood urea estimations were made and all were within the limits of normal. 15 of the 29 patients had a residual albuminuria. Microscopy revealed no casts in the urine specimens. Avertin at the time of administration appears to increase the excretion of urine.

I have not detected any evidence in this survey to suggest that avertin used in a dose of 0.09 ml per kg. of body weight causes hepatic or renal damage of either a temporary or permanent nature.

Foetal Loss in Relation to Follow-Up Maternal Findings.

When discussing the effects of age and gravidity upon the foetal survival rate, it was suggested that many elderly and multigravid patients had underlying hypertensive vascular disease. The follow-up data revealed in Table LV lend support to this view. Table LVI (page 127) shows the postpartum findings of the mothers whose infants did not survive. Only 8 of these mothers were seen 6 or more weeks portpartum. 3 of the 8 had neither residual hypertension nor albuminuria. 2 of the 8 had residual hypertension. The incompleteness of the follow-up precludes the forming of any definite opinion.

TABLE LVI.

The Follow Up in Mothers whose Infants did not Survive.

Maternal Age.	Foetal Result.	Duration Postpartum.	Residual Hypertension.	Residual Albuminuria.
*31	SB	12 months.	150/100	Trace
37	SB	18 days	160/120	+
22	SB	9 months	120/85	Solid
30	SB	9 days	160/130	++
38	SB	14 months	130/70	Nil
*25	NND	6 weeks	120/80	Nil
44	NND	10 days	180/120	Trace
35	NND	9 months	190/110	Nil
*20	NND	9 days	140/90	Trace
25	NND	7 weeks	130/80	Trace
*35	NND	12 days	180/120	++
30	NND	7 weeks	130/85	Nil
*27	NND	10 days	160/120	Trace
*21	NND	7 weeks	120/80	+
33	NND	6 days	150/110	+
35	NND	7 days	180/110	Trace
34	NND	9 days	120/95	Trace

*Primigravidae.

C O N C L U S I O N.

Imminent eclampsia is a clinical state in which the signs and symptoms of pre-eclamptic toxaemia develop to a degree sufficient to warrant special treatment to prevent the occurrence of convulsions. Retrospective diagnoses of such states are useful in providing criteria for the selection of patients, but add little to the assessment of the different drugs available for treatment. As treatment is always urgent and in the first instance taken to the patient, the diagnosis is made immediately on the presenting clinical symptoms and signs alone.

The incidence of imminent eclampsia is related to the standard of the available antenatal care in a given area. Where meticulous attention is paid throughout pregnancy to weight gain and changes in the blood pressure, the number of cases of imminent eclampsia developing is minimal. In Cape Town the relative frequency of the condition stems from the fact that many patients make no attempt to receive antenatal care, and secondly that the standard of antenatal care often falls short of basic, let alone superior requirements. A reassessment of the objectives of antenatal care with the accent on the maximum rather than the minimum that should be done for patients appears to be an urgent need in the services available in Cape Town. The remark applies equally to antenatal services administered by hospitals, municipal and other clinics, general practitioners and midwives.

In established cases, the objectives of treatment are to prevent convulsions and to deliver a live and as mature an infant as possible. As the aetiology is unknown, treatment is directed towards reversing the underlying pathological changes which are fluid retention and arteriolar vasoconstriction. It is possible that many cases of imminent eclampsia have also a cerebral dysrhythmia. Avertin was used for the treatment of the 100 patients in this survey. 3 patients nevertheless developed convulsions, which suggests that the treatment was ineffective. However, since the introduction of avertin for the management of imminent eclampsia, the numbers of cases of eclampsia who had their first fit in hospital, has fallen from a seven year average of 48% (Table 1) to 26.3% in the Maternity Units of the Department of Obstetrics of the University of Cape Town. A stricter application by the other hospitals in the department of the criteria for diagnosis and management established at the Peninsula Maternity Hospital would have resulted in an even greater improvement. Avertin has proved to be a successful

but certainly not an ideal drug for treating these cases. It effectively achieves sedation and lowers the blood pressure in about 90% of patients. Sedation is, however, probably only needed for the first six hours after which time a continuous reduction in the blood pressure appears to be the main need. Avertin certainly can maintain the blood pressure at lower levels for long periods, but sedation is an unwanted accompaniment in many instances. In those patients in whom I attempted to change from avertin to a specific anti-hypertensive agent, the switch-over was in most instances followed by a worsening of the signs to the pre-avertin clinical picture. In retrospect I think this was because I used either ganglion or adrenergic blocking anti-hypertensive drugs. Avertin acts directly on the blood vessels and I now believe that anti-hypertensive drugs acting in the same way should be used for the change over in patients in whom an attempt is to be made to delay termination of pregnancy. That such attempts are necessary is indicated by the fact that 11 of the 17 infants who failed to survive weighed less than 4 lbs.

The scheme of management that I would favour is as follows -

1. Avertin is administered to all patients who present in a state of imminent eclampsia The only exceptions are ptients in the late first or second stages of labour. In these patients, an intravenous anti-hypertensive agent is given and a general anaesthetic is administered at the onset of the second stage.

2. Avertin therapy is continued until delivery in 34 weeks or more mature patients who, if not already in labour, are induced.

3. In patients less than 34 weeks pregnant, immediate termination of pregnancy is withheld and the initial dose of avertin is followed by the intravenous administration of apresoline and a veratrum alkaloid. If there is no improvement within 24-48 hours, or if regression follows an initial improvement, induction of labour is performed.

The simplicity and safety of avertin for use in the initial domiciliary treatment of imminent eclampsia, and the satisfactory effects I obtained in this survey, are the reasons why I favour its retention

in the therapeutic regime. It has very obvious limitations in the management of patients where delivery is unlikely to occur within 24 hours.

The results of the survey indicate that vaginal delivery offers the best prognosis for the foetus in imminent eclampsia. Caesarean section should be reserved for patients in whom induction of labour fails or in whom an indication other than imminent eclampsia exists.

Imminent eclampsia is a preventable state and thoughtful, thorough antenatal care would largely eliminate the need for a special scheme of management such as I have suggested. Prevention is undoubtedly better than the most carefully planned and conducted 'cure'.

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ADDENDUM.

The Hospital Numbers of the
100 Patients in this Survey.

Peninsula Maternity Hospital.

1960.

1825	1140	1696	1984	2721
1820	2783	2800	1233	2622
2788	2900	986	2389	989
3025	3004	3551	3244	1764
3048	3204	1271	1281	2708
2685	2382	2383	2899	3154
3562	1362	2661	2188	1867
2285	1039	2471	988	1623
2580	917	2529	3369	2481
2766	3225	1355	2478	

1961.

434	1223	1992	1434	297
1397	1171	1847	120	1012
1876	615	1591	1977	1382
2337	2271	2190	427	2276
2052	1480	300	2074	322
1698	36	1620	1270	1549
1640	1519	1360	1663	2106
1650	1272	1157	1787	101
578	641	1455	2156	
262	2327	1047	725	

New Somerset Hospital.

1325/61.

St. Monica's Home.

607/61.

Karl Bremer Hospital.

61/10186.