ASPECTS OF LARYNGOTRACHEOBRONCHITIS IN AFRICAN CHILDREN.

A THESIS SUBMITTED FOR THE DEGREE
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IN THE UNIVERSITY OF CAPETOWN.

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CHAPTER I

CHAPTER 1

AN HISTORICAL REVIEW OF LARYNGOTRACHEOBRONCHITIS

Terminology and Aetiology

"Laryngotracheobronchitis" is a relatively recent term for infective upper airway disease (Baum, 1924).

Prior to this "croup" was used by both public and profession to describe a train of laryngeal symptoms which sometimes were due to infection. The word derives from the Anglosaxon "kropan" (Neffson and Wishik, 1934a) or "hreopan" (MacKenzie, 1880) and although used earlier by Blair (MacKenzie, 1880; Eisner, 1959), was popularised in 1765 by the Scottish physician Home (Cormack, 1875a). Both used the term in descriptions of what was probably diphtheria.

Early theories on the aetiology of croup included sewer poison (Johnson, 1878) and "an increased quantity of fibrine and albumin in the blood" (Drew, 1856). The association of measles with croup was noted (Adams, 1812; Hannay, 1840; Bell, 1879) and in 1826 Bretonneau clearly identified it as one form of diphtheria (Krugman and Ward, 1968).

There followed much discussion on the distinction of diphtheria from the old English disease of laryngitis (Kimbell, 1829; Hannay, 1840; Drew, 1856; Johnson, 1870; Bruce, 1875; Cormack, 1875a,b; Jenner, 1875; MacKenzie, 1880).

Further confusion arose over the correct meaning of the various prefixes attached to croup. True (or membranous) croup was used to refer to both a non-diphtheritic condition and to diphtheria (Ayres, 1852; Drew, 1856; Johnson, 1875; Cumming, 1875; Bruce, 1875). The French "false croup" was understood by some to refer to the English "spasmodic croup" (laryngismus stridulus) (Ayres, 1852; Cormack, 1875b; Bennett, 1875) and to inflammatory (but non-diphtheritic) croup by others (Johnson, 1875).

This ambiguity led to the plea that the term "croup" should be prefixed by the disease in question, for example, diphtheric croup (Bennett, 1875; Cormack, 1875a; Bruce, 1875), a recommendation not heeded universally until mid-twentieth century.

The terms "laryngotracheobronchitis" or "acute infective croup" (Neffson and Wishik, 1934a,b) to describe cases of non-diphtheritic croup have now been accepted by the English-speaking world. However, on the Continent "stenosing laryngitis" (Leegaard and Lindeman, 1954) and "pseudocroup" (Leegaard, 1960; Lindberg, 1963; Toth and Major, 1965; Roth 1966) are sometimes employed.

Re-apprasial of the sympton-complex was precipitated by the influenza pandemic of 1918 (Neffson, 1944; Eisner, 1959). Croup was described following influenza, where cultures for C.diphtheriae were negative, or where a pharyngeal membrane was absent (Glover, 1918; Lynah, 1919; Gittens, 1932). This led to the conviction that the micro-organism that caused influenza also was responsible for croup.

Over the next two decades a variety of bacteria isolated from pharyngeal cultures were claimed as causative agents (Tolle, 1930; Jackson and Jackson, 1936; Orton, Smith, Bell and Ford, 1941; Le Jeune and Bayon, 1941; Neffson, 1944).

Then followed the discernment of the entity later called "acute epiglottitis" or "supraglottitis" from other forms of infective croup (Sinclair, 1941). These cases were distinguished by severe toxaemia, a turgid cherry-red epiglottis and the culture of Haemophillus influenzae Type B from pharynx and blood.

Thus, by the early nineteen forties, only two organisms had regularly been shown to cause croup; C.diphtheriae and H.influenzae Type B.

About this time it was first suggested that a virus was responsible for the initial process in most cases of laryngotracheobronchitis and that bacteria were secondary invaders (Brighton, 1940; Neffson, 1944).

Rabe (1948a), in his classical contribution, found no constant organism in pharyngeal cultures. However, he observed the endoscopic picture of subglottic swelling so constantly that a single etiology was suggested and he predicted this would prove to be viral. In addition Rabe gave perspective to the aetiological problem: the largest group in his series was "viral" with the minority being due to C.diphtheriae and H.influenzae.

These early postulates have proved to be correct. Viruses were first isolated from cases of croup in 1956 by Charnock. Since then 50%-70% of pharyngeal cultures have been positive for viruses (Beale, McLeod, Stackiw and Rhodes, 1958; Vargosko et al,

1959; Parrott, 1963; McClean, 1964; Holzel et al, 1965; Toth and Major, 1965; Major, 1966). Those isolated so far have been Influenza A and B, Adenovirus 1,2,3, 5,7, Respiratory syncytial virus, enteroviruses, measles virus and most frequently, Para-influenza 1,2,3. The predominant agent has varied with the series and the season of the year.

In some children a predisposition to infective croup has been suspected, for recurrence is well-known. An inherent factor, whether allergic, neurophysical or emotional, may provoke croup (Turner, 1954; Philipson, 1958; Eisner, 1959; Martensson, Nilsson and Torbjär; 1960), as may sudden temperature changes (Windorfer, Lampert and Truckenbrodt, 1964) and the dry atmosphere of central heating (Turner, 1954). "Children of a gross and lax habit are most liable to it" (Buchan, 1812), an opinion shared by later observers (Eisner, 1959; Berg, 1963).

Treatment and Mortality Rates

Blood letting was practised up to the nineteenth century (Drew, 1856) and further routine treatment included the local application of silver nitrate to the tonsils and fauces (MacKenzie, 1825; Drew, 1856), emetics, sedation, calomel and mercurials (Adams, 1812; Hannay, 1840; Ayres, 1852; Drew, 1856; Jenner, 1875).

However, as early as 1829 Kimbell demurred. "Bleeding ... blistering ... drastic purging, calomel by cart-loads ... are quite enough to exhaust the life of an irritable and delicate infant." He recommended a warm atmosphere, achieved by inhaling steam from boiling water and the antispasmodics squill and valerian.

It was not until this century that there was general appreciation of the necessity for a humid atmosphere and plentiful fluids to combat the sticky secretions of laryngotracheobronchitis (Gittens, 1932; Brennerman, Clifton, Frank and Holinger, 1938; Davison, 1940; Orton et al, 1941; Rabe, 1948b; Everett, 1951; Rosales and Davenport, 1962). Oxygen-enriched inspired air was less emphasized (Gittens, 1932; Le Jeune and Bayon, 1941; Baum, 1945; Everett, 1951; Rosales and Davenport, 1962). The introduction of sulphonamides initiated the control of secondary bacterial infection in croup (Morgan and Wishart, 1947; Rabe, 1948b; Everett, 1951).

Tracheostomy was performed in ancient times (Voss, 1860). By the middle of the nineteenth century it had become a common procedure in the management of croup (Ayres, 1852; Drew, 1856; Voss, 1860; Bell, 1879). The survival rate was 10%-50%

and complications of tracheal ulceration and stenosis were described (Drew, 1856).

Earliest reports of intubation of the larynx via the nose or mouth came from France. Initially Desault, and later Bouchut, employed this technique (MacEwan, 1880b). It was condemned by contemporaries because the procedure was attended by a high morality rate.

The successful use of oral intubation in cases of oedema of the glottis was reported from Glasgow in 1880 (MacEwan, 1880a). O'Dwyer (1885) employed this technique in diphtheritic croup and found a supporter in Northrup (1894). These pioneers recommended intubation rather than tracheostomy as a simple procedure which could relieve tracheal obstruction, while the humidification of the inspired air was maintained by the nose and mouth.

The tracheostomy versus intubation debate has continued up to the present. The majority opinion regarded tracheostomy the method of choice (Gittens, 1932; Richards, 1938; Orton et al, 1941; Morgan and Wishart, 1947; Fearon, 1954; Rosales and Davenport, 1962; Windorfer, Lampert and Truckenbrodt, 1964; Fearon, MacDonald, Smith and Mitchell, 1966; Striker, Stool and Downes, 1967; Hatch, 1968; Parton, 1969). However, nasotracheal intubation was preferred by several authors (Baum, 1928; Richards, 1933; Neffson and Wishik, 1934; Baum, 1945; Roth, 1966; Halldorsson, Bushnell and Connelly, 1967; Abbott, 1968).

Although frequently recommended, the use of steroids has not been the subject of many controlled trials. Novik (1960) concluded that steroids did marginally reduce the need for tracheostomy, while Martensson et al (1960) found that only patients with a history of allergy benefitted. However, other controlled series (Eden and Larkin, 1964; Skowran, Turner and McNaughton, 1966; Eden, Kaufman and Yu, 1967) failed to show that steroids shortened the course of the illness or improved the prognosis.

Phenomenal success has been reported recently of a new management (Adair, Ring, Jordan and Elwyn, 1971). Nebulised racemic epinephrine was administered through a face mask and a Bird Respirator and thereby tracheostomy was avoided in over 300 patients. This was not a controlled trial.

Early writers regarded croup with apprehension (Drew, 1856). "There are no cases more trying to the young practitioner ... for death is, in every such case, imminent." (Jenner, 1875). "The immediate cause of death is a condition of brain .. that state

arises from non-oxygenation, the non-performance of which .. is .. mainly to be referred to the presence of mucus, and .. perhaps, to the peculiar effusion in the larynx and trachea." (Kimbell, 1829).

This century the prognosis of croup has improved. The total mortality rate of several large series ranged from 5% to 63%, with an average of 40% (Baum, 1928; Tolle, 1930; Gittens, 1932; Richards, 1933; Neffson and Wishik, 1934; Brennerman et al, 1938). The mortality rate of intubated cases was 14% - 33% and of tracheostomy cases 53% - 100%.

The prognosis depended on the proportion of cases in each series in whom tracheostomy or intubation was indicated and/or inflammation of the lower respiratory tract was present. Both these situations were accompanied by a high death rate.

Over the past two decades the average total mortality rate has fallen to 2% (Everett, 1951; Peach and Zaiman, 1959; Leegaard, 1960; Estola, Wasz-Hockert and Rinne, 1960; Rosales and Davenport, 1962; Hawkins, 1963; Lindberg, 1963; Windorfer, Lampert and Truckenbrodt, 1964; Garg and Sharma, 1965; Parton, 1969). The intubation/tracheostomy rate of these series was up to 31%. Ten per cent to 17% of those intubated and 3% to 37% of those tracheostomised succumbed.

While there remains a significant mortality rate amongst those patients requiring surgical relief of airway obstruction, the number of cases of such severity has declined.

CHAPTER II

CHAPTER II

THE DESIGN OF THE THESIS

INTRODUCTION

The reduction of morbidity and mortality rates of croup described in the previous chapter accompanied improvement not only in medical expertise but also in community health.

However, where socio-economic circumstances remain unsatisfactory children with poor nutrition are exposed to frequent infections at an early age, and are brought for medical attention late in the course of the disease. Treatment in such circumstances often achieves suboptimal results. Therefore laryngotracheobronchitis in African children has remained a formidable problem compared with the disease in White children.

Management of croup cases in the general wards of a busy institution was inadequate. In an attempt to improve prognosis concentration of these in one unit, and their care by a team, was undertaken.

A preliminary investigation done in this unit (Wesley, Bruce and Holloway, 1968) indicated that 3 aspects of croup in particular needed further examination :-

1. The value of certain physical signs in this syndrome.
2. The physical signs which led to the decision to intubate the trachea.
3. The blood gases and acid base pattern from admission through convalescence.

While numerous reports (see Chapters I and III) have dealt with clinical features of, and tracheostomy, in croup, guidance in the management of local patients was limited. Studies published to date on blood gases and acid base in croup have been restricted to a single observation on a small number of patients. Most workers were seeking assistance in the timing of surgical intervention to relieve obstruction. Neither the arterial carbon dioxide (Orton et al, 1941; Leegaard and Lindeman, 1954; Leegaard, 1960; Rees, Stead, Bush and Jones, 1966) nor the arterial pH (Owen-Thomas, 1966) were considered to be helpful.

DESIGN OF THE STUDY

1. Accommodation

A ward with six cots for the treatment of laryngotracheobronchitis was sited contiguous to the existing Respiratory Unit, King Edward VIII Hospital, Durban.

2. Staff

The nursing complement of the Unit is not subject to frequent rotation, giving opportunity for acquiring skill in special techniques necessary in respiratory care. Medical officers spend several months in the Unit. In 1969 a physiotherapist was seconded to the Unit.

3. Patient Selection

The patients for study were all children with croup, admitted either directly from home or from the general paediatric wards.

During the period under review 126 children with infective croup were treated in the Respiratory Unit and 63 with adequate data have been included in this study. Patients with diphtheria were excluded.

4. Clinical Aspects

Clinical data were recorded on a proforma designed so that observations would be standard (Appendix pages a1, a2).

Each child was assessed on admission and after one to 4 hours of selected treatment. Subsequent progress was recorded in the case notes. If intubation was undertaken clinical features present at the time were noted.

It was anticipated that the proforma based on limited experience might be imperfect, but would be a guide in the division of patients into treatment groups.

A laryngoscopy chart (Appendix page a3) used to record data was designed with the assistance of an otolaryngologist who worked in the Unit for a period.

The Clinical Signs Noted.

A. Signs for estimating severity of upper airway obstruction were :-
   1. Recession, which was divided into intercostal, subcostal, supra-clavicular and sternal.
   2. Reduction of air entry, assessed by auscultation. Experience made it possible to grade this into minimal, moderate and severe.

B. The child's ability to cope with his disease was assessed by :-
   1. Pulse and respiratory rates, noted with as little disturbance as possible.

2. Restlessness.

3. Alertness or otherwise to his surroundings.

4. Muscular tone. The method for assessing this was the arm-dropping test. If the child failed to resist the movement of his arm his tone was regarded as reduced.

C. Involvement of the lower respiratory tract in the disease process was recorded by the presence of rhonchi, bronchospasm, crepitations and bronchial breathing.

D. Cyanosis was noted.

E. Laryngoscopy findings were noted.

5. Classification of patients on Clinical Features.

Clinical division of patients was as follows :-

a. Mild : stridor and recession only.

b. Moderate : stridor and recession with reduced air entry on auscultation.

c. Severe : features of moderate cases but in addition cyanosis and/or indifference to surroundings and/or hypotonia.

The presence of lower respiratory tract involvement was not used in this clinical division.

6. Arterial Blood Gases

At the time of clinical assessment, arterial blood gases were analysed on all children while breathing air and, where feasible, daily thereafter until the seventh day.

Those children who were intubated had additional blood gas studies done as follows :-

Before intubation, breathing air.

Thirty minutes after intubation, breathing air.

After 10 minutes breathing 100% oxygen.

Four hours later, breathing air.

This routine was not possible in all cases as a 24 hour laboratory service was not available.

Blood specimens were collected from a femoral artery in heparinised small vein sets (Baxter, R35). Tests showed the polythene tubing of this set to be impervious to both oxygen and carbon dioxide over a 2-hour period, after which the tests were discontinued.

Blood Gas Analysis

A small research laboratory is attached to the Respiratory Unit. All blood specimens were analysed by a trained technician within 15 minutes of being obtained. Specimens taken on 100% oxygen breathing were examined immediately. The pH was measured using a microtechnique (Siggard-Anderson, Engel, Jorgensen and Astrup, 1960). The pH electrode was calibrated, using precision buffers of pH 7,381 and 6,840 at 38°C. The $PaCO_2$ was obtained by the interpolation method. The arterial oxygen tension was measured with a modification of the Clark electrode (Clark, 1956) which allows analysis of oxygen from microsamples (Laughlin, McDonald and Bedell, 1964). The calibration was done using thermostat water (Po_2 = 20,93 x B.P. - 47 mm.Hg) and a solution where the oxygen tension was taken to be zero (sodium sulphite in 0,04 molar borax). These calibrations were made at frequent intervals during the measurements. Less frequently, blood was tonometered with gases of known oxygen tension and the electrode checked by comparing the measured oxygen tension of the blood with the oxygen tension of the gas. In this way it was possible to establish that the difference was 1,1 ± 2,2 mmHg.

7. Management of Patients

a. Conservative Treatment

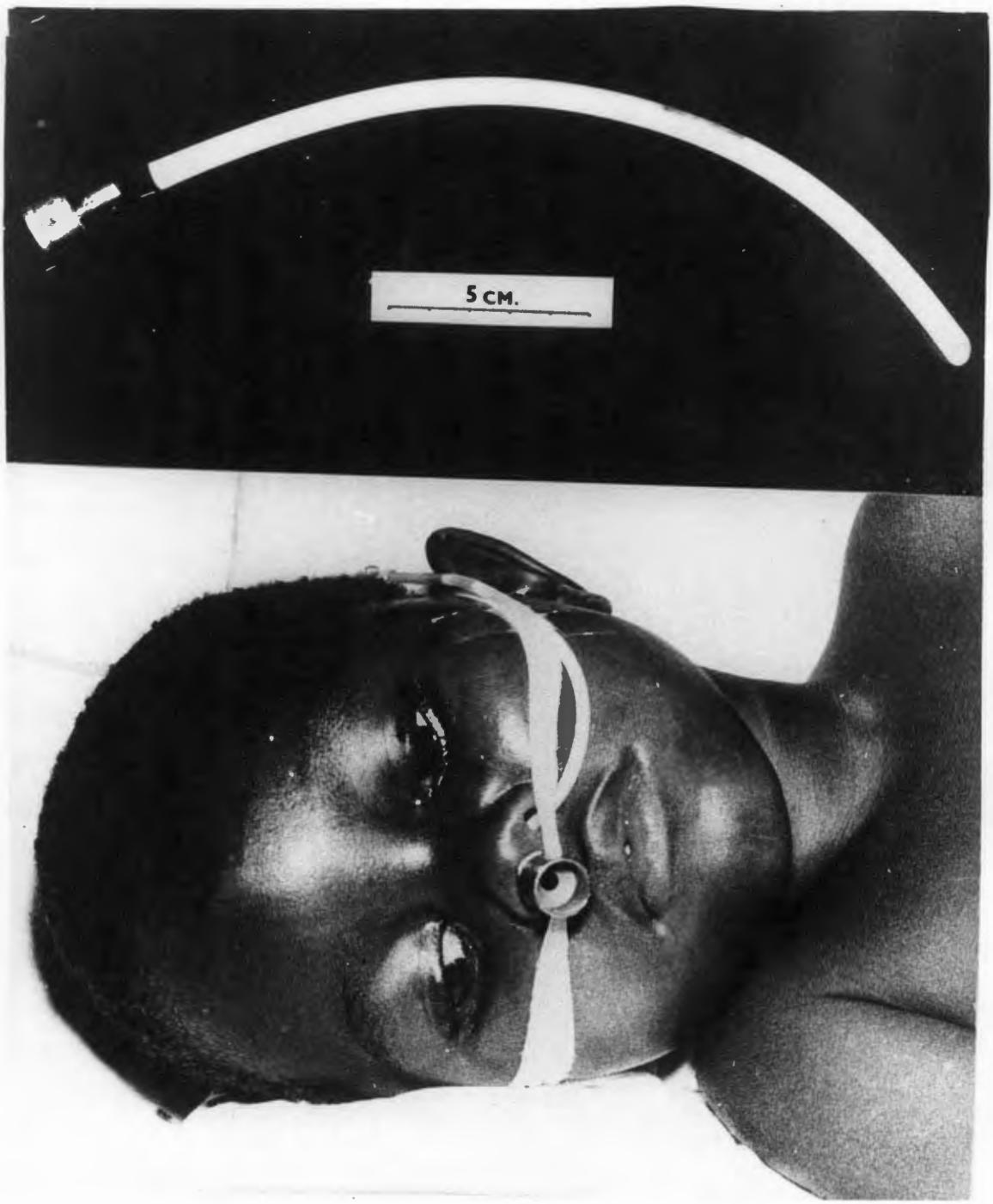
Treatment common to all patients was termed "conservative".

i. Fluid intake: In the more severe cases a nasogastric tube was passed to ensure adequate fluid intake. Most mild cases were so little distressed that bottle feeds could be continued. Cow's milk was given in an amount of 150 ml/kg/day divided into 7 feeds. If diarrhoea was present, electrolyte feeds (Appendix page a4) were substituted, or intravenous fluids were given until stool consistency improved.

ii. Initially all children were nursed in a tent which delivered humidified oxygen (see paragraph 9 below). When their condition allowed, the tent treatment was discontinued.

iii. Physiotherapy with removal of secretions by suction was performed about 4-hourly by nursing staff, sometimes assisted by a physiotherapist. The nasotracheal tube was cleared of secretions by a soft polyvinyl feeding catheter, while non-intubated patients were encouraged to cough by pharyngeal suction with a rubber catheter.

FIGURE II : 1 NASOTRACHEAL INTUBATION



Upper : A polyvinyl chloride endotracheal tube and metal suction connector.

Lower : The endotracheal tube held in position by metal connector and tape.

iv. Cold sponging was employed to reduce body temperature if it had risen above 40°C.

v. All patients were sedated with oral diazepam until the clinical condition improved. The dosage was :

Under 6 months of age : 2 mg 6 hourly

6 months - 3 years : 5 mg 6 hourly

Over 3 years : 5 mg 4 hourly or 10 mg 6 hourly.

vi. Antibiotics were prescribed from admission, as experience had indicated that the majority of patients had accompanying pneumonia. Initial penicillin or ampicillin was replaced by other antibiotics depending upon the response and tracheal secretion cultures. The antibiotic dosage used is given in the Appendix (Page a4).

vii. Hourly pulse and respiratory rates were recorded by the nursing staff and frequently checked by a medical officer.

b. Active Treatment

When relief of upper airways obstruction was thought necessary, nasotracheal intubation was undertaken. The indications for intubation were not decided upon prior to the study because this was one facit under review.

Method of Intubation

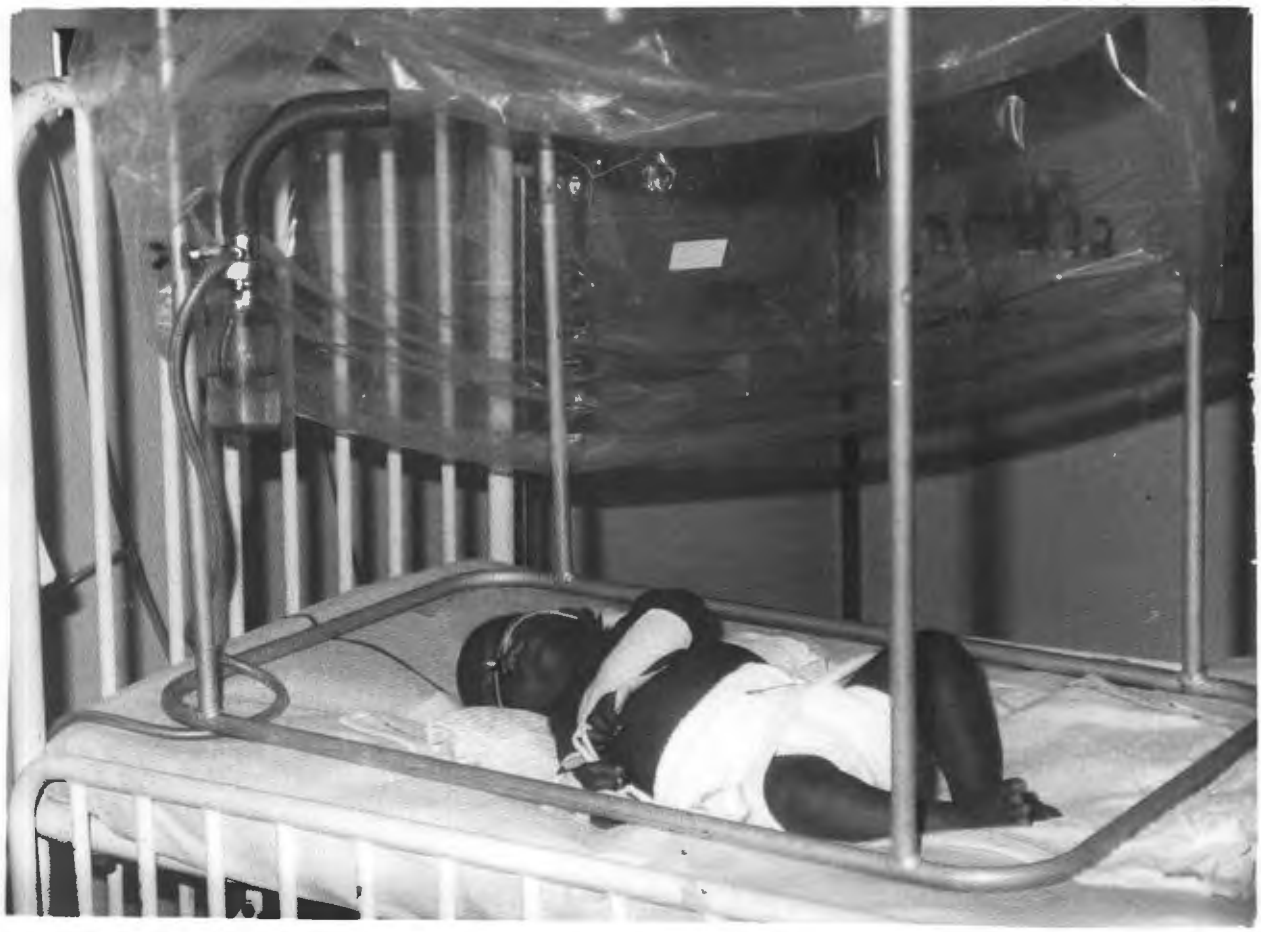
The patient was sedated with diazepam and given oxygen via a face mask for several minutes. The trachea was then intubated via the nose. A polyvinyl chloride tube, of a size that fitted comfortably in the larynx was used. The distal end was trimmed to prevent intubation of the right main bronchus and the tube was secured in place by a metal suction connector and tape (Figure II : 1).

A nurse then performed sterile tracheal suction while the attendant doctor carried out the initial physiotherapy. Five to 10 ml of sterile saline in 2 ml aliquots were usually instilled to soften and dislodge inspissated secretions. Physiotherapy and suction with a polyvinyl plastic feeding tube was performed thereafter at approximately 4-hourly intervals by the nursing staff, with or without a physiotherapist's assistance.

Extubation

Primary extubation was attempted on the seventh day. If this failed re-intubation

FIGURE II : 2 THE OXYGEN TENT



The non-collapsible frame, oxygen humidifier and disposable plastic canopy are shown.

or tracheostomy was performed. No previous policy was laid down concerning this aspect of treatment. If extubation was successful, sedation was stopped, although nursing in a tent continued until any residual stridor had diminished. Bottle feeds replaced nasogastric feeding as soon as the condition allowed.

8. Chest Radiograph Grading

Previous experience had shown that the majority of these patients had clinical and radiological evidence of pneumonia.

In order to record the extent of the pneumonic infection, a system of scoring the chest radiograph was devised. From the anterior-posterior and lateral films the number of segments showing complete or incomplete consolidation was assessed. Complete consolidation of a segment scored two points and incomplete consolidation, one point. For simplification the right lower lobe was taken to have four segments instead of five. Thus for example, with complete consolidation of both lungs the maximum score was 36, while incomplete consolidation of all segments scored 18. Other abnormalities, such as pleural effusion, atelectasis, lymphadenopathy and cardiac enlargement were also noted.

9. The Tent (Figure II : 2)

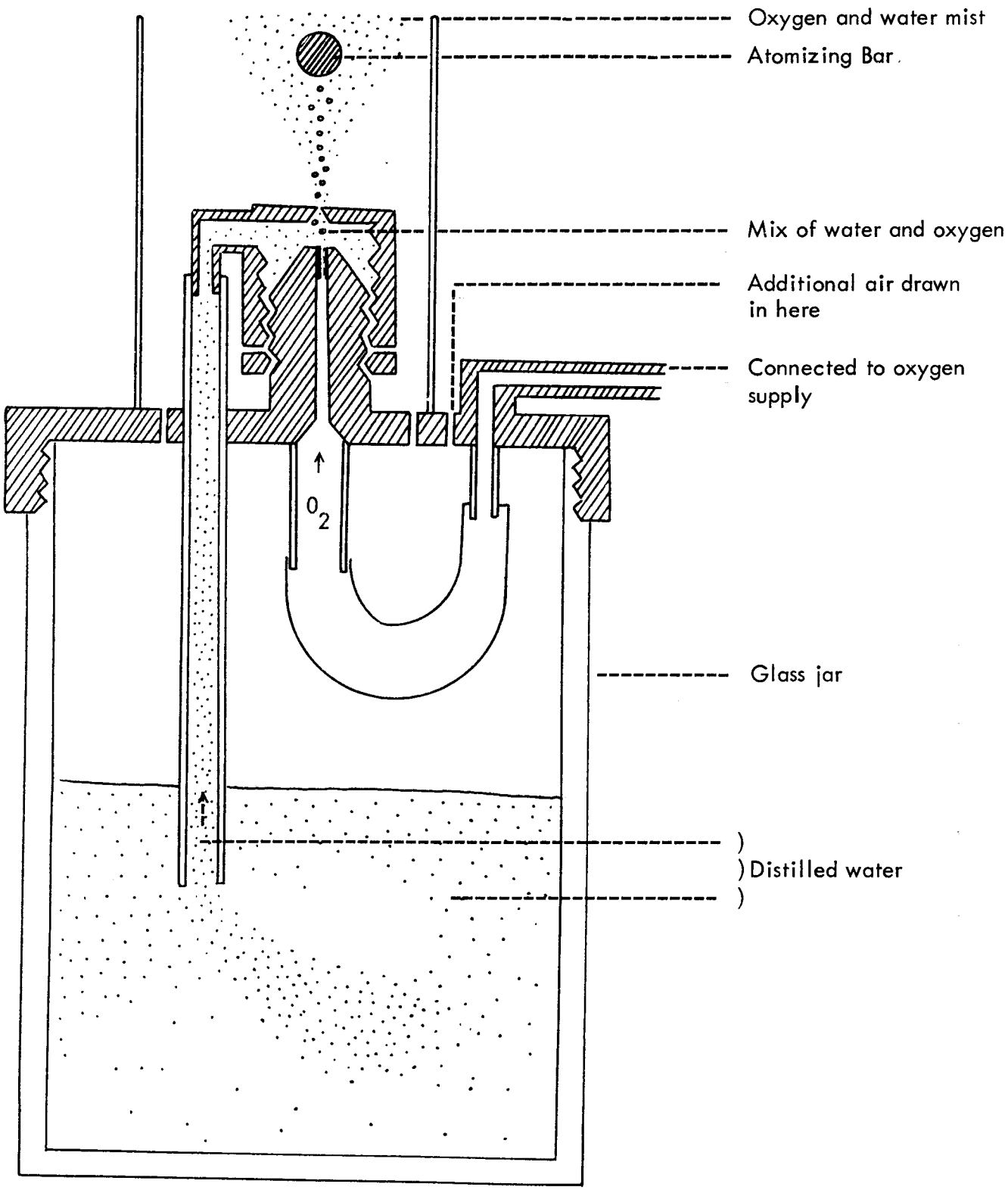
In 1967, despite the hot, humid climate of Durban, a canvas-sided tent and steam kettle was still in use in the hospital. In the gloom of this device the sweating patient was largely invisible to the observer, and the administration of oxygen was difficult. At that time the oxygen tents available were proprietary makes which delivered oxygen over an ice reservoir. Some were costly and all were difficult to sterilise.

A supersaturated atmosphere is widely accepted as necessary for nursing croup patients, to moisten the secretions in the upper airways. In addition, the frequency of hypoxaemia, even in mild cases, had been noted in the preliminary study (Wesley et al, 1968).

Consequently a tent was envisaged which would deliver a high humidity, a known oxygen concentration and also permit easy observation of the patient. It had to be inexpensive, simple and robust.

The tent employed, which was made to these specifications (Medical Engineering Company, Durban) consists of :

FIGURE II: 3 DIAGRAM OF HUMIDIFIER FOR THE TENT



1. Light non-collapsible tubular cube-shaped frame;
2. Disposable plastic canopy, which fits over the frame and tucks under the base of the frame.
3. Oxygen humidifier (Figure II : 3). This is connected to an oxygen supply and a venturi system entrains distilled water and mixes this with the oxygen at the nozzle. The spray is then thrown against an atomizing bar, which reduces the water particle size.

   The oxygen supply has a line pressure of 4,218 kg/cm^2 (60 lbs/sq.inch) and is connected to the humidifier by a high pressure hose of 6 mm approximate internal diameter. The oxygen passes through a number of restrictors positioned in the hose, and lastly through the nozzle, of diameter 0,4 mm, allowing a final flow of 24 litres per minute.

Tests on the efficiency of this tent were carried out in the Unit. It achieves a humidity of 115% (supersaturated) and an oxygen concentration of 50% within 5 minutes and 75% within 15 minutes of enclosing a patient in it.

SUMMARY

A favourable outcome can be expected from cases of laryngotracheobronchitis in developed countries. Amongst African children, however, this is not so and this thesis was designed to probe difficulties in assessment and management of these patients.

Accommodation and equipment was centralised in one ward where patients could be treated by a team of attendants.

A proforma was designed to record accurately the clinical manifestations.

The basic management of all patients was controlled. If intubation of the trachea was thought necessary, the features that led to this decision were carefully noted. The method of nasotracheal intubation with polyvinyl chloride tubes is described.

By these means appraisal of the clinical profile of croup in the local population was undertaken.

In addition, study of the arterial blood gases and acid base was planned. It was anticipated that information on the pathophysiology of croup would contribute to improvement in treatment and, consequently, in prognosis.

CHAPTER III

CHAPTER III (continued)

CHAPTER III

CLINICAL FEATURES

General Data

Sixty-three African patients were studied between 1967 and 1969.

1. Age: The age range was 5 months to 5 years (mean 19 months).

2. Sex: There were twice as many males (42) as females (21).

3. Nutritional State: The weights of 25 (40%) were below the 3rd percentile (Boston Scale) (Appendix page a5). The incidence of this degree of malnutrition (Lancet, 1970) is similar to that of the paediatric medical unit of this hospital. Forty-five per cent of the total admissions (approximately 5,000 a year) have weights below the 3rd percentile (Scragg and Rubidge, 1972).

4. Aetiology: Forty-seven (75%) either had measles or were in the post-measles state. Sixteen had "viral" laryngotracheobronchitis. This term denoted those whose illness was not related to measles, but where the laryngoscopic appearance was typical of viral croup as described by Rabe (1948a). Facilities for viral cultures were not available locally. There were no cases of acute epiglottitis (Sinclair, 1941).

5. Clinical Grading: On the clinical features described in Chapter II, cases were divided into 3 groups :-
   1. A Severe Group : 14
   2. A Moderate Group : 32

      These were further divided according to subsequent management :
      a. Nineteen requiring intubation were designated Moderate Intubated Group (M.IT)
      b. Thirteen who managed without intubation were designated Moderate Conservative Group (MC)
   3. A Mild Group : 17

The patients are described hereunder in their original grouping and comments are made on treatment, indications for intubation, complications and mortality rate. Individual case summaries are given in Tables. (Appendix, pages a6–a13).

TABLE III : 1. GENERAL SUMMARY

Group	No.	Aetiology Measles	Viral	Age in months	Poor Control Pneumonia	Cardiac Complications	Died
Severe	14	13	1	6–48	6 (5)*	8	7
M.IT	19	12	7	5–60	7 (5)	11	5
MC	13	9	4	7–48	3 (1)	4	1
MILD	17	13	4	5–60	4	4	0
TOTAL	63	47	16	5–60	20 (11)	27	13 (21%)

* Deaths in brackets

SEVERE GROUP

All but one of this group of 14 had measles croup. Twelve were cyanosed and one was stuporose on admission to the Unit; all 13 required emergency intubation. In the remaining patient airway obstruction increased during 5 days of conservative treatment; he was classified eventually as severe when muscular hypotonia developed.

Despite obvious clinical benefit from intubation, the mortality rate in this group was high, i.e., 50%.

Fatal Cases

The probable cause of death and the necropsy findings appear in Table III : 2. More than one potential cause of death was present in most of this group. Autopsy was relatively unhelpful in defining the actual cause of death.

TABLE III : 2 FATAL CASES : SEVERE GROUP

R/N	Day of Death	Cause of Death	Remarks
139	4	Tube blockage with secretions	Necropsy: Bilateral pneumonia; extensive atelectasis L. lung.
150	9	Pneumonia	Necropsy: refused.
234	29	Pneumonia	Primary extubation on D7; re-intubated for further 7 days. Pneumonia pursued a relapsing course. Necropsy refused.
406	13	Pneumonia	Cardiac failure developed. Necropsy refused.
410	2	Cardiac arrest	Death related to opening of oxygen tent and probable hypoxia. Necropsy: severe bilateral pneumonia. R. atrium and ventricle enlarged.
527	3	Tube blockage with secretions	Anaemia (4,5 gm%). Necropsy: extensive bilateral pneumonia and atelectasis. Right ventricle enlarged.
567	2	Cardiac arrest	Episode as for R/N 410. Necropsy: extensive atelectasis R. lung and bilateral pneumonia.

Survivors

Seven children survived (50%). Five ran an uncomplicated course with extubation on or before day 7. All had pneumonia, the control of which was established early.

One patient was extubated on day 7 but obstruction recurred and re-intubation was required for 3 days. The residual pneumonia took two months to resolve.

The remaining patient's course was complicated by myocarditis and pneumonia which was slow to respond to treatment. Extubation failed on day 7 and tracheostomy was performed. This tube was removed six days later.

MODERATE GROUP - INTUBATED

Of 19 children in this group the majority (12) had measles laryngotracheobronchitis.

Three were intubated on admission while the remaining 16 were given a trial of conservative treatment for varying periods.

The physical signs on which the decision to intubate was taken were:

(i) Rising pulse and/or respiratory rate. In 13 this was the primary indication. Two actually developed triple rhythm which disappeared after intubation. Contributory indications in two were severe restlessness and in one the development of hypotonia.

(ii) Muscular hypotonia. This was the major indication in 3. Additional signs were central pallor in 2 and decrease in restlessness in one.

(iii) Restlessness and recession. In 3 children severity of these physical signs in the presence of reduced air-entry was such that no trial of conservative treatment was given. One patient also had a mild degree of hypotonia.

The mortality rate of 5 (26%) was half that of the Severe group. Four of the five that died were not extubated. A common factor in all these was the poor control of pneumonia; one needed a tracheostomy and two assisted ventilation. A further complication of cardiac failure developed in two patients. Discussion of the cardiac complications arising during the course of the disease is given in Chapter IX.

One case (R/N 604) is particularly worthy of comment. This child, aged 3, required intubation and later assisted ventilation for complicating pneumonia. From admission he ran a hectic temperature despite antibiotics indicated by tracheal cultures. Finally, after 17 days, fever subsided. Extubation was possible on day 20. Changes compatible with myocarditis were present on serial electrocardiographs. Satisfactory progress once infection was controlled was interrupted abruptly on day 27 when acute pulmonary oedema developed, from which he died. This example of stubborn secondary infection and myocarditis, which finally tipped the balance and led to death, illustrates the prevalence of serious complications in this series.

Analysis of Survivors

(i) Primary extubation successful. (10 cases).

Nine were extubated on the seventh day. In all, secondary infection was controlled early. In one extubation was delayed to day 10 while pneumonia was brought under control. Two developed myocarditis.

(ii) Primary extubation failed. (3 cases).

In 3 primary extubation failed on day 7. One was re-intubated for a further 4 days. His severe pneumonia improved slowly and he developed myocarditis. The second was intubated for a further 7 days. His course was complicated by cardiomegaly and electrocardiographic changes of right ventricular overload. In the third patient secondary extubation on day 13 failed. Laryngoscopy revealed subglottic stenosis and tracheostomy was necessary. The stricture regressed completely in a month, permitting extubation.

(iii) One patient had congenital papillomata of the vocal cords, was tracheostomised and transferred for definitive treatment when he had recovered from infective croup.

ANALYSIS OF ALL INTUBATED CASES : SEVERE AND MODERATE

1. INDICATIONS FOR INTUBATION

(a) Those given a trial of conservative treatment :

Rising pulse and respiratory rate : 14 cases

Development of hypotonia : 3 cases

(b) Those intubated on admission:

Central cyanosis: 12 cases

Severity of recession and restlessness: 3 cases

Unawareness of surroundings: 1 case

2. COMPLICATIONS OF INTUBATION

(i) Blockage of nasotracheal tube was the terminal event in 2 (6%) and thus accounted for 15% of the mortality.

(ii) Subglottic stenosis occurred in one child (3%).

3. EXTUBATION ANALYSIS.

Twenty-three survived to extubation.

A. Primary extubation successful: 15 (65%)

B. Primary extubation failed: 8 (35%)

(i) Re-Intubated : 6

Marked residual pneumonia : 5

Two died after second extubation.

Maximum period of second intubation - 8 days.

Subglottic stenosis : 1

Followed by tracheostomy

(ii) Tracheostomy : 2

Pneumonia : 1

Congenital vocal cord papillomata : 1

4. CAUSE OF DEATH (Table III : 3)

Of the total 33 children who were intubated 12 died (36%). Only two had been extubated at the time of death.

TABLE III : 3

Bronchopneumonia	:	7	(2 on assisted ventilation)
Cardiac arrest	:	2	
Acute pulmonary oedema	:	1	
Blocked nasotracheal tube	:	2	

DISCUSSION ON THE INTUBATED PATIENTS

Pneumonia

The mortality rate was closely related to the control of associated pneumonia. This aspect has been noted in other series where the mortality rate from laryngo-tracheitis was low (1-3,5%), while the rate of those where the lower respiratory tract was involved was high (18-68%) (Neffson and Wishik, 1934; Rabe, 1948b; Lindberg, 1963).

Measles, especially complicated by laryngotracheobronchitis, carries a high mortality rate in malnourished children (Leary, 1966; Morley, Martin and Allen, 1967; Hendrickse, 1967, Lancet, 1968; Scrimshaw, Taylor and Gordon, 1968). Recently, measles (Burnett, 1968; Fireman, Friday and Kumate, 1969; Sellmeyer et al, 1972), protein-calorie malnutrition (Smythe et al, 1971) and viral upper respiratory tract infections (Thomas, Clements and Naiman, 1968) have been shown to depress cell-mediated immunity. This immunological debility would permit a high incidence of secondary bacterial infection.

Cultures of lung secretions obtained via a nasotracheal tube from these patients are detailed in the Appendix (pages a6-a13). The organisms recovered usually were staphylococcus pyogenes, E. coli and, less commonly, B.proteus, paracolon and pseudomonas species.

Initially it was uncertain whether these organisms were indeed the cause of the pulmonary super-infection. Tracheal secretions might have been contaminated by organisms originating from the oropharynx, the environment, or arising after antibiotic therapy. Therefore a study was undertaken in which children admitted to hospital with pneumonia associated with measles had percutaneous lung puncture aspirations cultured before treatment (Wesley, Sutton and Widrich, 1971). In this study the organisms obtained from untreated cases were similar to those in the present series. In addition, antibiotic sensitivities revealed that 50% of staphylococci were resistant to penicillin but sensitive to cloxacillin and cephaloridine. Further, almost all the gram-negative organisms were resistant to ampicillin but the majority were sensitive to gentamycin.

Therefore, a bold initial antibiotic attack is justified, consisting of a combination of cloxacillin or cephaloridine with gentamycin.

This antibiotic policy was progressively adopted as the study proceeded. Initially the dosage of gentamycin was small. The manufacturer's recommended dosage trebled over a few years (Appendix page a4).

Other complications of the disease

While the main problem of croup was reflected in the respiratory system, other complications had a significant effect on the course of the disease. The haemaglobin level of several patients was less than 9 gm%, one as low as 4,5 gm%. (For further discussion see Chapter V). Cardiovascular complications were frequent (See Chapter IX).

The decision to intubate

Sixteen children were judged to require intubation on admission. This decision was based on cyanosis (12), unawareness (1) and severity of recession and restlessness (3).

The remaining 17 children were given a trial of conservative treatment; failure was indicated by a rising pulse and/or respiratory rate (14) or the development of hypotonia (3).

Timing of intubation has not been specifically analysed in the literature. Terms used have been "advanced laryngotracheobronchitis" (Leegaard and Lindeman, 1954); "marked recession and restlessness" (Gittens, 1932; Rabe, 1948c); "increasing respiratory distress" (Brighton 1940) and "exhaustion" (Everett, 1951). Some authors have merely listed most of the physical signs commonly seen (Morgan and Wishart, 1947; Forbes, 1961). It is widely agreed, however, that cyanosis is a precise criterion to indicate tracheostomy (Morgan and Wishart, 1947; Forbes, 1961; Rosales and Davenport, 1962). Similarly the floppy, stuporose patient (the "exhausted child" quoted in the literature ?) requires tracheostomy. But these are late events in the progression of croup.

Therefore muscular tone and awareness of surroundings were noted in the hope that this would detect early "fatigue". These two signs were indeed found useful. The child with considerable upper airways obstruction, but who maintained an interest in his surroundings, for example, by playing with the humidifier in his oxygen tent, was regarded as not in need of intubation. If he became relatively disinterested he was intubated.

Similarly, the child with croup whose muscular tone was good, was managed conservatively, but if hypotonia developed he was intubated.

With the use of the arm-dropping test, lesser degrees of hypotonia were detected. Its presence should have classified the patient as Severe by definition, yet bedside impressions overruled this and the child was classified as Moderate. However, this deviation from the proforma was useful, as it showed that while hypotonia usually indicated the need for intubation, in some patients a minor degree was reversible without the aid of intubation. Thus, hypotonia is a good, though not invariable, sign that intubation may become necessary.

It is seldom possible at first assessment to define the degree of recession which indicates intubation. This sign cannot be reliably assessed by noting the area involved; for example, sternal recession in an infant may not indicate severe obstruction, while the four-year old child may be obstructed without much sternal movement.

Restlessness may be due not only to respiratory disease but also to hyperpyrexia, hunger and anxiety. The occurrence and subsidence of restlessness is discussed more fully in Chapter V.

Failure of recession and restlessness to respond to adequate conservative treatment is more easily appreciated.

A severe degree of reduction of air-entry on auscultation often, but not invariably, requires treatment by intubation. For example, some patients in the Moderate Conservative group had greatly reduced air-entry. This sign is best taken in conjunction with pulse and respiratory rates; if a patient is coping with his obstruction this will be indicated by these latter signs.

Monitoring of pulse and respiratory rate is important. While Everett (1951) thought these signs were not useful indications for tracheostomy, others have suggested an increasing pulse rate (Turner, 1954) or a rate of more than 140/minute and respiratory rate of more than 40/minute (Rosales and Davenport, 1962; Davison, 1967) are reliable indications. In this series the criteria for ending a trial of conservative treatment with intubation were commonly the pulse and respiratory rates; initially the critical rates were taken as 160/minute and 60/minute respectively. A rise above these levels was thought dangerous. The actual rates at which intubation was undertaken were higher and appear in Chapter V.

Loud stridor was not found to be a measure of the severity of obstruction, nor an indication for intubation. Many children in the Moderate Conservative group were relatively comfortable with loud stridor. Orton et al (1941) stressed the persistence of audible stridor during sleep, and Gittens (1932) its persistence during the day, as indications for tracheostomy.

In summary, cyanosis, obvious hypotonia and unawareness indicate the need for urgent relief of obstruction. It is more difficult to estimate the degree of recession and restlessness that is reversible without intubation. Such patients usually need a

trial of conservative treatment, and pulse and respiratory rates are most easily monitored during this period. The onset of "exhaustion" in the form of hypotonia or unawareness in such patients indicates that the need for intubation has arisen.

Complications of intubation

Complications of nasotracheal intubation occurred: in 2 patients (6%) the terminal event was blockage of the tube by secretions and in 1 patient (3%) subglottic stenosis developed.

Blockage of a tube by secretions depends mainly on two factors; the nature of the secretions and the care of the patient. Attention to environmental humidity and hydration is mandatory (McDonald and Stocks, 1965; Brown, Johnston and Conn, 1966; Stool, Striker and Downes, 1966; Rees et al, 1966). Secretions in this study were often thick due to complicating pneumonia. The humidity of the tent employed was super-saturated and fluid intake was carefully regulated. In this Unit the blockage of a tracheostomy or nasotracheal tube is about equal in incidence (5%) (Wesley, Desai, Holloway and Thambiran, 1972).

Several factors predispose to stricture formation. The site of the stricture is in the subglottic region and is thought to be due to the encirclement of the trachea at this level by the rigid cricoid cartilage (Bergstrom, Moberg and Orell, 1962; Way and Sooy, 1965; Abbott, 1968). Thus even minimally oedematous tracheal mucosa may be splinted between the cricoid shield and the endotracheal tube, and ischaemic ulceration may ensue.

The size of the endotracheal tube is important in the pathogenesis of laryngeal damage: it should not fit the trachea too tightly (Allan and Steven, 1955; McDonald and Stocks, 1965; Markham, Blackwood and Conn, 1967; Abbott, 1968).

Further, the material from which the tube is made is related to this problem. A high rate of tracheal damage followed intubation with red rubber tubes left in situ for more than a few hours (Dwyer, Kronenberg and Saklad, 1949; Stiles, 1965; Grillo, 1969). With the introduction of the relatively inert polyvinyl chloride tubes the incidence of this complication has lessened.

The presence of upper airways disease has been regarded as a relative contra-indication to nasotracheal intubation because of increased likelihood of stricture formation (Stool, Striker and Downes, 1966; Hatch, 1968).

TABLE III : 4 TRACHEAL STENOSIS FOLLOWING NASOTRACHEAL INTUBATION

Author	Type of Case	No. of Case	No. of Stenoses	Maximum length IT	Stenoses
McDonald and Stocks, 1965.	Mixed*	50	1	15 days	2%
Abbott, 1968	Mixed	26	9	?	35%
Owen-Thomas, 1967	Mixed	39	2	3 months	5%
Aberdeen and Glover, 1967	Mixed	62	2	?	3%
Markham, Blackwood and Conn, 1967	Mixed	74	3	?	4%
Brown, Johnston and Conn, 1966	Non-UAD+	160	4	43 days	2,5%
Striker, Stool and Downes, 1967	Non-UAD	98	3	42 days	3%
Hatch, 1968	Non-UAD	57	3	34 days	5%
Fearon et al, 1966	Non-UAD	29	7	42 days	24%
Allen and Steven, 1965	UAD^{x}	43	1	2 weeks in 80%	2,3%
Striker, Stool and Downes, 1967	UAD	18	4	42 days	22%

* Mixed = patients with and without upper airways disease.

\+ Non-UAD = patients without upper airways disease.

x UAD = patients with upper airways disease.

IT = Intubation.

Table III : 4 shows the reported incidence of this complication. In series where the upper airways were involved by disease, stenosis was diagnosed in 2-22% of cases. Where there was no tracheal abnormality intubation resulted in subglottic damage in 2,5-24%. Some series included cases both with and without upper airways disease (denoted "mixed" in Table III : 4) and an incidence of subglottic stenosis of 2,5-35% was reported. In the majority of patients constituting this last figure of 35% the tracheal damage was asymptomatic.

It appears from the above evidence that stenosis is not more common in the presence of upper airways inflammation.

Nasotracheal intubation versus tracheostomy in croup.

Croup often is recurrent, and in this series nasotracheal intubation was preferred to tracheostomy because re-intubation would be easier via the nasal route than via a closed tracheostomy stoma.

The alternative procedure of tracheostomy is not without hazard. Blockage of the tube and dislodgement occur. The reported incidence of permanent tracheal damage is 0,4-4% (Toremalm, 1960; Meade, 1961; Head, 1961; Oliver, Richardson, Clubb and Flake, 1962; Johnston, Wright and Hercus, 1967), which is less than in most accounts of nasotracheal intubation. The stenosis following tracheostomy is not subglottic, but at the carina and the site of the stoma or the tube cuff (Johnston, Wright and Hercus, 1967; Deverall, 1967; Pearson, Goldberg and da Silva, 1968; Grillo, 1969). Thambiran and Ripley (1966) in an experimental study showed severe mucosal damage followed tracheal suction alone.

Tracheostomy also carries an operative mortality of up to 5% (Bigler, Johnston and Schiller, 1954; Nelson, 1957; Head, 1961; Meade, 1961; Oliver et al, 1962; Watts, 1963; Aberdeen and Glover, 1967). Mediastinal emphysema and pneumothorax also occur, especially in patients with obstructed respiration, and even when endotracheal intubation precedes tracheostomy (Goldberg, Mitchell and Angrist, 1942; Forbes, Salmon and Herweg, 1947; Nelson, 1957; Toremalm, 1960; Oliver et al, 1962; McClelland, 1965). These problems have not been reported with nasotracheal intubation.

Failed extubation

In one-third of cases primary extubation failed. The chief reason for this was the inadequate control of pneumonia. In such cases, although residual upper airways obstruction often was minimal, a toxic, pyrexial child could not clear secretions adequately and so respiratory obstruction recurred.

With a shorter tracheostomy tube effective physiotherapy and suction are more easily achieved. Therefore, in view of other experience (Wesley et al, 1972) and that gained from this study, if extubation fails in the presence of pneumonia, or if pneumonia deteriorates, tracheostomy combined with bold antibiotic therapy should assist the rapid control of infection that is so vital in this disease.

CONSERVATIVE (NON-INTUBATED) PATIENTS

MODERATE GROUP

Thirteen patients classified as Moderate did not require intubation. Nine had measles. Stridor had been present 1-14 days (mean 4 days) before admission.

In 4 of the 13 response to conservative treatment was slow, and it was 2-3 days before their respiratory effort diminished. The remainder improved rapidly with treatment.

Pneumonia was present in 11, but control was achieved rapidly in 9, usually with penicillin or ampicillin. In 2 cases the reponse to treatment was poor. One died of pneumonia on day 13.

The main clinical feature which distinguished them from Mild patients was reduction of air entry on auscultation. In some it was markedly reduced, but the children remained alert to their surroundings with pulse rates less than 160/minute and respiratory rates less than 60/minute. The air entry returned to normal in 2-7 days (mean 4 days) after admission.

Features which differentiated them from Moderate patients who later were intubated, have been analysed in retrospect and are presented in Chapter V. Individual case summaries are given in Appendix (pages a12).

MILD GROUP

Seventeen of those studied were classified as Mild (Appendix page a13). The majority had measles. The age range and sex distribution was similar to the other groups. There were no deaths. The period of stridor before admission was 1-7 days (mean 3 days).

After assessment the severity of upper airways obstruction increased in 5 cases before recovery occurred.

All but one had concurrent pneumonia. In 10 adequate control of pneumonia was achieved with penicillin, ampicillin or chloramphenicol. The remainder required a change of antibiotic. In 3 cases the response was slow despite change of treatment.

Other complications of disease encountered were hypochromic anaemia, myocarditis and cardiac failure. These aspects are discussed in Chapter IX.

DISCUSSION OF THE NON-INTUBATED PATIENTS

Control of Secondary Infection

The most obvious difference in general progress of the conservatively treated groups compared with those intubated was the relative ease with which their secondary infection responded to treatment. It is unlikely that this can be attributed to the absence of a nasotracheal tube. Rather it is reasonable to surmise that their secondary bacterial invaders were gram positive organisms, as therapy with penicillin or ampicillin usually was effective. There was no confirmation of this, as sputum culture was not performed because it is widely regarded as an unreliable guide to the causative bacteria in pneumonia (Pecora and Yegian, 1958; Lees and McNaught, 1959; Laurenzi, Potter and Kass, 1961; Sinha and Hughes, 1966).

It is clear that the effectiveness of the initial chemotherapy regime has a critical influence on the subsequent clinical course. On the basis of the observations of the two treatment groups, the child whose infection is not rapidly controlled, and whose upper airway obstruction is classified as "moderate", will always require intubation.

The Value of Chest X-rays in Croup

Pneumonia was present in most patients. With the method of X-ray grading used in this study, the degree of pulmonary involvement was similar in all groups, whatever the severity. Yet the prognoses of these groups was very different. The important factor proved to be not so much the extent of pneumonia, but the control of infection. This was best judged by the physical signs and pyrexia. Deterioration in the chest X-ray was always preceded by a failure of the temperature to decline towards normal. Therefore chest X-rays were of limited value in estimating the outcome of any particular case.

As will be discussed in Chapter V, there was also no correlation between X-rays and blood gases obtained at the same time.

SUMMARY

The sixty-three children studied were divided into three groups, having been classified by the clinical features present at initial assessment. The groups were: Severe (14 cases), Moderate (Intubated 19 cases, Conservative 13 cases), and Mild (17 cases).

A high mortality rate of 50% occurred in the Severe group, while the rate in the Moderate Intubated patients was half this figure. One child in the Moderate Conservative group died. There were no deaths amongst the Mild patients.

Secondary bacterial infection was almost universally present and the deaths were closely related to the control of this complication. The nature of the super-infection was detailed.

The clinical features that led to the decision to intubate were tabulated. In this respect the physical signs of muscular hypotonia, awareness of surroundings, cyanosis and pulse and respiratory rates were valuable. Recession and restlessness were not as helpful.

Nasotracheal intubation and its complications (tube blockage and laryngeal stenosis) were discussed. Extubation problems were encountered in one-third of the survivors and were related chiefly to the control of the associated pneumonia.

The use of the techniques of nasotracheal intubation and tracheostomy in laryngotracheobronchitis was reviewed.

CHAPTER IV

TABLE IV : 1

MEAN BLOOD GASES AND ACID BASE ON ASSESSMENT

	Severe	M.IT	M.C.	MILD	NORMAL CONTROLS
pH	7,322 ± 0,102	7,386 ± 0,051	7,379 ± 0,069	7,426 ± 0,057	7,415 ± 0,043
			<0,05		
$PaCO_2$ mm.Hg.	41 ± 12	39 ± 11	39 ± 8	32 ± 6	37 ± 4
			<0,01	<0,05	
B.E. m.Eq/L.	-4,4 ± 7,3	-1,8 ± 3,1	-1,8 ± 4,3	-1,6 ± 4,6	-0,4 ± 2,2
PaO_2 mm.Hg.	51 ± 9	68 ± 9	69 ± 14	79 ± 13	87 ± 5
	<0,01		<0,01		
$[\Delta AaO_2]$ vols %	2,7 ± 1,5	1,1 ± 0,5	1,2 ± 0,8	0,7 ± 0,8	0,3 ± 0,1
	<0,01		<0,001		
Number	13	15	12	14	31

CHAPTER IV

ARTERIAL BLOOD GASES AND ACID BASE ON ASSESSMENT

Patients were graded clinically before treatment was commenced. At this time a sample of arterial blood was obtained while the patient was breathing air.

The Normal Control Values for Arterial Blood Gases and Acid-Base

Arterial blood was obtained from 31 children in hospital for minor conditions unrelated to pulmonary or metabolic disease. Their nutrition was considered satisfactory by local standards and their ages comparable with those in the study.

The arterial blood was obtained by the technique described in Chapter II and analysed by the same electrodes as used for the study subjects. These results appear in the Appendix (Page a14) and the calculated mean values in Table IV: 1.

RESULTS OF INITIAL ASSESSMENT MEASUREMENTS

TABLE IV : 1 shows the mean values obtained for each group. The Moderate patients are sub-divided further into those who subsequently needed intubation (M.IT) and those who did not (MC). The result for each patient appears in the Appendix (pages a47-a66).

pH: In general, the more severe the clinical disease the greater the acidaemia present. The mean pH of Severe Patients was 7,322, significantly lower than the normal control value ($p < 0,01$), but not significantly different from that of the Moderate groups.

The mean pH of the M.IT and MC patients was similar (7,386 and 7,379). Their combined mean was significantly less than the mean of the Mild group ($p < 0,05$) and the normal controls ($p < 0,05$).

Mild patients had a mean pH of 7,426, which was within normal limits.

Carbon dioxide tension ($PaCO_2$): The mean $PaCO_2$ of the Severe group was 41 mm.Hg. In this group 6 were hypoventilating ($PaCO_2$ >42 mm.Hg)

and 3 were hyperventilating ($PaCO_2$ < 32 mm.Hg).

The mean $PaCO_2$ of both Moderate groups was 39 mm.Hg. Of the 15 who were intubated subsequently, 5 were hypoventilating and 3 were hyperventilating.

Mild patients had a mean $PaCO_2$ of 32 mm.Hg, which was significantly less than that of the Moderate group ($p < 0,01$) and the normal controls ($p < 0,05$). Many of these cases were hyperventilators.

Base Excess (BE): Severe patients had the lowest mean base excess (-4,4 m.Eq/L) but this was not significantly less than that of the M.I.T group (-1,8 m.Eq/L). The figures for the Moderate and Mild groups were very similar, and not significantly different from the normal controls.

Oxygen Tension (PaO_2)

The mean oxygen tensions of the clinical groups were all significantly different from each other at $p < 0,01$ level.

The lowest mean PaO_2 was 51 mm.Hg. obtained in the Severe group. The two Moderate groups had identical oxygen tensions (68 and 67 mm.Hg) while the Mild group had the highest mean PaO_2 of 79 mm.Hg. This last figure was not significantly different from that of the normal controls (87 mm.Hg).

Alveolar to Arterial Gradient in Content: $[\Delta AaO_2]$

The $[\Delta AaO_2]$ was calculated by the method described in the Appendix (page a15). The gradient was wider than the normal in both Moderate groups (1,1 and 1,2 vols%) and the Severe group (2,7 vols%) ($p < 0,001$), while that of the Mild patients was within normal limits.

The mean gradient of the Severe patients was significantly greater ($p < 0,01$) than that of the Moderate groups.

DISCUSSION

At initial assessment the most deranged acid base status accompanied the Severe clinical grading, but the mean figures of the groups were not always significantly different.

The lowest pH, that of the Severe group, usually resulted from a mixed respiratory and metabolic acidosis. However, respiratory acidosis was not the dominant feature. Of the total patients who required intubation, less than half (12 out of 28) had a $PaCO_2$ above 42 mm.Hg. As a group, the Mild patients were actually hyperventilating on admission.

The mean $Pa0_2$ of each group was significantly different from the others. The lowest figure was associated with the Severe group and the highest with the Mild group.

The alveolar to arterial oxygen gradient of the Severe group was grossly widened. Undoubtedly the abnormal gradient was contributed to by this group's higher $PaCO_2$, displacing oxygen from the alveoli. But this cannot have been the only cause, for their gradient was double that of the two Moderate groups. The $[\Delta Aa0_2]$ will be discussed further in Chapters V and VI.

Analysis of blood gas and acid-base values obtained on initial assessment did not assist in sub-dividing the Moderate patients into their treatment groups, but the manner in which the blood gases altered as severity of the syndrome increased was evident.

SUMMARY

At the time of clinical classification arterial blood was taken from each patient.

Mean values of the blood gases and acid base of each clinical group were calculated. The Severe group, whose low pH resulted from a mixed respiratory and metabolic acidosis, showed the most abnormal acid base status. The Mild group had a respiratory alkalosis, while the Moderate group occupied an intermediate position.

The mean $Pa0_2$ of each group was significantly different, the lowest figure being obtained from the Severe group.

All the mean values of the Moderate group, when subdivided into those intubated and those conservatively managed, were almost identical.

The normal control values for acid base and blood gases used in the study were introduced.

CHAPTER V

CHAPTER V

CORRELATION OF CLINICAL SIGNS AND SPECIAL INVESTIGATIONS

The clinical signs and special investigations are considered in relation to each other and to the mortality rate.

1. PULSE AND RESPIRATORY RATES AT INITIAL ASSESSMENT.

TABLE V : 1

	SEVERE	M.IT	M.C.	MILD	IT	CONS.
Pulse Rate						
Mean and S.D.	179 ± 23	178 ± 19	156 ± 17	154 ± 17	178 ± 20	154 ± 17
		p < 0,01			p < 0,01	
Number	13	15	13	17	28	30
Respiratory Rate						
Mean and S.D.	60 ± 20	53 ± 13	47 ± 8	45 ± 11	56 ± 16	45 ± 10
		N.S			p <0,01	
Number	13	15	13	16	28	29

M.IT = Moderate Intubated Group

M.C. = Moderate Conservative Group

IT = Intubated (Severe and M.IT Groups)

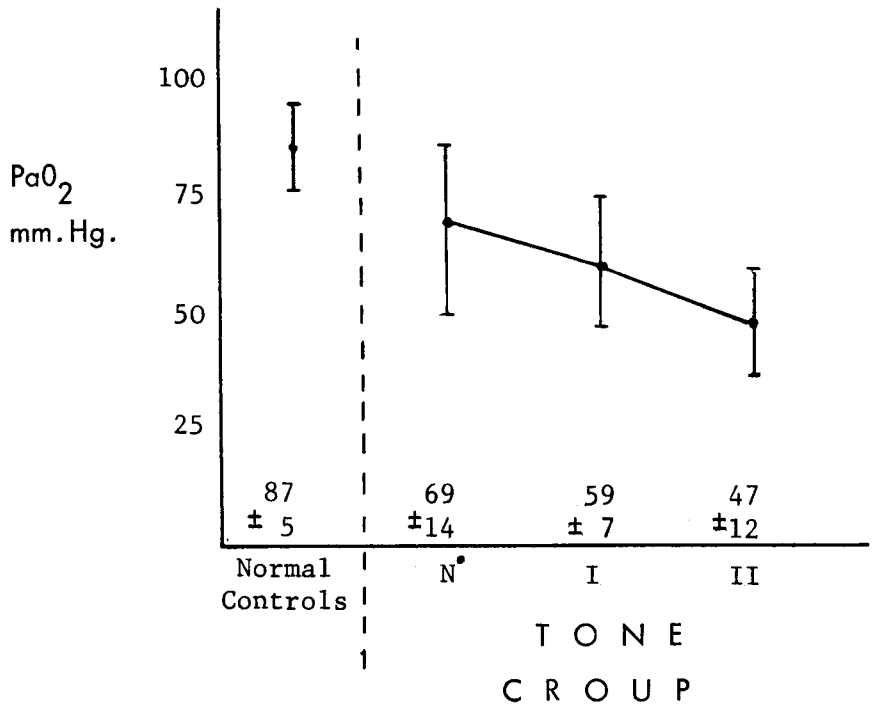
CONS = Conservatively Treated (M.C. and Mild Groups)

Mean pulse rates of the Severe and M.IT groups were similar, as were the rates for the M.C. and Mild groups.

The mean pulse rate of the M.IT group (178/minute) was significantly faster than that of the M.C. group (156/minute) ($p < 0,01$). This difference was again apparent

FIGURE V : 1

CORRELATION OF MUSCLE TONE AND PaO_2



• No mild patients included.

PaO_2 of patients with normal (N), with reduced (I) and with obviously reduced (II) tone were all significantly different at 0,05 level.

in the mean figures for the intubated compared with the non-intubated cases ($p < 0,01$).

Mean respiratory rates of the two Moderate groups (M.IT and M.C.) were not significantly different, but when the mean of the two intubated groups (56/minute) was compared with that of the conservative patients (45/minute) the difference became significant ($p < 0,01$).

Neither the pulse nor the respiratory rates correlated with the $Pa0_2$ or the $PaC0_2$ when taken at assessment.

II. CLINICAL FEATURES

The clinical features of individual cases appear in the Appendix (pages a16-a19).

TABLE V : 2 Incidence of various clinical features.

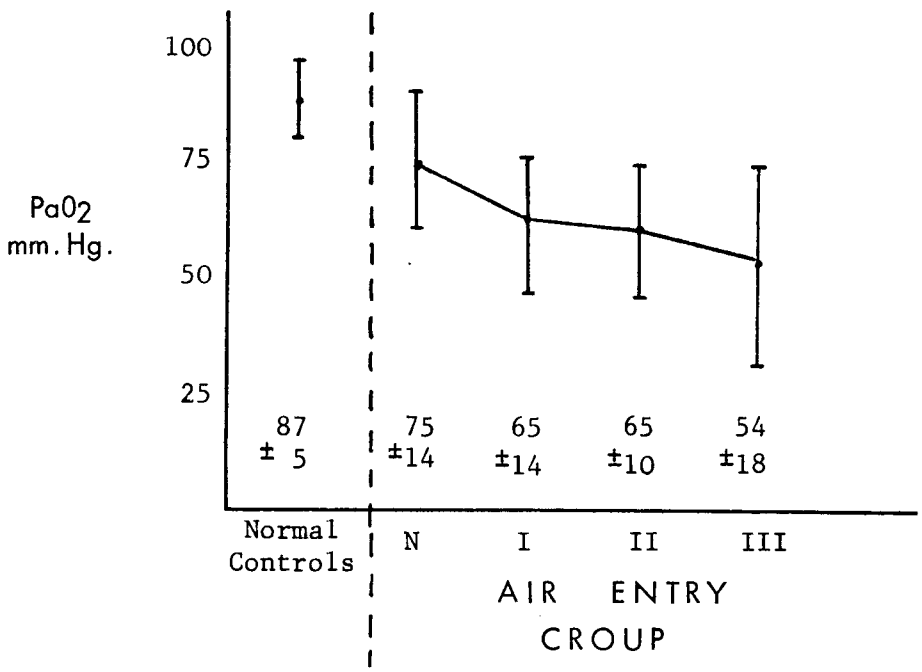
Group	Reduced Tone	Decreased Air-Entry	Unaware	Restless	Cyanosis (C) Pallor (P)
SEVERE n.14	9	13	8	4	C 11
M.IT n.19	7	14	0	9	P 4
M.C. n.13	3	13	0	9	P 1
MILD n.17	0	0	0	5	0

(a) Muscle Tone

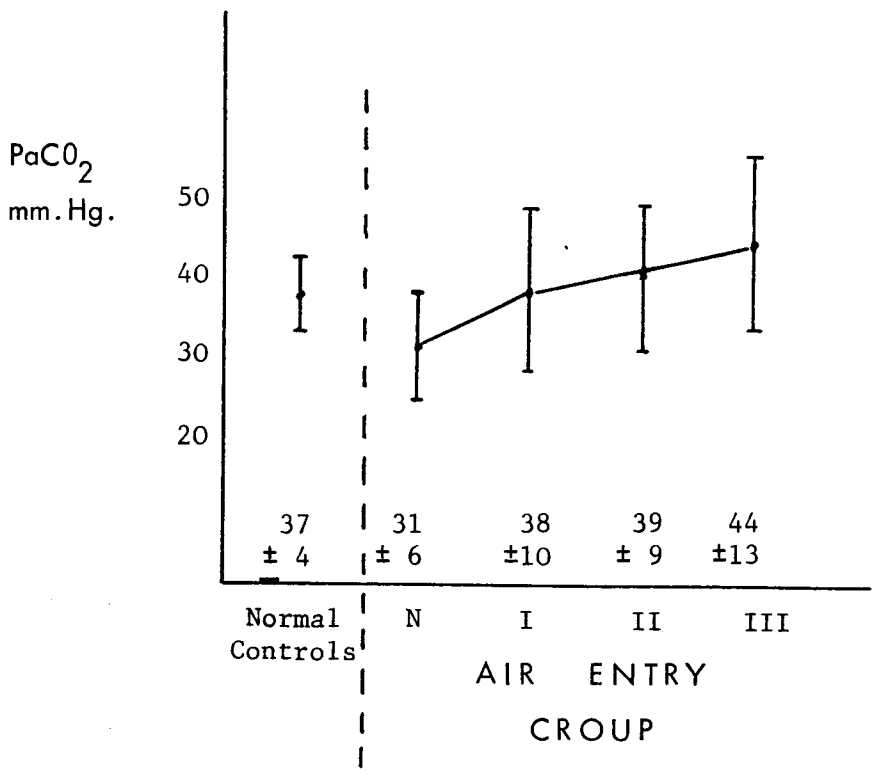
By the method of assessing muscle tone (Chapter II) patients could be divided into 3 categories: those with normal (N), slightly (I) and abviously (II) reduced tone. The mean $Pa0_2$ of these groups are significantly

FIGURE V : 2

CORRELATION OF AIR ENTRY, PaO_2 AND $PaCO_2$



Mean PaO_2 of the patients with normal (N) and those with severely reduced (III) air entry was significantly different ($p < 0,01$)



Mean $PaCO_2$ of patients with normal (N) air entry was significantly different from the mean of patients with air entry reduced I ($p < 0,05$) and III ($p < 0,05$).

different from each other at 0,05 level (Figure V : 1). Mild patients were not included in the analysis.

Obviously reduced tone was a feature of some of the Severe group while less marked reduction in tone occurred in all groups except the Mild patients. Normal tone was preserved in some patients of all severities.

Muscle tone did not correlate with $PaC0_2$ or pH.

(b) Reduction of air entry on auscultation

Air entry on auscultation was divided into normal (N), slightly (I), moderately (II) or greatly (III) reduced categories.

Air entry was greatly reduced in some children of all groups except the Mild.

It was reduced to some extent in all of the Severe and Moderate Conservative groups, in all but one of the Moderate Intubated and in none of the Mild group.

The mean $Pa0_2$, $PaC0_2$ and pH of each category was calculated.

(i) Relationship of Air entry to $Pa0_2$ (Figure V : 2)

The mean $Pa0_2$ was highest in those with normal (N) and lowest in those with greatly (III) reduced air-entry. The difference was significant ($p < 0,01$).

(ii) Relationship of Air entry to $PaC0_2$ (Figure V : 2)

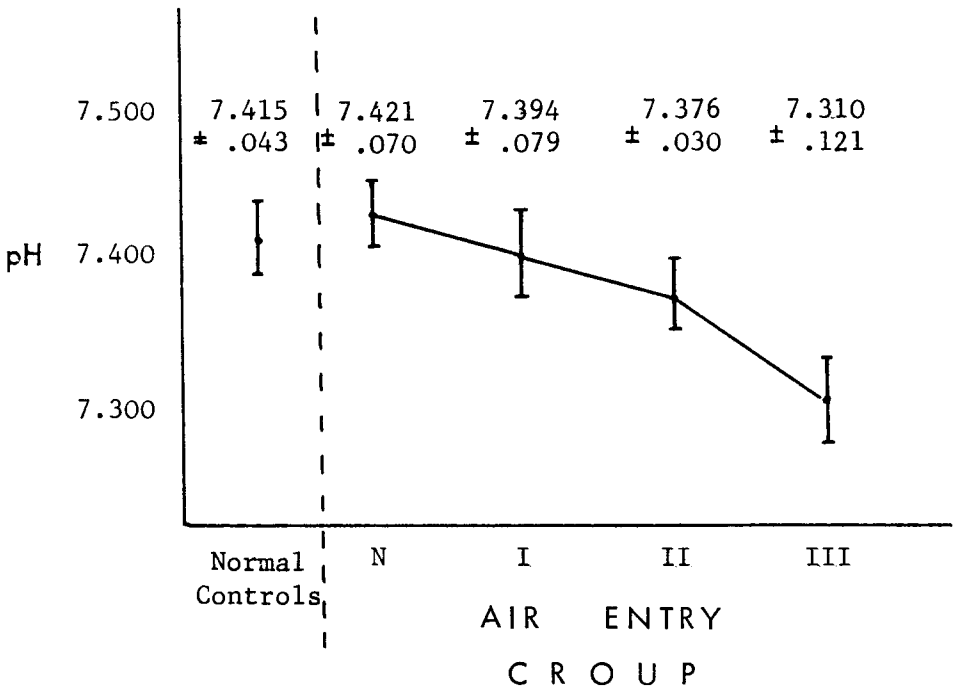
The mean $PaC0_2$ of the group with normal air-entry was significantly lower than those of Grade I ($p < 0,05$) and Grade III air-entry ($p < 0,05$). The combined mean $PaC0_2$ of those with normal and Grade I air-entry was significantly less than the combined mean of Grade II and III air-entry ($p < 0,01$).

(iii) Relationship of Air-entry to pH (Figure V : 3)

The mean pH of patients with normal air-entry was significantly higher than those with Grade III ($p < 0,05$). Likewise, the combined mean pH of those with normal and

FIGURE V : 3

CORRELATION OF AIR ENTRY AND pH



pH of patients with normal air entry (N) was significantly higher than those with reduced (III) air entry ($p < 0,05$).

The grand mean pH of patients with N and I air entry was significantly above that of patients with II and III air entry ($p < 0,01$).

Grade I air-entry was higher than that of the groups with Grade II and III air-entry ($p < 0,01$).

(c) Restlessness (Table V : 2)

Restlessness was more commonly present in the two Moderate groups than in the Mild and Severe patients. In some with other signs of distress, restlessness was absent. This physical sign did not correlate with $Pa0_2$ or $PaC0_2$.

(d) Unawareness (Table V : 2)

Only those in the Severe Group were unresponsive to their environment. In the intubated patients, those who were aware had a mean $Pa0_2$ (65 ± 10 mm.Hg) which was significantly higher than those who were unaware (49 ± 11 mm.Hg) ($p < 0,01$). (Appendix page a20).

(e) Cyanosis and Pallor

Cyanosis was the one sign that consistently classified a patient as Severe.

In 5 patients (4 M.IT and 1 M.C.) pallor of the mucous membrane was noted.

III. ALVEOLAR TO ARTERIAL OXYGEN GRADIENT

(a) $[\Delta Aa0_2]$ on Oxygen Breathing

i. In 9 of the Severe group the mean $[\Delta Aa0_2]$ on oxygen breathing was $1,32 + 0,5$ vols %; in 8 M.IT it was $0,89 + 0,2$ vols %. These means are significantly different ($p < 0,05$). (Appendix page a21).

ii. The mean $[\Delta Aa0_2]$ on oxygen breathing of the intubated patients who survived and those who died subsequently are dealt with under "Correlation with Mortality Rate" (see below).

(b) $[\Delta Aa0_2]$ on 100% Oxygen and Chest Radiograph Grading.

Chest X-ray grading and the calculated residual intrapulmonary shunting of blood on 100% oxygen breathing could be assessed in 15 of those intubated. The $Pa0_2$ on 100% oxygen breathing was measured shortly after intubation and chest X-rays were done within 24 hours of this procedure. No relationship between these two parameters was found (Table V : 3, page 43). In some a large gradient existed in the presence of normal X-rays.

(c) $[\Delta\ Aa0_2]$ Related to Pulse and Respiratory Rates before and after Intubation.

In 19 children pulse, respiratory rates and the calculated $[\Delta Aa0_2]$ on air were recorded before and after intubation.

There was no correlation between changes in either pulse or respiratory rate and the change in gradient (Appendix, page a22). The effect of intubation on pulse and respiration will be discussed further in Chapter VI.

(d) Alveolar to Arterial Oxygen Tension Gradient ($P\Delta Aa0_2$) on Air and Chest Radiograph : Steady State.

The $P\Delta Aa0_2$ of patients breathing air and their chest X-ray grading were considered when in a steady state compared with (b) above. The $P\Delta Aa0_2$ corresponding in time to the chest radiograph was selected any time between day 2 and day 15.

Again there was no relationship between these two measurements (Appendix page a23).

IV. MORTALITY RATE

(a) Haemoglobin: The haemoglobin values measured before blood transfusion correlated with the mortality rate of intubated patients. The mean haemoglobin of the survivors (10,3 gm%) was significantly higher than the mean haemoglobin of those who died (8 gm%) ($p < 0,01$). (Appendix page a24).

Only 2 who died had a haemoglobin of more than 9 gm%, while in only 2 survivors was the haemoglobin less than 9 gm%.

(b) $Pa0_2$ and $[\Delta Aa0_2]$ on 100% Oxygen Breathing : Intubated Patients.

Seventeen intubated patients had blood gas analyses while breathing 100% oxygen. The mean $Pa0_2$ of the survivors (404 ± 82 mm.Hg) was significantly higher than of those who died subsequently (277 ± 87 mm.Hg) ($p < 0,05$) (Appendix page a25).

Only one of 10 survivors had a $Pa0_2$ of less than 300 mm.Hg while only 2 of 7 who died had a $Pa0_2$ of more than 300 mm.Hg.

The mean $[\Delta Aa0_2]$ on oxygen breathing of the survivors was $0,88 \pm 0,3$ vols%, while in those who died later it was $1,46 \pm 0,4$ vols%; these figures are

significantly different ($p < 0,05$) (Appendix page a25).

(c) Neither the pH nor the $PaCO_2$ on admission correlated with death.

DISCUSSION

Pulse and Respiratory Rates

It has been noted previously that $Pa0_2$, $PaCO_2$, pH and $\Delta Aa0_2$ of the Moderate group did not detect those in need of intubation (Chapter IV). However, the mean pulse rates of the two Moderate groups (that of the M.IT measured before intubation) were significantly different, but not so their respiratory rates. If the pulse and respiratory rates of all who were subsequently intubated were compared with all those conservatively treated statistical difference was reached. It was evident that a pulse rate of 170-180/minute and respiratory rate rising above 50/minute indicated severity of disease and need for intubation.

It is instructive to compare the pulse rate of children stressed by disease with that resulting from exercise. Bicycle ergometer studies in children showed that at submaximal loads the pulse rate was about 170/minute, while maximal loads caused a rapid rise thereafter (Cumming and Danziger, 1963). Further, oxygen consumption was found to be related linearly to work capacity, and pulse rate to oxygen consumption. It appears that the dividing line between compensation for increased load, and exhaustion from it, is indicated by a pulse rate of about 170/minute. Implied also is that there is a similar critical oxygen consumption, whether observed in healthy children exercising for minutes, or sick children with airway obstruction endured for longer periods.

At the start of the present study a pulse of 160/minute and a respiration of 60/minute were considered indications of decompensation for the purpose of clinical monitoring. These estimates have proved to be moderately accurate.

Hypotonia and Unawareness

The presence of muscular hypotonia was one of the signs chosen as an indication of severity. Indeed, patients with obvious hypotonia were classified as Severe. The proforma was designed to define those whose disease was irreversible except by immediate intubation. However, mild hypotonia detected by the arm-dropping

test was noted in patients who, on completion of evaluation by other physical signs, were not considered to have such severe disease.

A correlation of the degree of hypotonia with the level of hypoxia was established. As would be expected, the incidence of hypotonia was greater the more severe the airway obstruction.

The mean $Pa0_2$ of those who were unaware of their surroundings was significantly lower than in responsive children.

Neither of these signs, unawareness or hypotonia, correlated with $PaC0_2$. Carbon dioxide narcosis evidently was not a factor, even in severe croup.

Air-entry on Auscultation

The clinical division of reduced air entry into several grades must be observer-dependent and, therefore, inaccurate. However, even if the division was limited to fewer grades, the correlation with blood gases still would be valid. The mean $PaC0_2$, $Pa0_2$ and pH of those with severely reduced and those with normal air-entry were always significantly different.

It is evident from Chapter IV that the alteration brought about by croup ranged from respiratory alkalaemia in the Mild to acidaemia (metabolic and respiratory) in the Severe. This pattern occurred again if blood gases were related to air entry. It follows that this physical sign correlated best with severity of croup, both biochemical and clinical. As the air-entry lessened the pH fell, as did the $Pa0_2$ whilst the $PaC0_2$ rose.

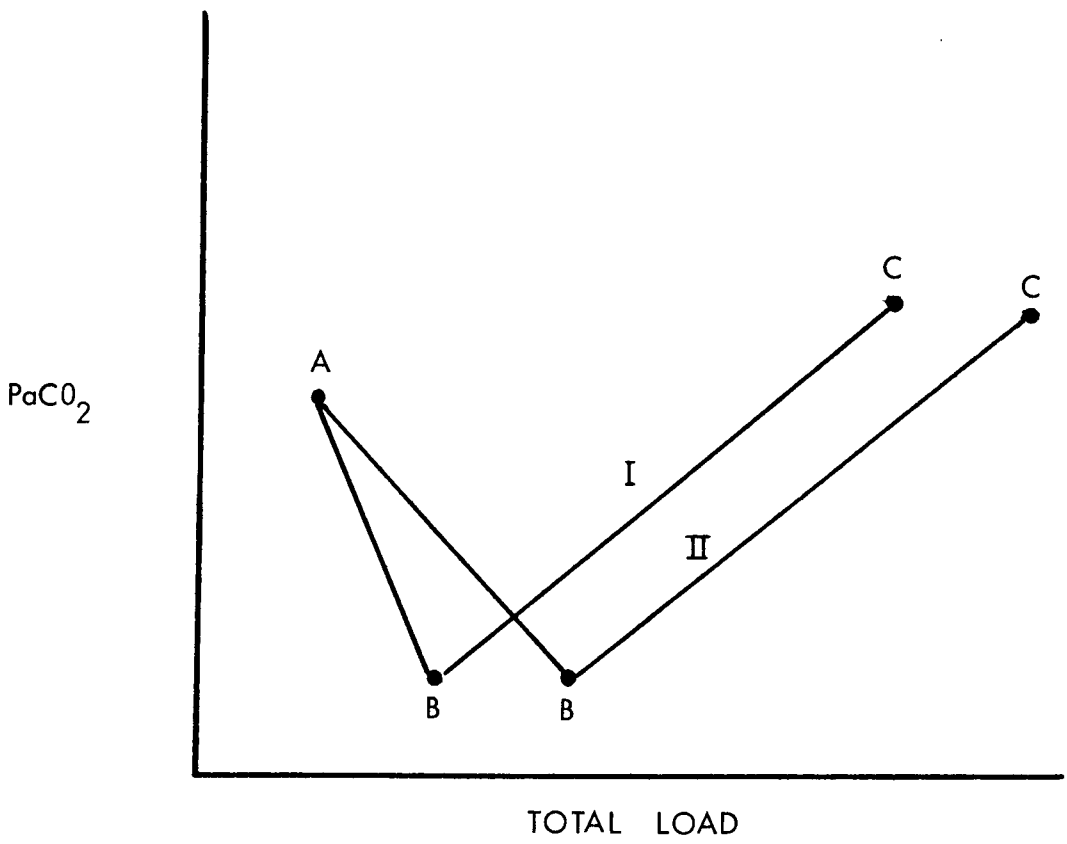
A relationship has been established between $PaC0_2$ and airway obstruction. Experiments on normal subjects breathing through resistive loads led to reduction of alveolar ventilation with consequent rise in $PaC0_2$ and fall in $Pa0_2$ (Zechman, Hall and Hull, 1957; Eldridge and Davis, 1959).

In croup, however, cases who were slightly obstructed actually hyperventilated and with increased obstruction (as judged by air-entry) the $PaC0_2$ rose. Perhaps because it had to rise from a low level, the $PaC0_2$ had seldom reached a hypoventilatory stage by the time the patient was in need of surgical relief of his obstruction.

A wider interpretation of the $PaC0_2$ in croup probably is valid. It reflects the patient's reaction to the total disease load (airway obstruction, length of illness,

FIGURE V:4

$PaCO_2$ AND TOTAL DISEASE LOAD



The graph ABC of a weak child (I) and a stronger child (II) showing the relationship of the $PaCO_2$ to the total disease load.

dehydration, malnutrition, secondary infection, etc.) Figure V : 4 illustrates this concept. The line ABC follows the course of $PaCO_2$ in its relationship to air-entry, as shown previously in Figure V : 2. "A" represents the healthy child; "B" marks his reaction to croup at a period when he is coping with his disease; "B" - "C" indicates the progress of $PaCO_2$ with an increasing total disease load.

In a strong child (II) the graph is shifted to the right so that although he might exhibit severe signs of obstruction he is in a better position than his weaker counterpart (I) in whom signs might be less severe but whose $PaCO_2$ starts to rise earlier, indicating earlier failure of compensation for disease.

Summary of significance of reduced air-entry and loss of tone.

The reduction of air-entry is perhaps the most important physical sign in croup. It is a good clinical quantitative guide and an expression of the degree of interference with gas exchange imposed by the disease.

The most important correlation with air-entry was $PaCO_2$. Clinical assessment of the capabilities of the patient can be augmented by measuring the $PaCO_2$. If it is low, the patient is withstanding his disease. If it rises (or if on first reading it is normal) it denotes more severe obstruction.

Hypotonia proved useful for it graded the severity of hypoxia. However, other factors may have affected tone (sedation, low serum potassium, dehydration) and therefore this sign loses some of its value.

Reduction in air-entry would tell the clinician that hypoxia was present: if hypotonia also was noted it indicated that the hypoxia was significant and presumably that cellular metabolism had been affected.

Restlessness

Not unexpectedly, restlessness developed as the severity of croup increased. Morrison (1955) has shown a good correlation between increasing oxygen desaturation and increasing restlessness. In the present series, however, restlessness often was absent in the most desaturated children and it appeared that the stage of restlessness had passed. This is a clinical hazard for the inexperienced but provided other physical signs are noted, misjudgement of a quiet child can be avoided.

Recession

An alarming degree of recession can develop in croup and in three cases recession was the primary indication for intubation. Yet some managed without intubation despite severe recession. Knowledge of the $PaCO_2$, as discussed above, will help to indicate whether the child with severe recession is, in fact, under as much stress as he appears to be. Further, in some, particularly the very young or malnourished, vigorous respiratory effort may diminish, not because their obstruction has improved but because they have become fatigued.

Cyanosis

All patients who became cyanosed were intubated. It is not known, therefore, whether cyanosis can be abolished by conservative management alone. Upper airway obstruction hampers efforts to clear secretions, the accumulation of which adds to the obstruction. Physiotherapy itself can be a stressful procedure (Holloway, Adams, Desai and Thambiran, 1969; Laws and McIntyre, 1969) and maintenance of adequate oxygenation with a face mask is difficult during manipulation, pharyngeal suction and coughing. Therefore intubation would seem justified in the presence of cyanosis. Central pallor may intervene before cyanosis becomes obvious. This sign, which could be detected by careful observation, served as an early warning of increasing respiratory stress.

Summary of the significance of restlessness, unawareness and cyanosis

These are striking signs in a sick child and comment on them might be expected from the mother. The uninitiated correctly pay great attention to them, but these signs are all of limited value: cyanosis and unawareness appear late and therefore the child could be in a precarious position before action is taken.

Both restlessness and recession initially are intensified by increasing obstruction, but later subside although the obstruction may not have lessened.

Anaemia

Anaemia, present in most patients, was usually attributable to malnutrition and infection. The haemoglobin of the fatal cases was significantly lower than that of the survivors. Oxygen transport therefore was an important variable and should be

taken into consideration.

The role of haemoglobin in the supply of oxygen to the tissues is shown by the equation of Nunn and Freeman (1964).

Available oxygen = Cardiac output x arterial oxygen saturation x 1,34.

The equation does not include dissolved oxygen which becomes important when the inspired air contains high oxygen tensions. Uncompensated changes on the right-hand side of the equation alter the available oxygen by a factor equal to the product of the individual changes.

Unless croup patients were able to compensate for anaemia, the available oxygen would drop. They had considerable intrapulmonary shunting (see below) which would handicap any attempt to increase haemoglobin oxygen saturation. Therefore the most obvious compensation was a rise in cardiac output. Unless this occurred hypoxia would result.

From the available evidence, restoration of the haemoglobin to normal is important and the level at which blood transfusion is mandatory would appear to be about 9 gm %.

Arterial oxygen tension and alveolar to arterial oxygen gradient on 100% oxygen breathing

Oxygen breathing proved a useful predictive procedure. A $Pa0_2$ of less than 300 mm.Hg while breathing 100% oxygen was usually associated with death. Evaluation of prognosis in the respiratory distress syndrome of the newborn has been achieved in the same manner (Boston, Geller and Smith, 1966; Robertson, Gupta, Dahlenburg and Tizard, 1968).

Oxygen breathing eliminates from the venous admixture two of its contributing components, ventilation to perfusion imbalance and diffusion defects, so that the true shunt remains (West, 1965b).

As recommended by West (1965a) completely non-ventilated but perfused aleoli (atelectasis) are not regarded as a ventilation to perfusion ratio of zero, but are included in the components of the true shunt. The other contributors to the true shunt are blood flow through right to left intracardiac communications and through arteriovenous pulmonary pathways. There was no evidence that these last two components of the true shunt were present in these children.

TABLE V : 3

TRUE SHUNT

Alveolar to arterial oxygen gradient on oxygen breathing compared with concurrent chest X-ray score and cardiac complications.

R/N	$[\Delta Aa0_2]$ vols %	Chest X-ray Score	Cardiac Complication
139	1,07	2	Heart enlarged on X-ray.
141	1,48	6	Nil.
150	1,27	6	ECG: L.V.V.O.
406	2,24	5	Cardiac failure.
527	1,34	0	Hb 4,3 gm %.
530	0,80	7	Myocarditis.
534	0,47	4	Nil.
140	0,76	1	Nil.
166	0,96	6	Nil.
202	1,11	0	Nil.
417	0,53	9	Cardiac failure : heart enlarged on X-ray.
497	1,06	10	Nil.
550	0,69	3	ECG: R.V.P.O., myocarditis.
558	1,14	18	Nil.
632	0,85	9	ECG : L.V.V.O.

L.V.V.O. = left ventricular volume overload.

R.V.P.O. = right ventricular pressure overload.

ECG = electrocardiogram.

Therefore it is deduced that the widened alveolar to arterial oxygen gradient on oxygen breathing was due mainly to atelectasis. However, the role of a relatively low cardiac output in producing a wide gradient might have been considerable (Kelman, Nunn, Prys-Roberts and Greenbaum, 1967) and is discussed further in Chapter VI.

An attempt to evaluate these two factors (cardiac output and atelectasis) appears in Table V : 3. Chest X-rays were examined to see if extensive lower respiratory tract involvement correlated with greater shunting. In addition, what evidence there was of cardiac decompensation is shown, whether clinical, radiographic or electrocardiographic. It will be seen that a large shunt was not necessarily associated with cardiac abnormality or with a high X-ray score. The reverse was also true: a relatively small shunt could occur with both a high X-ray score and cardiac strain.

SUMMARY

Several physical signs correlated with blood gas changes. This confirmed that these features did indeed relate closely to the disease and distinguished which biochemical alterations they represented.

Changes in pH, $PaC0_2$ and $Pa0_2$ accompanied a diminishing degree of air entry on auscultation. A cause and effect relationship could be assumed. The $PaC0_2$ was considered an estimate of the degree of airway obstruction.

Hypotonia and unawareness, but not restlessness, were found to be the clinical expression of hypoxia.

The prognosis for survival, after intubation had relieved the airway obstruction, depended upon factors affecting oxygenation. The haemoglobin level and the size of the residual shunt on 100% oxygen breathing oorrelated with the mortality rate.

CHAPTER VI

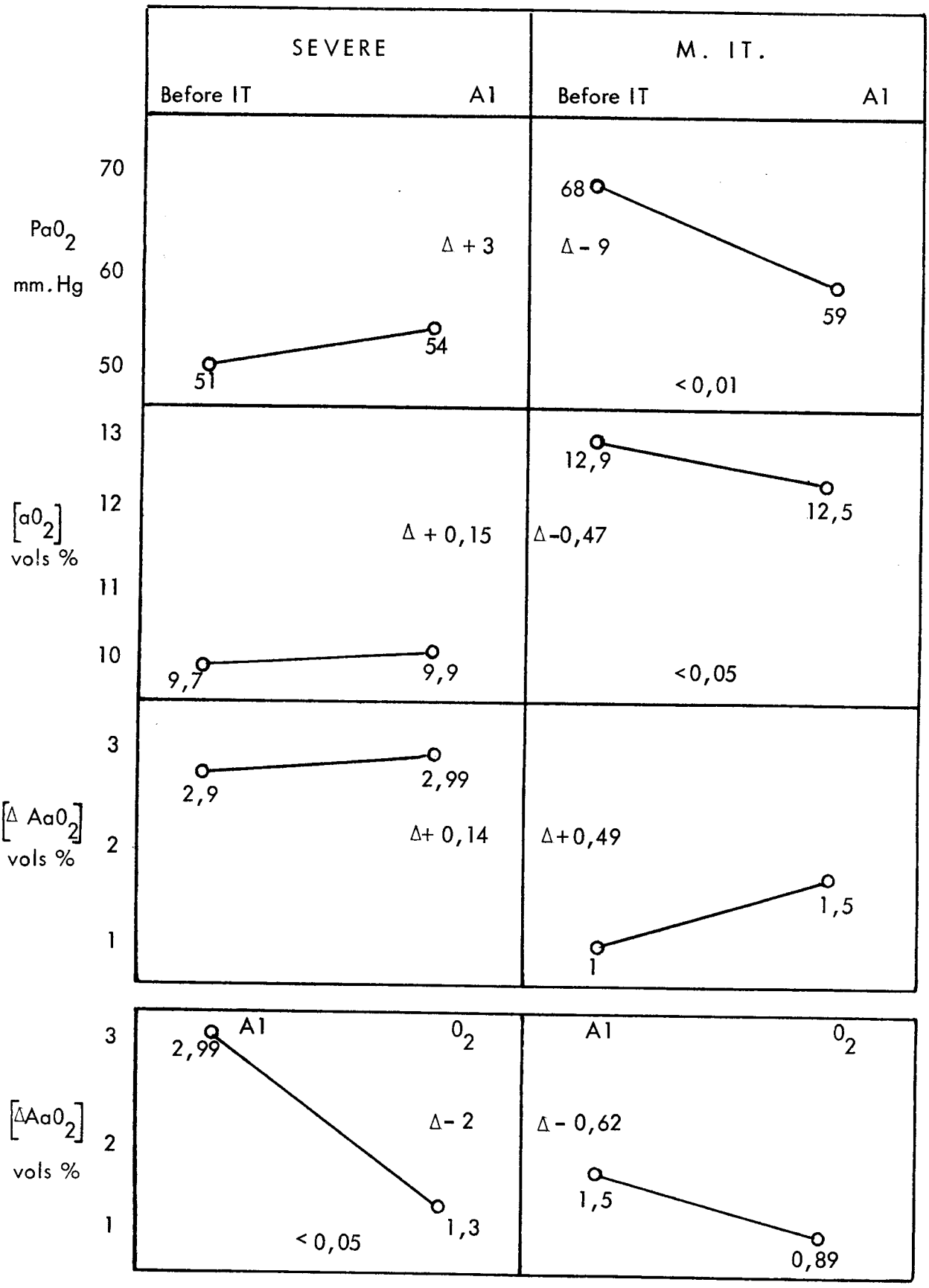
PAGE

THE EFFECT OF INTUBATION ON BLOOD GASES AND PULSE AND RESPIRATORY RATES

FIGURE VI : 1

THE EFFECT OF INTUBATION

OXYGEN



IT = Intubation

Δ = Mean of differences

A1 = After intubation

0_2 = 100% oxygen breathing.

CHAPTER VI

THE EFFECT OF INTUBATION ON BLOOD GASES AND PULSE AND RESPIRATORY RATES

Three specimens of arterial blood were obtained :

1. While the patient was breathing air before intubation.
2. Half an hour after the intubation procedure had been completed.
3. Thereafter a source of 100% oxygen was connected via a 2 litre bag to the endotracheal tube and after 10 minutes the third specimen was taken.

RESULTS

The results are summarised in Figures VI : 1 and VI : 2 and in the Appendix (pages a26,27). Individual results appear in the Appendix (pages a28-a32).

A. Severe Group

pH : The pH rose : the mean of the differences was significant ($p < 0,01$).

$PaCO_2$: The $PaCO_2$ fell : the mean of the differences was significant ($p < 0,05$).

There were no significant changes in the BE and PaO_2, or the ΔAaO_2, whether expressed as tension or content.

B. Moderate Intubated Group

$PaCO_2$: The $PaCO_2$ fell : the mean of the differences was significant ($p < 0,05$).

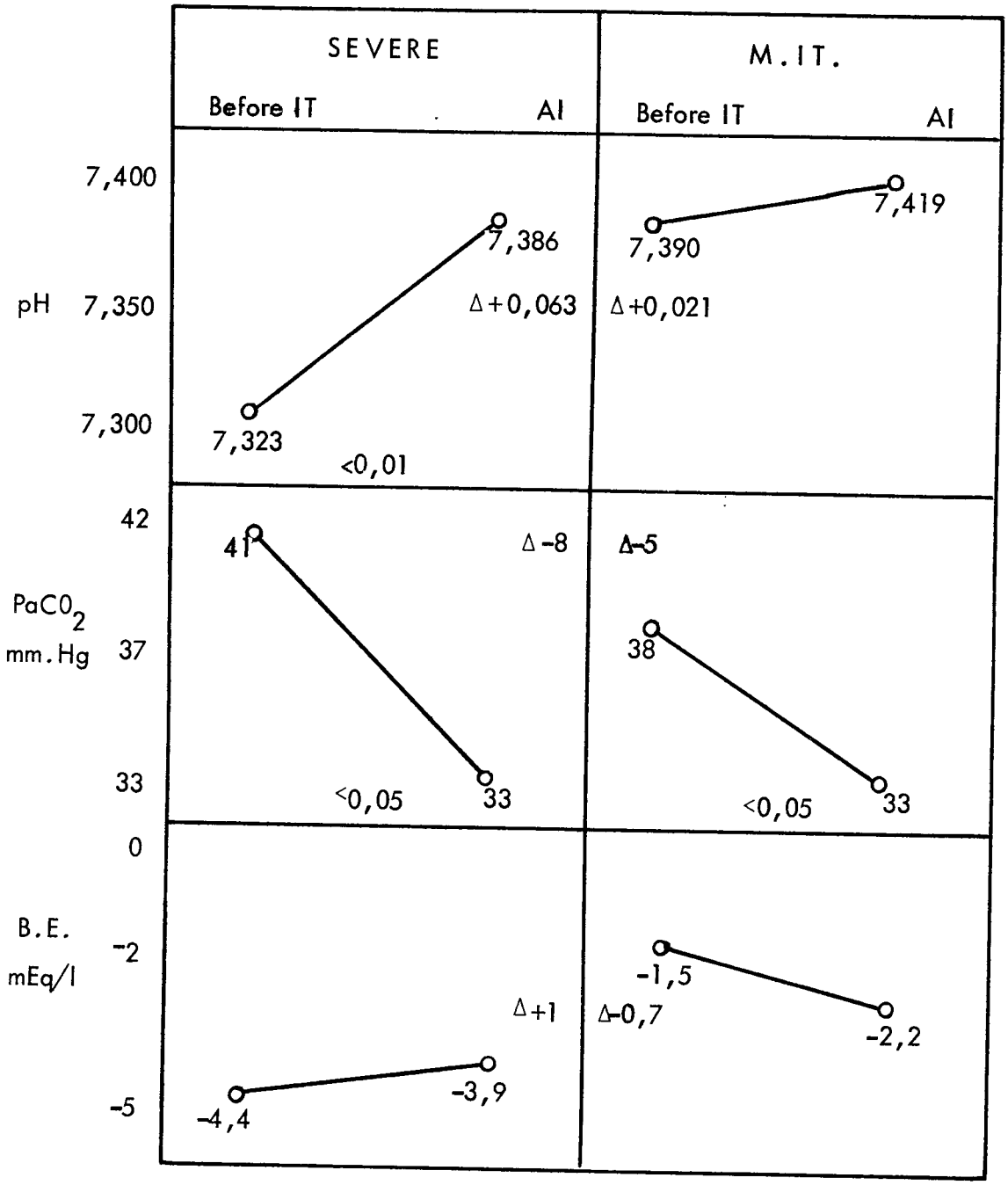
PaO_2 : Intubation was followed by a significant fall in PaO_2 ($p < 0,01$).
When oxygen was expressed as content, the fall was still significant ($p < 0,05$).

The changes in pH, BE and ΔAaO_2, whether expressed as tension or content, were not significant.

FIGURE VI : 2

THE EFFECT OF INTUBATION

ACID BASE



IT = Intubation

Δ = Mean of differences

AI = After intubation

C. Oxygen Breathing : $[\Delta Aa0_2]$ (Figure VI : 1)

In the Severe group breathing air after intubation the mean $[\Delta Aa0_2]$ fell from 2,9 ± 2,1 vols % to 1,3 ± 0,52 vols % breathing oxygen (Appendix page a33). The mean of the differences was significant ($p < 0,05$).

In the M.IT group, after intubation the mean $[\Delta Aa0_2]$ was 1,5 ± 0,8 and fell to a mean of 0,89 ± 0,22 vols % when breathing oxygen. (Appendix page a34). This change was not significant.

When both groups were considered together, the fall in mean $[\Delta Aa0_2]$ after intubation to that on breathing oxygen was significant ($p < 0,01$).

D. Pulse and Respiratory Rates

The pulse and respiratory rates were taken before and 1-3 hours after intubation. The results of the two groups (Severe and M.IT) were considered together.

There was a mean fall in pulse rate of -20 ± 34/minute ($p < 0,02$) and in respiratory rate of -7 ± 11/minute ($p < 0,01$) (Appendix page a35).

DISCUSSION

The striking change induced by intubation was the fall of $PaC0_2$ within one hour in both groups. There was an accompanying significant rise in the pH of the Severe group ($p < 0,01$).

Intubation of Severe patients was, therefore, followed by the return of the acid base not to normal, but towards that of Mild patients, that is, hyperventilation and alkalaemia.

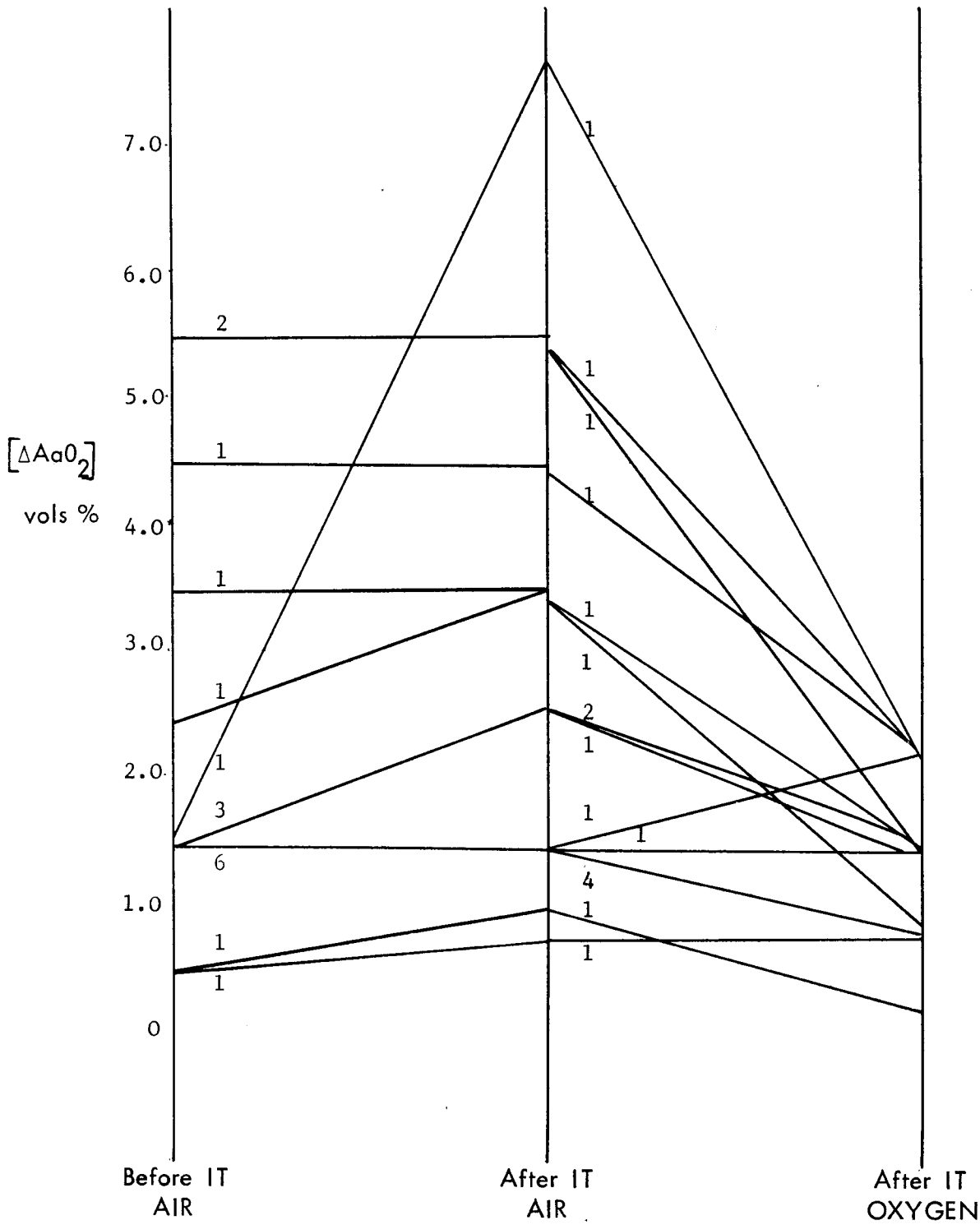
In view of the observations made in Chapter V, it is likely that the hyperventilation reflected the reduction of airway obstruction brought about by intubation and that the rise in pH was secondary. Hyperventilation will be discussed further in Chapter VIII.

Intubation also produced an effect upon oxygen metabolism. The $Pa0_2$ of the M.IT group fell significantly. While the change in the mean alveolar to arterial oxygen gradient of the M.IT and the Severe group was not significant, there was considerable alteration in individual cases (Appendix pages a33, a34). Therefore

FIGURE VI : 3

ALVEOLAR TO ARTERIAL OXYGEN GRADIENTS

Before and after Intubation and after 100% oxygen breathing



The numerals in the figure are the number of patients each line represents.

examination of these changes is indicated.

The method of calculating the alveolar to arterial oxygen gradient in tension and its conversion to content is given in the Appendix (page a15). The error involved in obtaining the $[\Delta Aa0_2]$ by this means has not been accurately defined. For the purposes of this discussion it has been assumed to be 30%. The gradients were reconsidered in a manner designed to minimise incorrect conclusions arising from this conversion error.

The gradients that changed (after intubation) by less than 30% were regarded as unaltered and are represented in Figure VI : 3 as a straight line. Gradients that changed by more than 30% are shown to alter by units of Δ30%, that is, by an amount expressed in errors. The error is considered to be non-cumulative.

The gradients are grouped into those starting at <1 vol %, between 1-2 vols %, etc., before intubation.

Treating the data thus, in 7 of the 11 cases where the $[\Delta Aa0_2]$ increased this was unlikely to have been due to the error of converting tensions to contents. But in all 6 cases where the gradient lessened, the change could have been due to this error. Thus the immediate effect of intubation was not to reduce the gradient: if there was an alteration it was in the direction of widening.

Several factors must be considered in this $[\Delta Aa0_2]$ change. Hyperventilation itself, which followed intubation, might have been expected to raise the alveolar oxygen content according to the alveolar air equation, with a subsequent rise in arterial oxygen content. Although only 3 of the patients did not lower their $PaC0_2$, the mean alveolar oxygen content of the group did not alter significantly (Appendix page a36).

Indeed, neither in normal subjects (Holloway, 1968) nor in patients with obstructive airways disease (Holloway, Valjee and Singh, 1972) has hyperventilation been associated with a decrease in $[\Delta Aa0_2]$, for while the alveolar oxygen increased, for various reasons the arterial oxygen did not follow suit.

If the alveolar oxygen content did not increase, the arterial oxygen content must have changed via alteration of the venous admixture. The important components of the venous admixture in croup are ventilation to perfusion imbalance and the true shunt (previously discussed in Chapter V).

In addition, the cardiac output affects the venous admixture in the following manner: if oxygen consumption remains unaltered a fall in cardiac output allows increased oxygen extraction and therefore reduction in the mixed venous oxygen content. Thus blood in the venous admixture will have a lower oxygen content (Kelman et al, 1967).

The relationship of $\left[\Delta Aa0_2\right]$, venous admixture (QS) and cardiac output (QT) is evident from the following equation :-

$$\frac{QS}{QT} = \frac{(c'0_2 - a0_2)}{(c'0_2 - a0_2) + (a0_2 - \bar{v}0_2)}$$

where the $\bar{v}0_2$ = mixed venous oxygen content and $c'0_2$ = pulmonary capillary oxygen content. If alveolar oxygen content ($A0_2$) is assumed to be equal to $c'0_2$, this can be rewritten :

$$\frac{QS}{QT} = \frac{A0_2 - a0_2}{A0_2 - \bar{v}0_2}$$

Therefore widening of the $\left[\Delta Aa0_2\right]$ following intubation might have arisen from an increase in the size of the venous admixture or a fall in the cardiac output, or both.

Intubation and physiotherapy caused improvement in ventilation; air entry on auscultation increased immediately, and there was a significant fall in $PaC0_2$. The pulmonary vascular resistance, probably initially high in these hypoxic, acidotic patients, should have decreased after intubation; but any decrease possibly was suboptimal in the period under consideration, for while the pH rose, the $Pa0_2$ did not. Perhaps the increase in pulmonary perfusion was marginal and did not match the increase in ventilation.

The other component of the venous admixture, the true shunt, should have decreased, for intubation and physiotherapy could have allowed atelectatic areas of lung to re-expand. But the opposite probably occurred. Some patients with respiratory disease employ continuous positive intrathoracic pressure to hold open their alveoli despite reduced surfactant, and thereby help preserve alveolar ventilation. This has been achieved by the employment of the expiratory grunt (Harrison, Heese and Klein, 1968; Knelson, Howatt and DeMuth, 1969) or by means of mechanical ventilation (Ashbaugh, Bigelow, Petty and Levine, 1967;

Ashbaugh, Petty, Bigelow and Harris, 1969).

Some children in this study may have relied upon expiration through the reduced calibre of their upper airway to maintain positive intrathoracic pressure. Intubation of the trachea would have interfered with this manoeuvre, with resultant increase in atelectasis, and therefore of true shunt.

The effect on cardiac output brought about by intubation was likely to have been a fall. Physiotherapy itself can reduce the output (Laws and McIntyre, 1969) and manipulation of these children, certainly those in the Severe group, would be likely to have had similar results. Indeed, occasionally after intubation there was a transient deepening of cyanosis and bradycardia. This could have paralleled a low cardiac output.

Further, a direct correlation of $PaCO_2$ and cardiac output has been established (Theye, Milde and Michenfelder, 1966; Prys-Roberts, 1970; Prys-Roberts, Kelman, Greenbaum and Robinson, 1967; Prys-Roberts, Kelman and Greenbaum, 1967; Morgan et al, 1967). Therefore the cardiac output should have fallen with the significant drop in $PaCO_2$ that immediately followed intubation.

The pulse rate of these patients slowed after intubation. This reflected either a fall in cardiac output or a rise in stroke volume. The latter seems more likely, for the reduction of intrathoracic pressure swings after intubation would have favoured an increased stroke volume. However, the pulse rate usually was taken 1-2 hours after the $\Delta Aa0_2$ measurements and therefore did not relate closely to the period of acute change under discussion.

The hypothesis that a drop in cardiac output was the major reason for the widening of the $\Delta Aa0_2$ on intubation was tested. Mixed venous oxygen tensions ($P\bar{v}0_2$) were calculated after intubation, when the change in $\Delta Aa0_2$ was assumed to be entirely due to a fall in cardiac output. If this calculation resulted in a $P\bar{v}0_2$ below 20 mm.Hg, the level at which cellular death occurs, it was deduced that the change in $\Delta Aa0_2$ would have been unlikely to be entirely cardiac dependent.

The details of this calculation appear in the Appendix (page a37-a40). In 4 of the 7 cases where the $[\Delta Aa0_2]$ widened after intubation, the $P\bar{v}0_2$ was physiological (i.e. above 20 mm.Hg). This suggested that in the remaining 3 a fall in cardiac output could not have been the only factor in the increase in $[\Delta Aa0_2]$.

Thus the increased $[\Delta Aa0_2]$ after intubation probably resulted from changes both in the components of the venous admixture and the cardiac output. It has not been possible to define the relative importance of these factors with the information available.

The $[\Delta Aa0_2]$ also was calculated on 100% oxygen breathing and treated in the manner described above to minimise the error involved in expressing results in content.

The gradient lessened in all but 3 patients: in 2 it was unchanged and in one it actually increased (Figure VI : 3).

The reduction in the $[\Delta Aa0_2]$ occurred because oxygen breathing eliminated the contribution made to the venous admixture by ventilation to perfusion imbalance (West, 1965b). The residual $[\Delta Aa0_2]$ therefore indicated the size of the true shunt.

Thus croup was demonstrated to cause not only considerable ventilation to perfusion imbalance, but also a significant amount of intrapulmonary shunting, as the $[\Delta Aa0_2]$ after oxygen breathing was still grossly widened.

Once again, the cardiac output may have altered. As these children were not manipulated at this time, any change would have been entirely due to the administration of oxygen. The cardiac output has been shown to fall during oxygen breathing (Whitehorn, Edelmann and Hitchcock, 1946; Daly and Bondurant, 1962; Cotes, Pisa and Thomas, 1963). Therefore the resultant reduction in mixed venous oxygen content may have negated some of the effect that the elimination of ventilation to perfusion imbalance would have produced upon the $[\Delta Aa0_2]$.

SUMMARY

In those children who required intubation, the effect of this procedure upon the arterial blood gases and acid base was analysed.

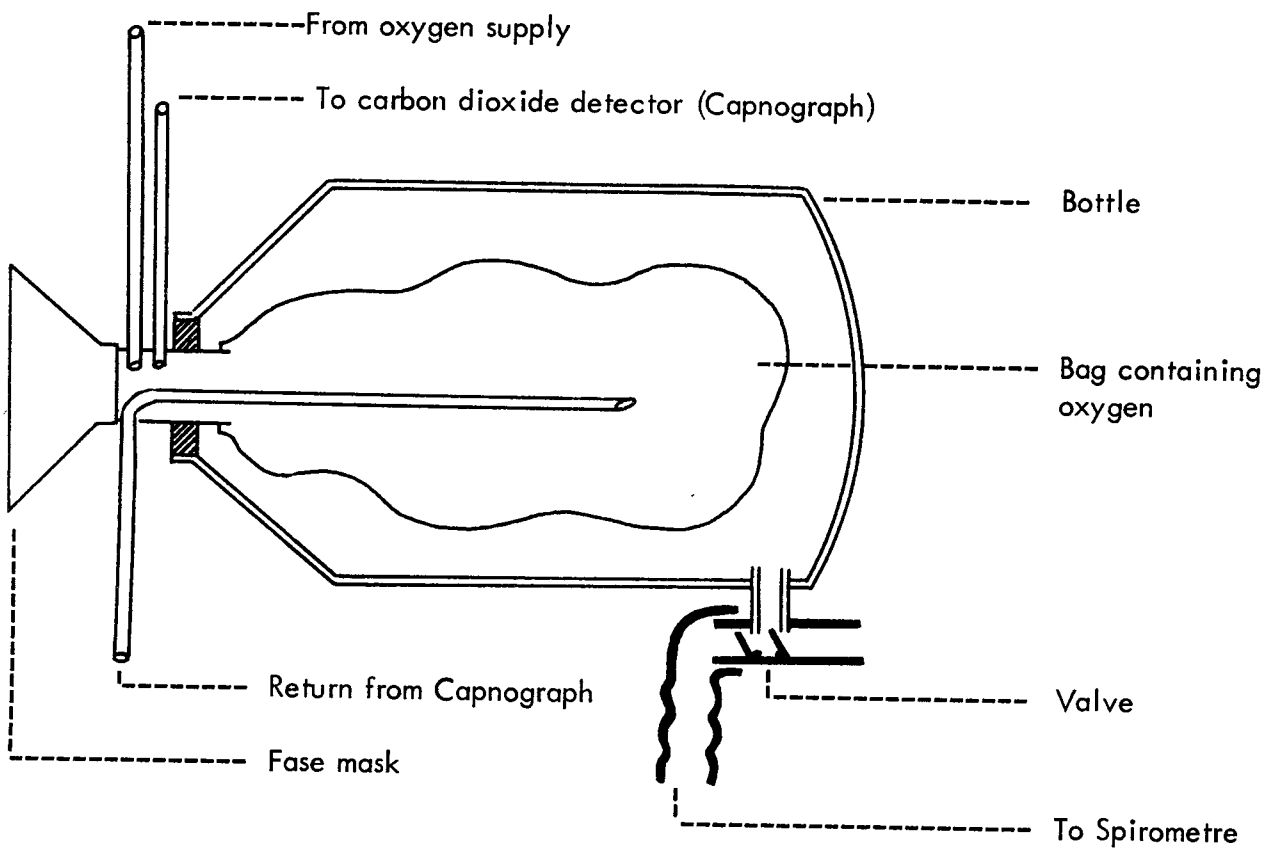
Intubation allowed immediate hyperventilation in most children, which, in the Severe group, led to a significant rise in pH in the short period under study.

Another significant change was a fall in arterial oxygen content of the Moderate Intubated group. When all patients were considered as one group, the alveolar to arterial oxygen gradient widened, if it altered at all. Possible mechanisms of this feature were discussed.

Oxygen breathing demonstrated a considerable ventilation to perfusion imbalance and also a large true shunt in croup.

CHAPTER VII

FIGURE VII : 1 BAG IN BOTTLE APPARATUS



Apparatus for measuring ventilatory response to carbon dioxide.

CHAPTER VII

THE EFFECT OF INTUBATION ON THE VENTILATORY RESPONSE TO CARBON DIOXIDE

Several patients were given a carbon dioxide challenge before and after intubation.

Principal of the Method

The method used was that of Read (1967). The subject rebreathes from a bag in which carbon dioxide is allowed to accumulate. If the bag contains a gas mixture whose initial PCO_2 is close to that of mixed venous blood, equilibrium is soon established between alveolar, arterial, mixed venous and bag CO_2. This is followed by a linear rise in PCO_2 and the consequent increase in ventilation is measured.

Despite ventilation/perfusion imbalance, equilibrium between alveolar gas, blood and chemoreceptor tissue is complete (Read, 1967; Clark, 1968). Changes in medullary tissue PCO_2 can be monitored by end tidal PCO_2. Therefore arterial sampling is not required.

A high initial concentration of oxygen in the bag prevents the occurrence of hypoxic stimuli to ventilation.

Method

A 2-litre bag was sealed in a large bottle (Figure VII : 1). The patient was connected to this apparatus by means of a tight-fitting face mask. The bag was filled initially with oxygen so that the residual oxygen in the bag after the experiment was higher than the initial alveolar oxygen tension. Priming of the bag with carbon dioxide was not done. Each patient was his own control, so that alineality due to absence of carbon dioxide prime was rendered unimportant.

As the patient rebreathed gas was sampled continuously as it passed to and from the lungs and was analysed for CO_2 by an infra-red carbon dioxide analyser

TABLE VII : 1

THE EFFECT OF INTUBATION ON THE VENTILATORY RESPONSE TO CARBON DIOXIDE AND ON BLOOD GASES

	BLOOD GASES				VE/CO_2 Δ Litres/ Δ % CO_2		
R/N	Δ $PaCO_2$ mm.Hg.	Δ pH	Δ B.E. M.Eq/L	Δ $PaCO_2$ mm.Hg.	PRE-IT	POST-IT	Δ
33	-	-	-	-	1,666	1,252	+ 0,086
140	- 5	+ 0,003	+ 0,5	- 5	1,428	1,431	+ 0,003
150	+ 10	+ 0,020	- 5	- 9	0,927	0,818	- 0,109
166	- 3	- 0,025	+ 4	- 8	2,180	4,693	+ 2,513
170	+ 2	0	+ 1	- 24	0,498	1,054	+ 0,559
191	- 7	+ 0,060	+ 1	- 4	1,204	1,463	+ 0,259
202	- 22	+ 0,125	+ 1,5	- 4	0,943	2,415	+ 1,472
234	- 3	- 0,005	+ 0,5	- 4	0,392	0,752	+ 0,360
451	-	-	-	-	0,729	1,980	+ 1,251
497	- 2	+ 0,030	+ 1	- 13	0,074	1,123	+ 0,049
450	-	-	-	-	1,780	3,926	+ 2,146
558	- 13	+ 0,080	+ 0,2	- 8	1,434	2,042	+ 0,608

$p < 0,02$

(Capnograph). Oxygen content of the bag was measured at the end of the experiment by a paramagnetic oxygen analyser (Servomex). By means of a low resistance valve and a spirometer, ventilation was recorded from the excursions of the air in the bottle surrounding the bag.

The patient rebreathed from the bag for periods of 2 to 3 minutes. Two measurements were made before and after intubation.

The change in ventilation (VE in litres) from the beginning to the end of the period of rebreathing was expressed as a ratio of the change in percentage end-tidal $C0_2$ over the same interval, i.e., litres VE/% $C0_2$. This ratio was calculated before and after intubation, and the latter subtracted from the former to give the alteration in response to $C0_2$ allowed by the procedure of intubation.

Material

Twelve patients were studied. In 9 of the 12 arterial blood gases were also done before and after intubation.

Results

The results of the $C0_2$ challenge and of blood gases for each child appear in Table VII : 1. The details of measurements made during the $C0_2$ challenge are given in the Appendix (page a41).

1. The mean ventilatory response to a carbon dioxide challenge increased after intubation ($p < 0,02$).
2. Although this increase for the whole group was significant, there were important exceptions (see discussion).
3. The changes in blood gases produced by intubation were identical to those of the series as a whole and were discussed fully in Chapter VI.

There was no correlation between these results and length of history of obstruction, age, clinical severity of obstruction, degree of pneumonia, or level of $PaC0_2$, $Pa0_2$ or pH before intubation.

DISCUSSION

Clark (1968) defined three factors which govern the ventilatory response to a carbon dioxide challenge :-

i. The magnitude of the challenge ($PAC0_2$) produces an increase in ventilation by altering the pH of the cerebrospinal fluid, which stimulates a chemosensitive centre situated on the ventero-lateral surface of the fourth ventricle. In addition, peripheral chemoreceptors also are stimulated by the rise in $PaC0_2$ but the magnitude of their contribution is uncertain.

ii. The central conversion of the input signal to the output signal. The comparison of the same subject in different circumstances is valid only if the blood perfusion and $C0_2$ production of the receptor areas have not changed.

iii. The motor output which, in man, is generally equated with alveolar or minute ventilation. This relationship is affected by the presence of airflow obstruction.

The method of expressing the change in ventilation as a ratio of the change in end-tidal $C0_2$ ensured that the challenge was comparable in each experiment. It was assumed that the central transfer was unchanged in each child. Therefore any alteration in the ventilation to carbon dioxide ratio must have been produced by the effect of intubation on the motor output.

Normal subjects breathing through artificial resistances (Zechman, Hall and Hull, 1957; Eldridge and Davis, 1959; Milic-Emili and Tyler, 1963) and patients with chronic obstructive airways disease (Cherniack and Snidal, 1956; Godfrey, Edwards, Copland and Gross, 1971) have been shown to have a reduced ventilatory response to any given carbon dioxide stimulus. The debate as to whether this reduced response was due to chemical effects on the central and peripheral chemoreceptors or to mechanical factors has crystallised in favour of the limiting factor being the latter (Cherniack and Snidal, 1956; Eldridge and Davis, 1959; Howell, 1966; Godfrey et al, 1971).

TABLE VII : 2 VE/CO_2 and $PaCO_2$ Changes due to Intubation

VE/CO_2	$PaCO_2$	Cases : R/N
9 ↑	3 ↓	191, 202, 558
	3 →	166, 170, 234
	3 not done	33, 451, 540
2 →	↓	140
	→	497
1 ↓	↑	150

The majority (9 out of 12) of croup patients increased their ventilatory response to inhaled CO_2 after upper airway obstruction had been reduced by intubation (Table VII : 2). This was to be expected in the light of the work quoted above, and indicated that in these patients an airway obstruction had been relieved. However, in some, the increased capacity to ventilate was not immediately used. That is, they did not promptly lower their $PaCO_2$. It is possible that these children might have managed without intubation, although clinically there was ample evidence that they benefitted from the procedure.

In 2 of the 12 cases the VE/CO_2 ratio was unaltered by intubation (Table VII : 2). In these 2 cases the following points must be considered :-

i. It is known that some normal subjects have a lesser response to CO_2 than others (Schaefer, 1958; Howell, 1966; Ingram and Bishop, 1970).

ii. Patients with the most severe pulmonary disease had the least response to CO_2. (Godfrey et al, 1971).

iii. Response to inhaled CO_2, when related to the level of the initial $PaCO_2$, has been found to be greater the lower the $PaCO_2$ (Brodovsky, McDonell and Cherniack, 1960; Tandon, 1969).

iv. Impedance to airflow might have been only partially in the upper airways. Obstruction, for example by secretions, further down the bronchial tree may have persisted after intubation.

The level of initial $PaCO_2$ in these two children did not correlate with the result of the challenge, nor were they more severely ill than other patients. They may have been relative non-responders, but more probably had residual distal airways obstruction, limiting their ventilatory response after intubation.

In one case the VE/CO_2 actually lessened after intubation and his $PaCO_2$ rose. Although clinically the immediate effect of intubation was beneficial, the physiological effect was not. It is possible that this child was relying upon an end expiratory positive pressure to maintain his ventilation and that this was abolished by intubation.

SUMMARY

Twelve children were given an increased concentration of carbon dioxide to inspire before and after intubation.

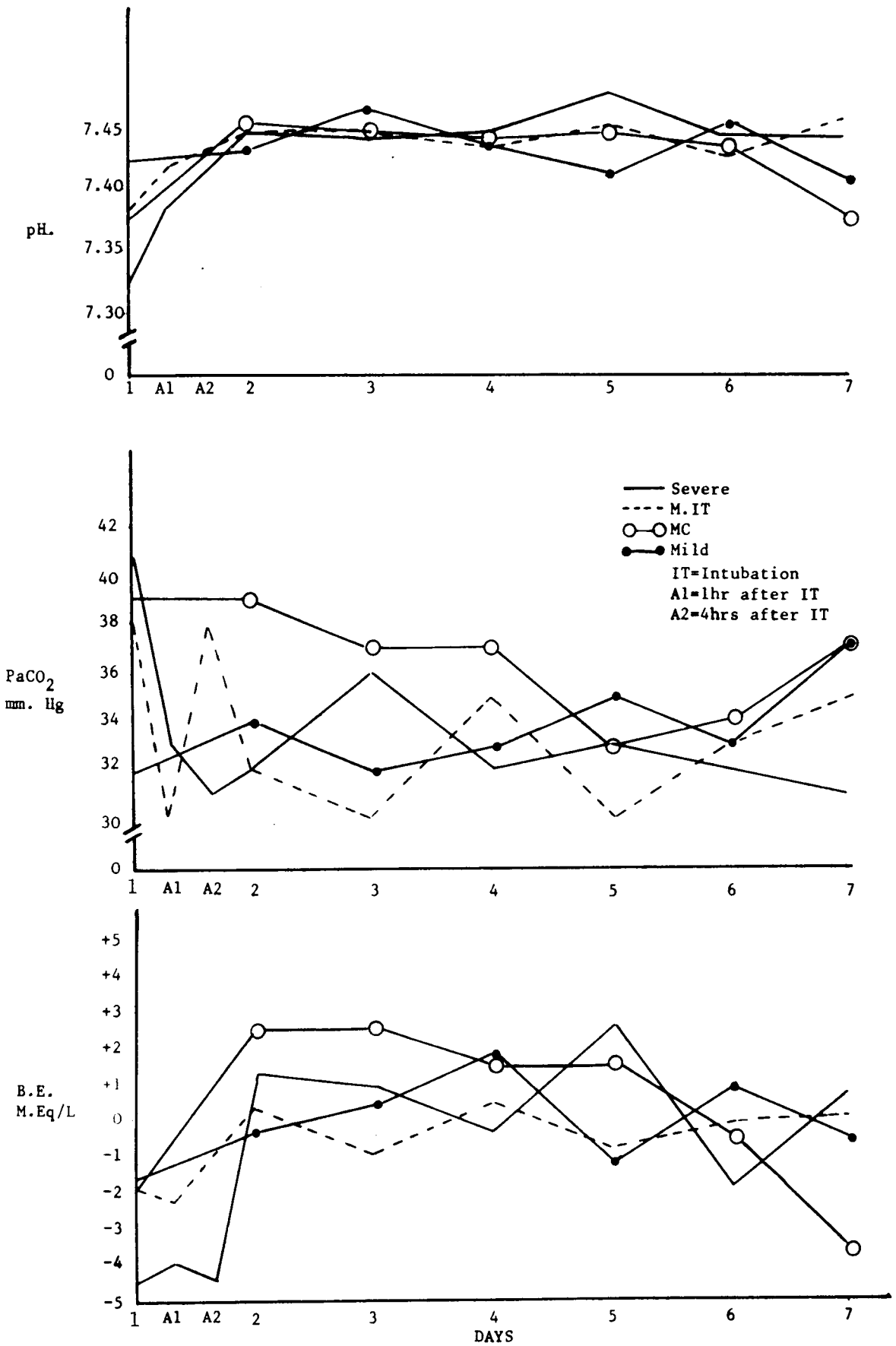
The majority had a considerable degree of upper airways obstruction as evidenced by the increase in possible ventilation that followed intubation. However, some did not make use of this improved ability to ventilate, for they failed to lower their $PaCO_2$. Presumably this was not needed and it is probable they might have managed without intubation.

Exceptionally ventilation did not increase following intubation and was probably due to obstruction persisting further down the bronchial tree.

The possibility that some croup patients maintained an end expiratory positive pressure in their lungs has been discussed in Chapter VI. In the small sample of patients given a CO_2 challenge the results from one lent support to this hypothesis.

CHAPTER VIII

FIGURE VIII : 1 DAILY MEAN VALUES



CHAPTER VIII

THE PROGRESS OF THE DISEASE

ARTERIAL BLOOD GASES AND ACID BASE

In addition to arterial blood samples obtained on admission and after intubation, blood gas analyses, with patients breathing air, were done daily for 7 days, where this was possible.

RESULTS

Figures VIII : 1 and VIII : 2 show in graphic form the acid base and blood gases from admission to the seventh day. Tables of daily means of each parameter and individual daily analyses appear in the Appendix (pages a42-a66).

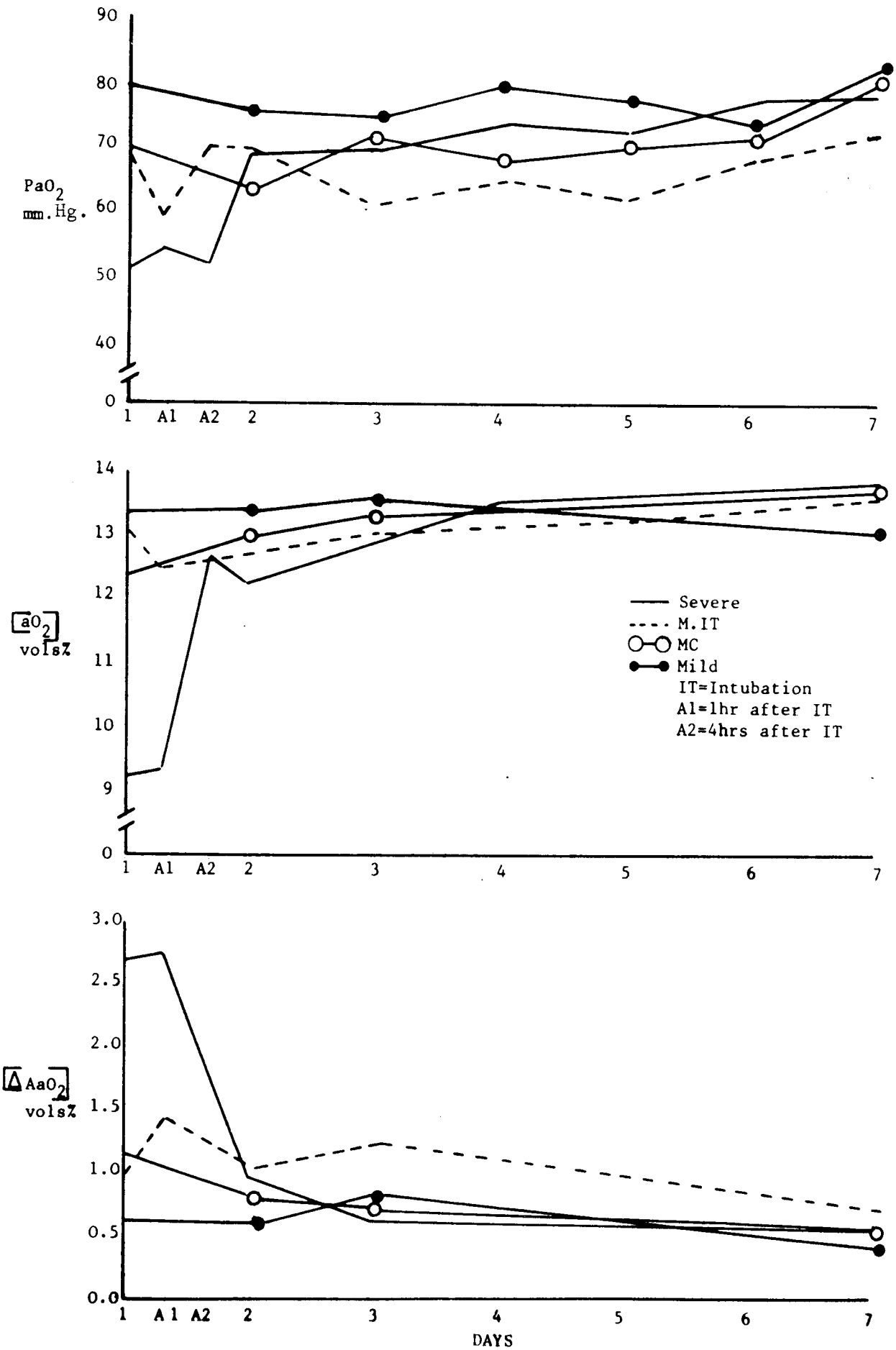
A. ACID BASE

The most striking feature was that the mean pH in all clinical groups rose from the various values on admission (Chapter IV) to very similar figures at the end of 24 hours, the grand mean of which, $7,451 \pm 0,053$, was significantly above normal ($p < 0,01$). Forty-eight hours after admission the pH of all groups was still above normal ($7,452 \pm 0,05$ $p < 0,01$). The pH of the intubated patients (Moderate and Severe) remained high ($p < 0,05$) until the seventh day.

a. Intubated Patients

The rise in pH during the first day of treatment from 7,322 to 7,443 (Severe) and 7,386 to 7,448 (Moderate Intubated) is accounted for by the fall in the $PaCO_2$ that immediately followed intubation. In addition, Severe patients had a significant decrease in base deficit from -4,4 to + 1,3 m.Eq/L ($p < 0,05$). The base deficit of the M.IT group decreased less. Thus there was both a respiratory and metabolic component to the pH change.

FIGURE VIII : 2 DAILY MEAN VALUES



For 24 hours after intubation the mean $PaCO_2$ of those intubated was significantly below normal ($p < 0,05$). Then followed a slow rise until day 7 when it was within normal limits. Study of the individual results shows that $PaCO_2$ fell on intubation in all but four. The initial $PaCO_2$ measurements of these four were the lowest (<31 mm.Hg) and rose on intubation.

The shape of the base excess graph of the intubated children was exactly the same as that for oxygen tension over the 7 days. In the first 24 hours the changes in PaO_2 of the two intubated groups correlated significantly with their B.E. changes ($\Delta BE = 0,15.\Delta PaO_2 + 0,27$. $r = 0,62$. $p < 0,001$) (Figure VIII : 3.)

Neither the BE nor the $PaCO_2$ of these children was different from normal on day 7 but the pH was still high. This resulted from a slightly low $PaCO_2$ coupled with a small base excess.

b. Moderate Conservative patients pursued a different course. Here the mean pH rose from 3,379 to a level (7,451) comparable with the intubated patients. This rise was not accounted for by a fall in the mean $PaCO_2$ but by a large decrease in mean base deficit ($p < 0,01$).

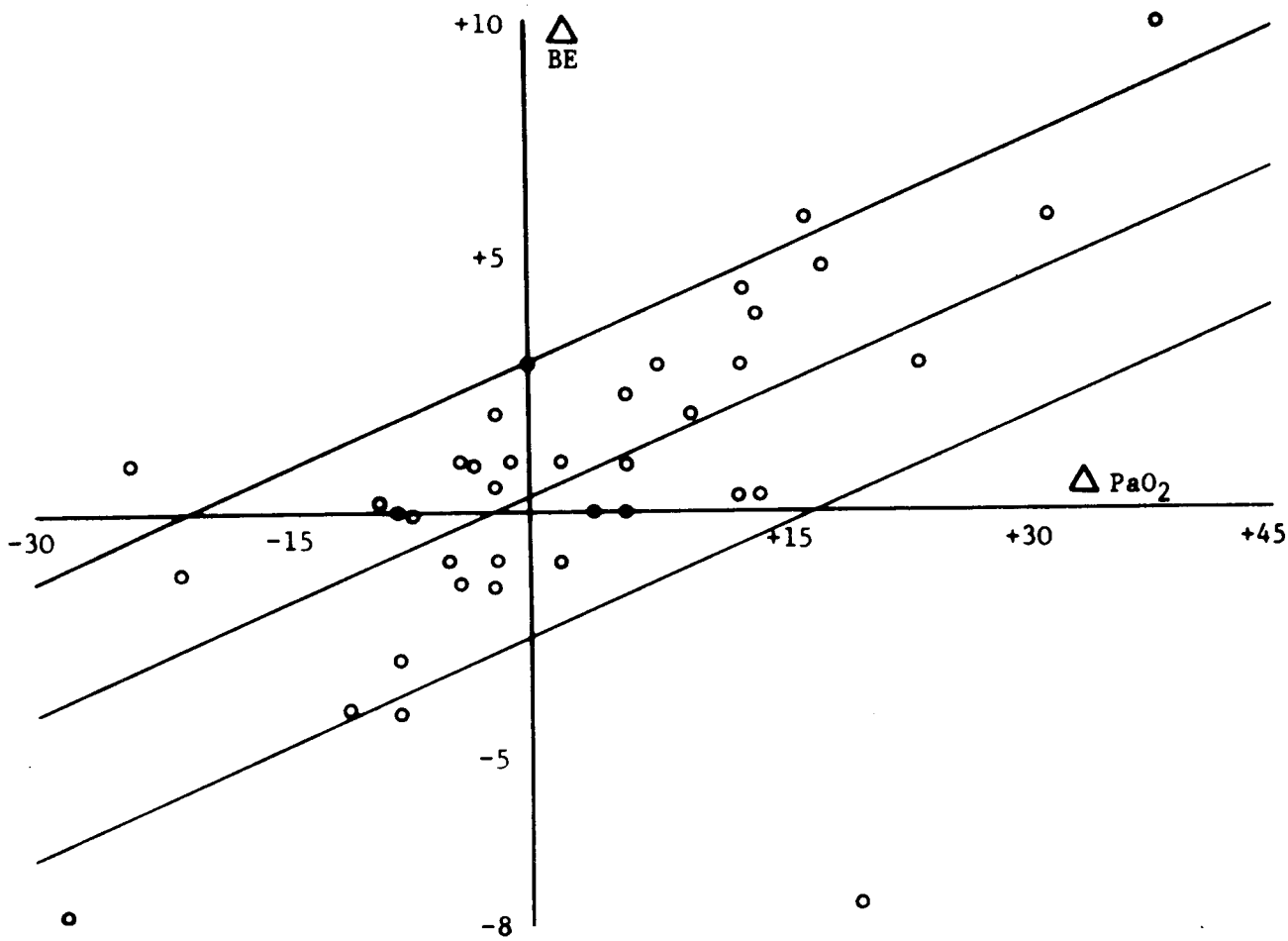
By day 7 the mean $PaCO_2$ of this group had fallen to the same figure as that of the Moderate Intubated group (35 mm.Hg) without passing through a hyperventilation phase. The base excess, after the initial sharp rise, decreased slowly to a mean of -3,6 m.Eq/L on day seven.

Unlike the intubated children, no correlation was established between base excess and PaO_2 changes.

c. Mild cases

The mean pH commenced at 7,426, the upper limit of normal, and rose further over the next 2 days to 7,464. This pH resulted from the sustained low $PaCO_2$ of this group as well as a small decrease in the base deficit. Over the week of study the pH gradually fell to normal as the $PaCO_2$ rose.

FIGURE VIII : 3 CORRELATION OF CHANGES IN ARTERIAL OXYGEN TENSION AND BASE EXCESS IN THE FIRST 24 HOURS, IN INTUBATED PATIENTS.



$$\Delta BE = 0.15\ \Delta PaO_2 + 0.27$$
$$r = 0.62$$
$$p < 0.001$$

B. OXYGEN

1. Oxygen Tension

a. Intubated Patients: Four hours after intubation the mean PaO_2 of the Severe group was no different from the admission level of 51 mm.Hg, but by 24 hours it had risen to a mean of 68 mm.Hg. There followed a further rise to 76 mm.Hg by day 7, a level still significantly below normal. ($p < 0,01$). Many individual cases had not recovered their admission level of PaO_2.

b. Non-intubated Patients

The mean PaO_2 of the M.C. Group rose during the week from 67-78 mm.Hg. In some individual cases the PaO_2 fell markedly over the first 2 days, while in 4 it rose sharply.

The mean PaO_2 of Mild cases did not vary significantly and was within normal limits throughout the study period.

2. Arterial Oxygen Contents

The lowest mean oxygen content on admission was that of the Severe group (9,27 vols %), which increased to 12,09 vols % in 24 hours. ($p < 0,05$). The rise thereafter was slower to 13,83 vols % on day seven.

The Moderate and Mild groups had higher oxygen content levels on admission, which rose over the week to 12,8 vols % (M.IT), 13,5 vols % (M.C.) and 12,9 vols % (Mild) on day seven.

At the end of one week the content of all groups was still significantly below that of the normal controls (16,5 vols %) ($p < 0,01$).

3. Alveolar to Arterial Oxygen Gradients (in Contents)

On admission, the Severe and both Moderate groups had significantly widened alveolar to arterial oxygen gradients ($p < 0,001$) but that of the Mild group was normal. The admission figures have been shown in Chapter IV.

Severe cases showed a rapid decrease of the gradient over the first 24 hours of treatment, while in the others the decline was gradual. On day 7 all were within normal limits except the M.IT group ($p < 0,01$).

DISCUSSION

Hyperventilation

The striking feature of most patients was their hyperventilation (Figure VIII : 1).

The Mild cases had a low mean $PaCO_2$ from the first day of study. In the more severe patients, who required intubation, hyperventilation followed immediately upon this procedure. The only patients who did not hyperventilate were the Moderate group, who managed without intubation despite a considerable degree of obstruction.

Several of the conditions associated with hyperventilation were present in these croup patients. Fever (Cotes, 1968) and apprehension are unlikely causes because in the least affected, the Mild group, hyperventilation occurred as frequently as in other groups.

Hyperventilation was not consequent upon acidaemia (Cotes, 1968) for the mean base excess of those with a $PaCO_2$ < 32 mm.Hg and of those with a normal figure (32–42 mm.Hg) was not significantly different (Appendix page a67).

Most cases had some lower respiratory tract involvement, but those with severe pneumonia did not hyperventilate more than the less seriously affected. The mean pneumonia grading of chest radiographs of those with a $PaCO_2$ < 32 mm.Hg was not significantly different from those with a higher $PaCO_2$ (Appendix page a68).

The presence of the endotracheal tube itself was not the stimulus, because Mild cases, without tubes, also hyperventilated. The possibility that, at least in some patients, a rise in left auricular pressure (or cardiac failure) might have initiated hyperventilation will be discussed in Chapter IX.

Hypoxaemia may have led to hyperventilation and needs careful analysis.

The critical level of acute hypoxia that results in over-ventilation lies in the range 55-65 mm.Hg of alveolar oxygen tension (Tenney and Lamb, 1965; Weil et al, 1970). Subtracting a normal alveolar to arterial gradient, no hyperventilation should occur with arterial oxygen tensions above 45 mm.Hg. Cases in the Mild group had the lowest $PaCO_2$ but a $Pa0_2$ well in excess of the critical level. Indeed, if all patients are considered, the mean $Pa0_2$ of the hyperventilators and that of the non-hyperventilators was not significantly different (Appendix page a69).

It could be argued that if some patients had not been hyperventilating they would have been hypoxaemic. From Figures VIII : 1 and VIII : 2 it will be seen that the arterial oxygen tension of the Severe and M.IT groups had risen considerably within 24 hours of intubation, but their hyperventilation continued for longer. However, this could have been due to the known time lag between the alteration in peripheral chemoreceptor stimulus to ventilation and the return of cerebrospinal fluid pH to normal (Leusen, 1972).

Further support of the argument that hyperventilation was not secondary to hypoxaemia is that, although nursed in oxygen tents, the patients continued to hyperventilate. The period they spent out of oxygen for the purpose of obtaining arterial blood samples was too short for any ventilatory control mechanism to alter.

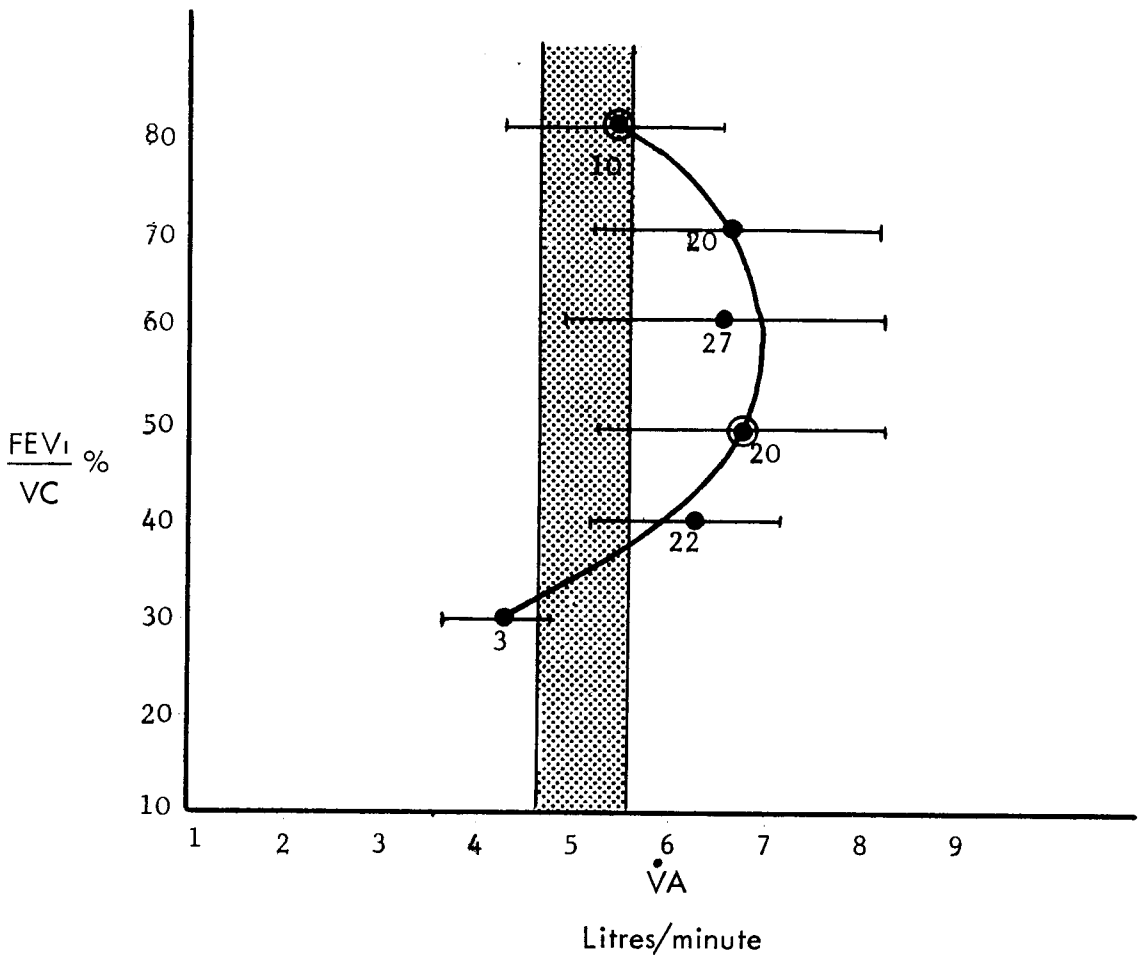
Some of the factors discussed above may have contributed to hyperventilation in individual patients, but the uniformity of hyperventilation, present in three-quarters of the patients, suggests a common cause. The basic abnormality of croup (upper airway obstruction) could be this factor.

Obstruction, as assessed by reduced air entry, bore a relationship to $PaCO_2$ (see Chapter V). With a mild degree of obstruction, the $PaCO_2$ was not normal but significantly below normal. Greater obstruction was accompanied by a higher $PaCO_2$. Furthermore, intubation converted the blood gases of the severe patient, not to normal, but to that of a mild case. The endotracheal tube presumably represented a lesser degree of airway obstruction than had been present previously.

Support for this observation was found in an experimental study of resistance breathing, where a few subjects hyperventilated at the lightest load (Eldridge and Davis, 1959).

FIGURE VIII : 4

THE RELATIONSHIP OF AIRWAYS OBSTRUCTION TO ALVEOLAR VENTILATION



The means marked by ◉ are significantly different ($p < 0,05$).

The numerals under each mean are the number of observations. The total number is 102.

The shaded portion marks the normal limits.

$\dot{V}A$ = alveolar ventilation

FEV_1 = forced expiratory volume in one second

VC = vital capacity.

To examine this theory further, pulmonary function tests of adult hospital patients with airways obstruction (asthma, non-specific obstructive lung disease, recovered tuberculosis) were analysed (Holloway and Wesley, 1972). The relationship of ventilation to airways obstruction in these cases is shown in Figure VIII : 4. The measurement of obstruction was Forced Expiratory Volume expressed as a percentage of Vital Capacity. It is evident that in this group of patients a small degree of obstruction also led to hyperventilation and a greater degree to relative hypoventilation.

Only the Moderate Conservative croup patients did not hyperventilate. It follows from the discussion above that their degree of obstruction was such that their $PaCO_2$ was normal. Without intubation they were unable to hyperventilate.

Therefore it is postulated that in croup, hyperventilation resulted from a certain degree of laryngeal obstruction. The mechanism whereby this was achieved is not known.

Hypoventilation

While hyperventilation was the commonest feature of croup, some patients did the opposite.

There were two categories of hypoventilators. In the first were 12 children who had developed a high $PaCO_2$ before intubation. The explanation could be that their airway obstruction had become so severe that they were developing ventilatory failure.

The second category consisted of 3 of the 13 M.C. cases where the $PaCO_2$ rose above 42 mm.Hg (for short periods) although they were not considered severe enough for intubation. This unusual phenomenon needs consideration.

It has been demonstrated that some normal subjects have decreased sensitivity to carbon-dioxide challenge and are prone to hypoventilate in the face of obstruction to airflow (Howell, 1966; Clark 1968; Ingram and Bishop, 1970). Also, the ventilatory response to carbon-dioxide has been found to be less the higher the initial $PaCO_2$ (Brodovsky, MacDonell and Cherniack, 1960; Tandon, 1969).

Another possibility is that the increase in $PaCO_2$ may not have been primarily a respiratory mechanism. Compensation for disease in the hypoventilators of the

M.C. group may have been via their cardiac output. The high $PaCO_2$ may be evidence that the cardiac function of these children was particularly good, and was their means of dealing with their disease.

Alveolar to Arterial Oxygen Gradient

The low arterial oxygen tension and wide alveolar to arterial oxygen gradients of the intubated children returned rapidly towards normal after intubation. By day 7 all groups were within normal limits, except the M.IT children.

In the majority the continuing factor contributing to the gradient was likely to have been a low ventilation to perfusion ratio secondary to pneumonia and mucus plugging of small airways. This factor would have recovered more slowly than cardiac output, the other cause of a widened gradient in croup.

Blood Acid Base

The restoration to normal of the arterial pH within 24 hours was found to be the common result of treatment in all but the Mild group, where the pH was normal from the first day. Three mechanisms were used to achieve this change. The first was hyperventilation: where possible the $PaCO_2$ was lowered. Only the Moderate Conservative group did not employ this method (Figure VIII : 1).

The second mechanism, the alkalinising effect of oxygen, was apparent in the intubated, and therefore more severely affected, patients. A significant ($p < 0,001$) degree of correlation between changes in base excess and in arterial oxygen tension occurred in the critical first 24 hours. Most of these patients were hypoxaemic, and presumably the oxygenation of undersaturated haemoglobin that followed intubation increased the buffering capacity of haemoglobin with the release of oxygen and the uptake of acid (Peters and van Slyke, 1931a; Davenport, 1958). Further, Naeraa, Petersen and Boye (1963) showed that a decrease in $PaCO_2$ led to an increase in oxygen affinity for haemoglobin which was independent of pH change. With improved oxygenation any anaerobic metabolism would have been reversed and lactate reconverted to pyruvate.

The third mechanism of pH elevation was employed by the Moderate Conservative group. Over the first 24 hours there was a significant rise in their base excess. In this period the group did not lower their $PaCO_2$, or raise their $Pa0_2$.

TABLE VIII : 1

MODERATE CONSERVATIVE GROUP

CHANGES IN ACID BASE OVER THE FIRST TWO DAYS OF TREATMENT

R/N	$\Delta (H^+)$ m.Eq/L	$\Delta PaCO_2$ mm. Hg	Δ B.E. m.Eq/L
552*	+ 8,94	+ 9	- 4
570	- 7,79	-14	- 0,5
513	- 1,29	+ 3	+ 4
592	+ 2,66	+ 2	+ 3
414	+ 1,79	+16	+ 5
438	- 8,43	+ 5	+ 9
920	-26,52	+14	+11
520	- 7,32	- 5	+ 5
540	-10,69	- 5	+ 6
557*	-12,97	- 4	+ 4
571	- 4,13	- 1	+ 4
628	- 5,76	+ 1	+ 5
748	-10,23	- 1	+ 7

The pH has been expressed in hydrogen ion concentration (H^+).

The acid base data have been shown as the difference (Δ) between day 1 and day 2.

* Data from day 1 and day 3.

Nevertheless, this base excess rise might still have been an oxygenation phenomenon. Therefore the oxygen content was calculated to see if it increased with the rise in pH, for alkaline blood with the same oxygen tension would hold more oxygen. The rise of the mean content from admission to days 2 and 3 was not significant. Thus it appeared that these patients did not rely on the haemoglobin buffering mechanism.

The derivation of the mean values of the M.C. group might have been obscured multidirectional acid base changes with a fortuitous mean in the alkali range.

Therefore individual case data are presented in Table VIII : 1. In 11 the data is for the first two treatment days, and in 2 the data for the second day was not obtained, but days 1 and 3 are considered. The pH has been expressed in hydrogen ion concentration for clarity.

With two exceptions the uniformity of the decrease in base deficit can be seen, which resulted in the significant change in the mean over this period (Figure VIII : 1). Two groups of patients can be discerned :-

1. In 2 there was no metabolic component to the pH change. The first showed a rise in pH in response to hyperventilation and the base excess was unchanged (R/N 570). The second showed the pH actually fell, due to a rise in $PaCO_2$ with a fall in base excess (R/N 552).
2. In 11 patients the pH change could only partially, if at all, be explained by a change in $PaCO_2$.
   i. Two were in a steady hyperventilatory state yet they raised their base excess (R/N 513, 592).
   ii. In 3 the $PaCO_2$ rose. In each the base excess increased, and the pH moved to normal or alkaline levels. (R/N 414, 438, 920). It must be considered whether the change in the metabolic component in these 3 cases could have been due to renal compensation for respiratory acidosis. The time period (24 hours) was too short for maximal renal compensation (Polak, Haynie, Hays and Schwartz, 1961) and even the maximum renal compensation would fall short of restoring the pH to normal (Winters, 1967) as occurred in these children.

Compensation for acute respiratory acidosis, over a time period when renal mechanisms could not be involved (Giebish, Berger and Pitts, 1955), would lead to a rise in bicarbonate in vivo, which would be less than expected in vitro (Winters, 1967). This difference results from a leak of bicarbonate into the interstitial fluid compartment, and leads to an actual fall in base excess. In the patients under consideration the base excess rose. Therefore neither this mechanism, nor renal compensation, could entirely explain the acid base changes that occurred. An alternative means must also have been involved.

iii. In the remaining 6 patients the $PaCO_2$ was relatively stable and in the normal range. In these there was no possible respiratory stimulant for the increase in the metabolic component that occurred. Also it was not an oxygenation phenomenon (see above).

Thus in these 11 detailed above, a primary metabolic alkalosis apparently was present as the partial or complete mechanism whereby the pH was elevated.

Metabolic alkalosis can result from external loss of acid, as in vomiting, but this was not a feature of these children. It might have followed a high alkali intake, which indeed they had, for they received 3-hourly milk feeds. But this regime was common to all; and in none of the other groups was there an unexplained rise in base excess.

As this metabolic alkalosis is a phenomenon unexplained by simple means, unusual mechanisms must be considered. Five-sixths of the body's buffer capacity exists outside the blood (Peters and van Slyke, 1931b; Relman, 1966). These cellular buffers might have been mobilised, but the stimulus for this remains obscure.

Alternatively, these cases may have lost acid into their cells (Darrow, Schwartz, Iannucci and Coville, 1948; Berliner, Kennedy and Orloff, 1951; Cooke et al, 1952). Hydrogen ions usually enter cells if there is a shift of potassium out of cells. This results in intracellular acidosis with extracellular alkalosis. Despite the alkalosis, the renal tubular cells continue to excrete hydrogen ions and the urine remains acid. The common causes of potassium loss were not operating in this group, for example diuretics, diarrhoea or vomiting. Steriods, chiefly aldosterone, but cortisone also, lead to potassium loss in the urine (Sprague et al, 1950; Bayliss, 1958;

Williams, 1968). Grollman and Gamble (1959) showed adreno-cortical hormones to have a specific alkalinising effect, apart from causing potassium loss. These children did not receive exogenous steroids. However, endogenous increases are known to occur in varying circumstances. Immobilisation (Knigge, Penrod and Schindler, 1959) physical and emotional strain (Renold, Quigley, Kennard and Thorn, 1951) malnutrition (Leonard and MacWilliam, 1964; Alleyne and Young, 1966; Rao, Spikantia and Gopalan, 1968) and infections (Klein, Papadatos and Fortunato, 1953) all result in high serum cortisol levels. Klein et al (1953) found the levels circulating during pharyngitis and pneumonia to be increased five fold above normal. Measles has been suspected of evoking high cortisol levels (Feingold, 1949; Starr and Berkovich, 1964; Holt, 1965). It has not been established whether this degree of endogenous secretion could lead to alkalinisation.

In summary, the Severe and Moderate Intubated groups used both their respiratory and haemoglobin buffer systems to return their acid base status to normal. Intubation allowed them to do this.

Mild cases used their respiratory apparatus only. Neither their oxygen tension nor base excess altered significantly over the week. Most interesting of all, the Moderate Conservative group returned their pH to normal by means of primary metabolic alkalosis.

it was not surprising that the fundamental drive in croup patients was to restore their blood pH towards normal. However, they did more than this; they raised their pH significantly above normal ($p < 0,01$). While alkalinity was a uniform reaction, the possible explanation would have to be twofold.

Patients with a certain degree of laryngeal obstruction had to overventilate and therefore their pH was above normal.

In those who could not hyperventilate, a steroid-induced intracellular acidosis could be postulated. The renal tubular cells being acid, failed to conserve hydrogen ions, so increasing the pH of the extracellular fluid to alkalaemic levels. These two mechanisms resulted in an alkaline acid base status in all patients, until their disease (upper airway obstruction or increased steroid secretion) subsided, and their arterial pH returned to normal.

SUMMARY

The pattern of the arterial blood gases was followed for a period of seven days.

The arterial pH of all groups rose over the first twenty-four hours of treatment to alkalaemic levels.

This resulted from hyperventilation and the haemoglobin buffering system in those children who were intubated. The Mild patients hyperventilated without the aid of intubation. The Moderate Conservative group alone did not hyperventilate, but their base excess rose significantly and with it their pH.

In most patients the blood gases had returned to normal within the week.

The alveolar to arterial oxygen gradient was significantly widened in all but the Mild group. This decreased rapidly in twenty-four hours and thereafter more gradually. The gradient of the Moderate Intubated group was still abnormal at the end of the week.

The possible reasons for hyperventilation in some children and metabolic alkalosis in others were discussed.

There was a small number of patients who actually hypoventilated, the mechanism for which was also discussed.

CHAPTER IX

TABLE IX : 1

CASES WHERE DIAGNOSIS OF CARDIAC ABNORMALITY WAS MADE BY MEANS OTHER THAN CLINICAL.

R/N	Group	ECG	Heart Size on X-Ray	Outcome	Autopsy
139	Severe	Not done	Large	Died	Myocardial cell hypertrophy
150	Severe	L.V.V.O.	Normal	Died	Not done
234	Severe	R.V.P.O.	Normal	Died	Not done
410	Severe	Normal	Normal	Died	R.A. & R.V. large, myocardial oedema.
458	Severe	L.ÅQRS	Normal	Alive	
581	Severe	R.V.P.O.	Normal	Alive	
144	M.IT	Biventricular overload	Normal	Died	Myocardial oedema and cell hypertrophy
191	M.IT	R.V.P.O.	Normal	Alive	
514	M.IT	?Myocarditis ?Anaemia	Normal	Alive	
519	M.IT	L.V.V.O.	Normal	Alive	
550	M.IT	R.V.P.O. and Myocarditis	Normal	Alive	
414	M.C.	R.V.P.O.	Normal	Alive	
557	M.C.	Lost	Large	Alive	
570	M.C.	L.ÅQRS	Normal	Alive	
603	Mild	R.V.P.O.	Normal	Alive	

Abbreviations

L.V.V.O. : Left ventricular volume overload

R.V.P.O. : Right ventricular pressure overload

L.ÅQRS : Leftward QRS axis

R.V. : Right ventricle

CHAPTER IX

CARDIAC COMPLICATIONS

There were indications of abnormal cardiac function in many patients. The evidence consisted of clinical, radiological, electrocardiographic and pathological features.

The cases have been divided into those where a clinical diagnosis of cardiac failure or myocarditis was made (Table IX : 2) and others without clinical signs particularly referable to the cardiovascular system, but in whom abnormalities were found in the electrocardiograph (ECG), chest X-ray or at necropsy (Table IX : 1).

The data on the abnormal electrocardiographs with concurrent arterial blood gases, haemoglobin and chest X-ray scores are given in the Appendix (pages a70-74).

RESULTS

1. A total of 27 cases had evidence of abnormal cardiac function. This was 42% of the total series.

2. Symptom-free Group (Table IX : 1).

   It was striking that half (15) had no clinical evidence of cardiac involvement. Four of these died. Twelve had electrocardiographic changes, 2 an enlarged cardiac shadow on radiograph and one hypertrophy of the right atrium and ventricle at necropsy.

   Summary of ECG changes in Symptom-free Group:

R. ventricular pressure overload	:	5*
L. ventricular volume overload	:	2
Isolated left QRS axis	:	2
Myocarditis	:	2*
Biventricular overload	:	1

   * One patient had R. overload pattern with localised L. ventricular myocarditis.

3. Cardiac failure was the clinical diagnosis in 9.

   The relevant ECG, radiograph and necropsy features appear in Table IX : 2

TABLE IX : 2

CASES WHERE DIAGNOSIS OF CARDIAC ABNORMALITY WAS MADE CLINICALLY

	R/N	Group	ECG	Heart Size on X-Ray	Outcome	Autopsy
Clinical Failure	406	Severe	S.T.	Normal	Died	Not done
	225	M.IT	L.$\dot{A}$QRS	Large	Died	R.V. dilated; Liver suggestive CCF.
	417	M.IT	S.T.	Large	Died	R.V. dilated Histo : normal
	604	M.IT	Myocarditis	Normal	Died	Not done
	705	M.IT	Biventricular overload	Large	Alive	
	592	M.C.	Not done	Not done	Died	Not done
	200	Mild	S.T.	Normal	Alive	
	216	Mild	?Myocarditis ?Hypoxic damage	Normal	Alive	
	496	Mild	Myocarditis	Normal	Alive	
Clinical Myo-carditis	530	Severe	Myocarditis	Normal	Alive	
	497	M.IT	Normal	Normal	Alive	
	632	M.IT	L.V.V.O.	Normal	Alive	

Abbreviations

S.T. : Pulse >180/minute

L.$\dot{A}$QRS : Leftward QRS axis

L.V.V.O. : Left ventricular volume overload

R.V. : right ventricle

CCF. : cardiac failure

and abnormalities in these were present in 6 of the 9 cases.

4. Myocarditis.

(a) This diagnosis in 3 cases was based on the following findings :-

R/N 497: Soft first heart sound and prominent third heart sound initially; bradycardia later (ECG normal).

R/N 530: Relative bradycardia with soft first heart sound which persisted for some days (ECG compatible with myocarditis).

R/N 632: Triple rhythm just before intubation. Thereafter bradycardia with a prominent third heart sound, both features disappearing with recovery. (ECG: left ventricular volume overload).

(b) A further 3 had evidence of myocarditis on ECG, which changes were unlikely to have been caused by metabolic factors (See discussion). (R/N 604, 496, 550).

(c) Two had electrocardiographic changes compatible with myocarditis but were also hypoxaemic (R/N 216) or anaemic (R/N 514).

5. Relationship to the Severity Group.

The higher incidence of cardiac abnormalities in patients with more severe upper airway obstruction, compared with those with less obstruction, was statistically significant ($p < 0,05$).

GROUP	NO. WITH CARDIAC ABNORMALITIES		
Severe (14) *	8	19	$p < 0,05$
M.IT (19)	11		
M.C. (13)	4	8	
MILD (17)	4		

* Total cases in Group.

6. Mortality Rate.

Of the 27 cases under consideration 9 died (33%). As there were 13 deaths in the whole study, it follows that in only 4 fatal cases was there no evidence of cardiac dysfunction.

DISCUSSION

A summary of the incidence of cardiac abnormalities in this series is given in Table IX : 3.

TABLE IX : 3

Cardiac abnormalities in total series	:	27 (42%)
Cardiac abnormalities in fatal cases	:	9 (69%)
Cardiac abnormalities in intubated cases	:	19 (58%)
Cardiac abnormalities in non-intubated cases	:	8 (27%)

It was evident that cardiac involvement was most common in the more severely affected, and an important contributory cause of death. However, in only half the affected patients was cardiac embarrassment clinically obvious. In the remainder the evidence was usually electrocardiographic. Therefore the interpretation of the ECG is important.

The standards for normal tracings in the paediatric age group, and the criteria used for right and left ventricular overload, were taken from standard references and are given in the Appendix (pages a75, a76).

In one-third of cases there was evidence of ventricular overloading. In a further 3 the only abnormality was leftward deviation of the QRS axis. While this feature is not necessarily abnormal, an axis of 0 to + 20° in the age group under consideration is so unusual that left ventricular overload should be suspected (Cassels, 1966). In addition, left axis deviation has been described as an isolated abnormality in children with respiratory diseases, including asthma (Moller, Carlson and Elliot, 1968).

There is no electrocardiographic pattern characteristic of myocarditis, but disturbances in conduction and rhythm, with T wave inversion or flattening and occasionally ST depression or elevation are indications, especially when subsequent tracings show variation (Diehl, 1966). In addition, ventricular premature beats, low voltage and left ventricular preponderance have been noted (Saphir and Amromin, 1948; Fine, Brainerd and Sokolow, 1950).

ST-T wave changes are not specific for myocarditis and have been described

with alkalaemia (Barker, Schrader and Ronzoni, 1939; Thomson, 1943) and with hypoxic or anaemic myocardial damage (Goldman, 1970). In only 2 of the 8 possible cases of myocarditis was there likelihood of these factors contributing to the electrocardiographic changes. One patient had a sustained low PaO_2 and one a moderate anaemia (7,7 gms%). The electrocardiographic abnormalities persisted despite treatment of these patients in oxygen tents.

Potassium deficiency also can lead to similar ST segment and T wave alterations (Ferencz, 1966). This cause cannot be definitely eliminated as serum electrolytes were not measured, but other electrocardiographic features of hypokalaemia were absent.

In the remaining 12 patients the evidence of cardiac involvement was based on clinical findings (Table IX : 1).

Cardiac failure developed in 9. Diagnosis of right, left or biventricular failure in the presence of respiratory disease is difficult. If two or more of the following signs occurred, failure was thought to be present: sustained pulse rate of 200/minute or more; sudden increase in respiratory rate or change in character of dyspnoea; rapid appearance and disappearance of wide-spread crepitations; enlarging liver; and triple rhythm (Rudolf, 1965; Rao, Srikantia and Gopalan, 1968).

A clinical diagnosis of myocarditis was made in 3 patients. In a further 5 this condition was thought to be present. The difficulties in making an electrocardiographic diagnosis of myocarditis have been discussed previously. Similarly the histological diagnosis of this condition is not an easy one. None of the 8 children in whom myocarditis was suggested came to necropsy. In a further 2 in whom this was undertaken some individual myocardial cell hypertrophy was noted. Generally, however, the poverty of histological change militates against the seemingly high incidence of myocarditis suggested by other means.

Myocarditis is a well described complication of infectious diseases and pneumonia (Neubauer, 1944; Painton, Hicks and Hantman, 1946; Saphir and Amromin, 1948; Fine, Brainerd and Sokolow, 1950; Ross, 1952). Damage to the myocardium may be either bacterial or viral in aetiology (Diehl, 1966). In this series the evidence tended to favour a bacterial cause. All but one with

myocarditis had severe secondary infection which was slow to respond to treatment. Further, the mean chest radiograph score of this group was double that of patients without myocarditis, but did not reach statistical significance ($0,1 > p > 0,05$). (Appendix page a77).

There are many other factors besides myocarditis that may lead to cardiac dysfunction or failure. On the evidence available in this study it is not possible to do more than discuss these factors separately. To predict the result of a combination of variables on cardiac function would be extremely difficult.

In this patient population several unfavourable factors were present, which would increase the likelihood of respiratory stress having a significant effect on the heart.

Malnutrition, present in the majority, has a direct effect on myocardial function (Smythe, Swanepoel and Campbell, 1962; Alleyne, 1966; Wharton, Howells and McCance, 1967).

Most of the children were anaemic, some quite severely so; another factor detrimental to cardiac performance. A compensatory rise in cardiac output in the more severely anaemic patients, would have been an unfavourable base-line from which a further rise would have had to occur as a result of respiratory disease and infection (Rodman, Close and Purcell, 1960; Duke and Abelmann, 1969; Cropp, 1969).

Probably most important in croup would be the depressant effect of hypoxia and acidaemia on the myocardium. (Darby, Aldinger, Gadsden and Thrower, 1960; Karis, Harmel and Hoffman, 1960; Stewart, 1964; Jones, 1966; Rees, Stead, Bush and Jones, 1966). Further, hypoxaemia and hyperventilation, the commonest blood gas pattern in croup, has been called "the inappropriate ventilation of the critically ill" and is conducive to the occurence of arrythmias (Ayres and Grace, 1969).

Against this background, the mechanical effects of obstructed respiration should be considered. Large intrathoracic pressure swings must have occurred, with an effect on the blood vessels of the lung.

A small increase in negative intrathoracic pressure would be accompanied by an increase in pulmonary blood flow, with a resultant small rise in cardiac output

(Guyton, 1963b; Daly and Hebb, 1966a). A larger increase in pressure would not lead to any additional rise in cardiac output, the venous return being determined by the collapse of veins entering the thorax (Guyton, 1963b).

The primary effect of positive intrathoracic pressure, on the other hand, restricts the inflow of blood from the systemic vessels to the right heart and leads to a fall in cardiac output. Such a fall would be restored to normal, provided compensatory mechanisms were effective (Guyton, 1963b).

Thus while a rise in cardiac output would be needed in response to increased metabolism from infection (Guyton, 1963a) and hypoxia (Asmussen and Neilson, 1955; Kahler, Goldblatt and Braunwald, 1962; Guyton, 1968) this would be hampered by the mechanical effects of breathing in croup.

The results of resistance breathing were directly investigated by Visscher and his co-workers. In studies on dogs they demonstrated that breathing against a resistance, whether inspiratory or expiratory, produced pulmonary oedema (Zinberg, Nudell, Kubicek and Visscher, 1948; Haddy, Campbell and Visscher, 1950). In these experiments a rise in pulmonary venous pressure regularly occurred, sufficient to overcome the pulmonary capillary osmotic pressure, and they postulated that this was the explanation for the pulmonary oedema.

Probably more important than these mechanical considerations were the finer adjustments of the pulmonary circulation which depend on blood gases and acid base. Hypoxia of a degree of 80% saturation, acidaemia and hypercarbia elevate pulmonary artery pressure. Their effects are augmented if they occur simultaneously. The mechanism is via carotid and aortic chemo-receptors and the sympathetic nervous system. But alveolar gas mixtures, acting locally and directly, also regulate the pulmonary circulation (Liljestrand, 1958; Fishman, 1961; Enson et al, 1964; Cournand, 1964; Aviado, 1964; Daly and Hebb, 1966b; Comroe, 1966b).

But, whatever the effect produced by respiratory disease, the pulmonary vascular bed has enormous reserves. Doubling of the pulmonary blood flow need not be attended by a significant increase in pulmonary artery pressure or alteration of cardiac output (Charms, Brofman, Elder and Kohn, 1958; Comroe, 1966b).

Both mechanical and biochemical factors affect the pulmonary vasculature and exert their main influence on the right heart.

However, the left heart does not escape involvement in pulmonary disease, and there was evidence, chiefly electrocardiographic, that in one-third of the children under consideration, left heart strain occurred.

The function of the left heart in pulmonary disease has been the subject of fewer investigations than that of the right heart. The earliest observation of left ventricular hypertrophy was noted at necropsy on adults with chronic obstructive airways disease. (Altshule, 1962; Fishman, 1971). With the improvement of techniques for measuring left ventricular performance, disturbed function of this ventricle has been found in conditions when only abnormal right ventricular function would have been expected (Olson, Ellenbogen and Iyengar, 1961; Rao, Cohn, Eldridge and Hancock, 1968; Graham, 1970; Urschel et al, 1971; Kelly et al, 1971; Salel, Mason, Amsterdam and Zelis, 1971; Baum, Schwartz, Llamas and Castillo, 1971). Right ventricular overload is thought to lead to encroachment by the septum on the left ventricular cavity and outflow tract. This effect, called the "reversed Bernheim phenomenon" (Dexter, 1956) is unlikely to be involved in acute respiratory disease, because very severe right ventricular hypertrophy is required to achieve this result.

A large body of opinion supports the direct effect of hypoxia, hypercarbia and/or acidaemia upon the myocardium as the cause of left ventricular dysfunction (Altshule, 1962; Fishman, 1971; Baum, Schwartz, Llamas and Castillo, 1971). But this opinion is concerned with chronic, not acute respiratory disease.

In other chronic pulmonary conditions, for example, bronchiectasis, proliferation of bronchopulmonary anastomoses has been demonstrated, and a left to left shunt of considerable proportion created. The burden of this increased blood flow falls on the left heart (Roosenberg and Deenstra, 1954; Cudkowicz, Calabresi, Nims and Gray, 1959; Nakamura et al, 1961). In acute respiratory disease anatomical anastomoses would not be expected. But the existing bronchopulmonary circulation could dilate secondary to hypoxia (Daly and Hebb, 1966c). There appears to be no published study of the magnitude of augmented flow through this system in acute disease, or the possibility that it might cause stress to the left heart.

A rider to the above concept needs consideration. In heart disease it is known that ventilation is increased. This phenomenon is related to raised pulmonary venous pressure secondary to increase in left auricular pressure (Gazetopoulos, Davies,

Oliver and Deuchar, 1966). The actual cause is unknown. If augmented bronchopulmonary flow with subsequent left atrial pressure increase occurred it might explain, at least in some of these cases, the hyperventilation commonly observed in croup.

Notwithstanding the above considerations of right and left ventricular involvement in respiratory disease, it has been established that cardiac output is directly related to the $PaCO_2$ (Theye, Milde and Michinfelder, 1966; Prys-Roberts, 1970; Norman and Atkinson, 1970). It would appear that this occurs via reduced sympathetic nervous activity but the exact mechanism is not clear (Moster, Reier, Gardier and Hamelberg, 1969).

Finally, pulmonary oedema can be a feature of respiratory disease. An established cause of pulmonary oedema is resistance breathing, discussed previously. Inflammatory hyperaemia and altered permiability of vessel walls also have been incriminated in the aetiology of pulmonary oedema (Guyton, 1966; Hinshaw, 1969). Subsequently, damage to alveolar and bronchiolar cells, including Clara cells, has been found to interfere with surfactant production (Cutz and Cohen, 1970). This derangement of active surface material predisposes to pulmonary oedema (Wang, Huang and Thurlbeck, 1970), and could be an important factor in croup, when extensive secondary infection was present.

Lastly, pulmonary oedema can occur as a result of hypoxia, possibly through pulmonary venous constriction (Hultgren, Spickard, Hellriegel and Housten, 1961; Greene, 1965). However, the degree of hypoxaemia necessary ($Pa0_2$ 34-40 mm Hg) was seldom observed in the present study.

In summary, clinical recognition of abnormal cardiac function in croup was not infrequent but, in addition, a number of patients had only electrocardiographic evidence of cardiac embarrassment.

That right heart strain should occur was expected. But the left heart was frequently involved, the mechanisms of which were less obvious. A sequence of events leading to left heart strain in croup could include myocardial damage from hypoxia, anaemia, acidaemia or infection, an increase in bronchopulmonary flow with left atrial overload, and subsequent hyperventilation. The reduction in $PaCO_2$ would be accompanied by a fall in cardiac output.

SUMMARY

Cardiac function in croup was assessed by clinical and electrocardiographic means, and from chest radiographs and necropsy results.

Some indication of cardiac embarrassment was present in 42% of children, although in only half of these was this obvious clinically.

The incidence was higher the more severe the airways obstruction, but there was suggestive evidence that it was influenced also by the degree and control of the secondary pulmonary infection.

Factors which might have contributed to the high incidence of cardiac complications in this patient population were discussed.

The possible mechanisms for cardiac involvement in pulmonary disease, especially airway obstruction, were reviewed.

CHAPTER X

CHAPTER X

A LINEAR-DISCRIMINANT SCORING SYSTEM FOR CROUP

INTRODUCTION

Clinical signs likely to attract the attention of the inexperienced have been shown to be relatively unhelpful in the assessment of how to treat a patient with croup.

Familiarity with the syndrome permits judgment of a case based upon several variables. But where croup is seen sporadically or where the decision must be made by a relatively inexperienced observer, there is either no opportunity or insufficient time for the development of clinical acumen.

However, there are variables which alter with the severity of the disease and which can be measured. These have been examined to see whether a simple scoring system could be devised which would be helpful in the assessment of patients.

METHOD AND MATERIAL

The linear-discriminant function is a regression relation that allows an efficient binary classification of a population of which each member can be described by a set of variables.

A weighting co-efficient for each variable is determined so that a subject's discriminant score, that is, the sum of weighted variables for that subject, is the maximally efficient linear combination that may be used to classify that subject into one of two mutually exclusive sub-sets of the population. No numerical method would allow perfect segregation into these two groups, but even in the presence of overlap, an objectively derived estimation of disease severity can be obtained.

By means of the linear-discriminant method (Kendall, 1957) weighting factors were calculated for 5 variables: arterial pH, $P0_2$, $PC0_2$ and pulse and respiratory rates. These data, obtained at the initial clinical assessment, were those of the 2 most widely separated clinical groups : one group defined by death

TABLE X : 1

LINEAR-DISCRIMINANT SCORES

SCORE	DEAD	OTHERS	MILD
	R/N	R/N	R/N
-55-59	406*		
-50-54			
-45-49			
-40-44	224*	530*	
-35-39	567*		
-30-34		534*	
-25-29	417*, 139*	458*	
-20-24	225*	558*	
-15-19	150*, 604	170*, 665*	216
-10-14	411*, 527*, 410*	628, 570, 540	
-10 Line			
-5-9	592	191*, 632*, 505* 552*, 141*, 550*	532, 496
-4-0		520, 920, 166*	466
0-4		438, 557, 571	463
5-9		469*, 202*, 140* 497*, 705*	603
+10 Line			
10-14			233,639
15-19		748	590, 248, 577
20-24		513	468, 547, 224
25-29			200, 629
30-34		414	416

*Intubated Patients

and one group with almost no likelihood of death, that is, the Mild patients.

With the equation derived from the data of these two groups, all the patients were scored. The equation was then mathematically manipulated so that the maximum number of patients who were neither dead nor those who were Mild fell in a certain range of the score (-10 to + 10).

The equation derived by the method described above for calculating the discriminant score was

$$y = 0,57.Pa0_2 - 0,29.PaC0_2 + 35,41\ pH - 0,27.\text{Pulse Rate} - 0,51.\text{Respiratory rate} - 222,3.$$

RESULTS

The discriminant scoring of each patient appears in Table X:1. In the left-hand column are the dead patients and in the right-hand column the Mild patients. The middle column consists of the remainder of the patients.

i. -10 Line

All those who died scored less than -10 except one. All the Mild patients scored more than -10 except one. Of the survivors who were not Mild, 10 scored less than -10 : 3 of these were unintubated.

ii. Between +10 and -10 Lines

The majority were clinically Moderate (whether or not they were intubated). But 5 Mild cases also fell into this area, as did 2 Severe patients. (R/N 141, 469).

iii. +10 Line

Most of the clinically Mild patients scored more than +10, but so did 3 conservatively treated Moderate cases.

DISCUSSION

The clinical features used to assess the degree of upper airway obstruction were cyanosis, muscular tone, alertness and air entry reduction on auscultation. Three groups emerged from this clinical exercise.

No difficulty was experienced in dividing those with severe from those with mild obstruction. Much more helpful would have been the clinical division of the Moderate group into those who needed intubation and those who did not. However, often this was not possible on initial assessment.

The linear-discriminant scoring was based on different variables from the clinical classification. By this method the same patients were again divided into 3 groups, which could be thought of as mild (score > + 10) moderate (score between -10 and +10) and severe (score < -10). The populations of these groups, which will be called L-D groups, were somewhat different from those determined by clinical means.

However, the severe L-D group had a mortality rate (50%) identical to that of the clinical Severe group. Furthermore, the clinical Moderate Conservative and the moderate L-D groups had similar mortality rates.

Measles, with its immunological incompetence, might have biased the prognosis of any one of the clinical groups, by having an inordinately high measles population. Chi-Square statistical method applied to this problem showed that the fluctuations of disease (measles and "virus") were consistent with a random variation.

Thus, by applying discriminants of quantifiable measurements, the most severely affected patients could be detected without any information dependent upon previous experience of the syndrome.

Examination of "Misclassifications" by the Linear-Discriminant scoring method.

i. Clinically Mild case in the L-D severe group: This child had mild airway obstruction, but also cardiac failure which resulted in the discriminant variables (pulse and $Pa0_2$) being adversely affected. Clinical examination of air-entry would have been needed to indicate that medical treatment and not intubation was required.

ii. Three clinically Moderate Conservative patients in L-D severe group: (R/N 540, 570, 628). All the discriminant variables of these 3 tended to be at variance with the average for the M.C. group. The reason for this was not obvious, although 2 of the 3 had moderately severe underlying pneumonia. They responded rapidly to conservative treatment.

iii. Fatal case in L-D moderate group.
Fatal cases used for calculating the variable weights were uncorrected for time of death. The patient in question was clinically moderate, but his secondary infection was uncontrolled and he died of pneumonia two weeks after assessment.

iv. Five clinically Mild cases in the L-D moderate group.
All had favourable (for croup) blood gases but high pulse and respiratory rates. These high rates might have been accounted for by severe infection present in 3. The presence of normal air entry would have indicated that their score was affected by a complication of croup and not by upper airway obstruction.

Comment on "Misclassification"

The variables used for scoring were relatively non-specific and could be affected by the presence of complications of croup (cardiac failure, infection, anaemia, etc.).

Therefore, the scoring method apparently registered the total load of the syndrome more accurately than by clinical means, which latter method had been aimed specifically to assess the degree of upper airway obstruction.

The scoring method placed several M.IT patients in the L-D severe group, which suggests that their condition was more precarious than had been thought on clinical grounds.

Also there were several intubated children amongst those with a moderate score, which group had a mortality similar to that of the M.C. group. It is possible that some were intubated unnecessarily.

Use of the Score

If a patient scored less than -10 intubation would be needed. A score of more than +10 should suggest that conservative treatment was sufficient.

A patient with a score -10 to +10 might require intubation. If a clinical decision were difficult, re-scoring in 3 to 4 hours would detect a favourable or otherwise trend, perhaps earlier than by clinical criteria. If the score had moved in the direction of minus, intubation should be undertaken.

Conclusions

To the clinician who may be unaware of the nuances of blood gas changes and some of the clinical features of croup, the value of the linear-discriminant classification would be to alert him to severe illness. By observing the degree of air entry reduction in conjunction with the score, it should be possible to decide between intubation and careful conservative management.

Croup is not a static disease, and re-scoring after a time interval would assist in decisions on treatment in difficult cases.

SUMMARY

A scoring system for croup was investigated, using the linear- discriminant method. The variables chosen for statistical weighting had been established as useful in the assessment of the severity of croup, and were measurable.

The data used to calculate the weights were taken from two mutually exclusive groups: the patients who died, and those who were classified Mild.

The discriminant equation that resulted was applied to all the patients in the series. By this means, three severity groups were achieved which had identical prognoses and similar constituent patients, as the original clinical divisions.

However, there was some overlap in the scores of the patients who were intubated and those who were not.

This overlap arose from the complications of croup, which affected the variables in the equation. Nevertheless, the scoring system should prove useful when taking decisions on the management of cases, for little clinical experience need be invoked.

CHAPTER XI

SUMMARY AND CONCLUSIONS

CHAPTER XI

SUMMARY AND CONCLUSIONS

In children handicapped by poor socio-economic circumstances, malnutrition and recurrent infections, laryngotracheobronchitis is a formidable problem.

To improve the prognosis of such patients a ward was established with equipment for standardising therapy, and staffed by a relatively stable team of personnel.

A preliminary study, done in this unit, indicated the problems that a more comprehensive investigation into croup should encompass.

Standard observations of the clinical signs of infective upper airway obstruction were noted in all patients. On the basis of these features children were divided into 3 groups according to the severity of airway obstruction. If a decision to overcome the obstruction (by intubating the trachea) was made, the physical signs present at the time were also recorded.

A study of the arterial blood gases sought to establish an understanding of the underlying pulmonary patho-physiology. Arterial blood specimens were obtained at frequent intervals over one week. The results were not used in the classification of patients into severity groups. Clinical and biochemical features were correlated later.

Change in ventilation in response to a carbon dioxide challenge was measured in some patients before and after intubation.

Information on cardiac function was collected from clinical and electrocardiographic features, chest radiographs and necropsy examinations.

Sixty-three African children were studied, aged 5 months to 5 years. All had viral croup, two-thirds being due to measles. When graded clinically there were 14 with Severe, 32 with Moderate and 17 with Mild croup.

All the Severe and 19 of the Moderately classified patients required intubation. Twelve of these (36%) subsequently died. In one-third of the survivors primary

extubation on the seventh day failed and this usually resulted from severe or uncontrolled underlying pneumonia.

Of the 30 children that were managed conservatively (that is, without intubation) 13 were in the Moderate group and the remainder were mildly affected. There was one death from pneumonia. Characteristic of these patients was the ease, in contradistinction to the intubated group, with which their secondary bacterial infection was controlled.

The physical signs of airway obstruction were considered in conjunction with the concurrent blood gases. As air entry on auscultation diminished the arterial pH and oxygen tension fell while the carbon dioxide tension rose. This correlation was considered important but this physical sign is particularly observer-dependent and confirmation by quantitative methods is required.

Reduced muscle tone and lack of interest in surroundings were accompanied by a significantly lower PaO_2 than that of children without these features.

Restlessness and recession were not reliable signs for grading severity of obstruction. They were often more marked in Moderate than in Severe cases. Neither of these signs correlated with blood gases.

An haemaglobin of less than 9 gm% and PaO_2 of less than 300 mm.Hg. on pure oxygen breathing were related significantly to the deaths in this series.

Aspects of intubation were considered. This procedure led to immediate clinical relief from the laboured breathing of croup and, therefore, appeared to be beneficial. As judged by the increase in ventilation on carbon dioxide challenge, intubation was indeed shown to overcome a considerable degree of upper airway obstruction. A few patients, however, did not make use of this improved ability to ventilate, which suggested that they did not need to do so, and possibly that intubation had not been necessary.

The immediate effect of intubation was, if anything, detrimental to the alveolar to arterial oxygen gradient. An increase in both ventilation to perfusion imbalance and in true shunt, with a fall in cardiac output were likely to have contributed to this feature. The possibility that the gradient widened in some patients because maintenance of positive end-expiratory pressure had been interrupted by intubation

was supported by the results of one subject given a carbon dioxide challenge.

Another effect of intubation was to allow the blood gases of these more severely obstructed children to revert, not to normal, but to the pattern of the mild disease. That is, it permitted hyperventilation and thus recovery of the arterial pH.

An analysis of the blood gases and acid base in croup was a previously neglected field of study.

The early response to treatment of all severity groups was not the achievement of a normal acid base status, but that of alkalaemia. After intubation the rise in arterial pH was accomplished by the Severe and Moderate Intubated groups via hyperventilation and the haemoglobin buffer system. The Mild cases were hyperventilating from the first day of study.

The Moderate Conservative patients, with a degree of upper airway obstruction which apparently precluded hyperventilation, nevertheless also raised their pH as far and as fast as the other groups had done. They achieved this via a metabolic route, the trigger for which mechanism could only tentatively be suggested.

Several days were required for the acid base of the more severely affected patients to return to normal.

The most striking aspect of croup, the preference for alkalaemia, was accompanied by an increased alveolar to arterial oxygen gradient composed of considerable ventilation to perfusion imbalance and significant intrapulmonary shunting of blood. This feature had not recovered at the end of a week in some children.

The initial effect of the disease process, that is, of mild airway obstruction, was hyperventilation and some degree of hypoxia. If obstruction increased it was then accompanied by a rise in $PaCO_2$, a further fall in PaO_2 and the development of metabolic acidaemia. The alterations of $PaCO_2$ in croup are now better understood. In the presence of clinical evidence of obstruction, if the $PaCO_2$ is low, the patient is coping with his disease load. If normal, it frequently indicates significant obstruction and such a value should be regarded as high for croup, having risen from hyperventilation levels. The movement of the $PaCO_2$, first down and then up, is thought to be related to mild followed by more severe airway obstruction.

Indications for intubation have been derived from this study. They can be divided into two categories. In the presence of obstruction (stridor, recession and

reduction of air entry on auscultation) they are :-

Absolute Indications :

Cyanosis, obvious muscular hypotonia, unawareness of surroundings. If any of these are present intubation is urgently needed.

Additive Indications :

If two or more of these are present, then intubation is needed :-

Pulse rate > 170/minute and respiratory rate > 55/minute.

"High" $PaCO_2$ i.e., > 37 mm.Hg.

PaO_2 < 50 mm.Hg.

The presence of a complication :

i) Cardiac failure

ii) Uncontrolled infection

iii) Severe clinical pneumonia.

It is unlikely that a child with croup will need to be intubated if he has :-

Good muscle tone and interest in his surroundings.

A pulse rate of <160/minute and respiratory rate of < 50/minute.

An alkali pH (whether due to metabolic or respiratory factors).

$PaCO_2$ < 32 mm.Hg.

Croup is not a static condition. Therefore repeated assessment of a child is necessary until his condition has stabilized.

In some patients intubation alone may be insufficient and may need to be followed by tracheostomy and mechanical ventilation. This was suggested by two deaths from cardiac arrest in probable hypoxic circumstances. Also, severe clinical lower respiratory tract involvement was not unusual, as confirmed by the degree of intrapulmonary shunting of blood present in some patients.

The complications of nasotracheal intubation that occurred were blockage of the tube by secretions (2 cases) and laryngeal stenosis (1 case). This technique was compared with the older method of tracheostomy. It was concluded that the hazards of both procedures had similar incidence, in our hands. If the nasotracheal method is used, tracheostomy should be proceeded to in the following situations :-

i) Blockage of the nasotracheal tube, indicating unusually copious secretions.

ii) Failure of primary extubation after 7 days.

iii) Inadequate control of lower respiratory tract infection.

To simplify the decision to intubate for the relatively inexperienced practitioner, a scoring system was devised, employing the linear-discriminant method. The variables used were measurable and therefore independent of previous experience of the syndrome.

The discriminant equation obtained from the data in this study was :

$y = 0,57.PaO_2 - 0,29.PaCO_2 + 35,42.pH - 0,27.\text{Pulse rate} - 0,51.\text{respiratory rate} - 222,3.$

By means of this scoring system the study patients could be divided into 3 groups which had somewhat different populations from the groups obtained by the clinical classification. But a severe group, defined by either method, had the same prognosis.

However, there was some overlap of the scores of patients who had been thought to require intubation and those who had not. This overlap apparently resulted from the frequent occurrence of complications in the patients studied, which affected the variables used in the equation.

These complications contribute to the problem of therapeutic management that the African child presents, and adds to the burden of his airway obstruction. There was an almost universal occurrence of secondary bacterial infection, frequently by gram-negative organisms and often difficult to control. This aspect was presumably related to the known depression of immune responses caused by malnutrition and measles. Anaemia and cardiac decompensation, with or without myocarditis, were frequent problems.

Nevertheless, the relatively inexperienced doctor would obtain guidance from the use of the discriminant equation in the management of the occasional case of croup.

FUTURE WORK

Cognisance must be taken of the importance of lower respiratory tract involvement in prognosis. The problems that need study are concerned with the selection of cases for management by mechanical ventilation and the possibility that positive end-expiratory pressure would be beneficial.

The application of the linear-discriminant equation to a prospective series is in progress and should result in more precise assessment of patients. The equation might be recalculated with increased data. The addition to the discriminants of air entry on auscultation must improve the value of the equation. A method of quantitative measurement of this physical sign is being developed.

The probable correlation of hyperventilation and the degree of upper airway obstruction might be clarified by a study of gas flow to volume "wash-in" relationships.

More information is required on the metabolic alkalaemia exhibited by a small group of children and on the role of the cardiovascular system in croup. The techniques involved in such research are difficult and therefore these fields are likely to remain neglected for the present.

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APPENDIX

KEH. 2157(a)

KING EDWARD VIII HOSPITAL, DURBAN

CROUP QUESTIONAIRE

NAME: HOSP.NO. N-Tet.No: AGE SEX RACE

Date of Admission to Hospital:
Date of Admission to Special Care Unit:

HISTORY:

First symptom and onset date:
Date of onset of croupy cough:
Time between first symptom and croup:
Previous hospital admissions:
Previous respiratory infections:
Other previous illness:

Is measles suspected? YES NO. Is Diphtheria suspected? YES NO.

Illness of other members of family within last two months.

EXAMINATION: Ring correct answer.

Hoarseness	YES	NO	Resp. Rate		
Brassy cough	YES	NO	Pulse rate		
Stridor	YES	NO	Cyanosis	YES	NO
Recession: Intercostal:	YES	NO	Hypotonia (arm test):		
Supraclavicular	YES	NO	Falls on face		
Substernal	YES	NO	Falls away from face		
Sternal	YES	NO	Resists		
Coarse rhonchi	YES	NO	Restlessness (position changing):-		
Wheezing	YES	NO	YES		
Crepitations	YES	NO	NO		
Bronchial breathing	YES	NO	Painful stimuli (Thigh pinch)		
Culture taken	YES	NO	Awareness		
Air Entry reduced	YES	NO	Indifference		

ASSESSMENT OF SEVERITY (BEFORE TREATMENT) : INDICATE:

Mild Stridor + recession only

Severe Stridor + recession; and/or indifference and/or hypotonia and/or cyanosis

Moderate Inbetween mild and severe

RELIEF AFTER TREATMENT: (a) Intubation

(b) Moist 0_2 and sedation (within 4 hours)

Delete which not applicable.

Recession:	Complete Only quiet breathing
Restlessness:	Partial Goes to sleep
Hypotonia:	ISQ Improved
Painful stimuli:	Awareness Indifference
Cyanosis:	Partial Complete

Pulse rate _____

Respiratory rate _____

EXAMINATION OF LARYNX:

1. Superior aperture:

   (Cuneform and Corniculate tubercles + Aryepiglottic folds + epiglottis).
   N.A.D. Oedematous Reddened Membrane Present Lumen narrow.

2. Vestibular folds:

   N.A.D. Oedematous Reddened Membrane Present Lumen narrow.

3. Rima glottidis + Cords:

   N.A.D. Oedematous Reddened Membrane Present Narrow.

4. Infra glottic area:

   N.A.D. Oedematous Reddened Membrane Present Lumen narrow.

   Viral Picture: (Infraglottic oedema/inflammation).

   Bacterial Picture: (Supraglottic oedema/inflammation).

INTUBATION/TRACHEOSTOMY NOTES:

Operation:

Time and Date:

Sedation:

Tube:

Respiratory Unit. King Edward VIII Hospital.

EXAMINATION OF THE LARYNX AND TRACHEA.

Name: Age: Sex: Race:

Hospital No.:

Respiratory Unit No.:

Date of Examination:

Indications for Examination:

Provisional Diagnosis:

LARYNGOSCOPY:-

Type of Anaesthesia:

Supraglottic area: (includes epiglottis, aryepiglottic folds, arythenoid region and vestibular folds)

Vocal cords: (indicate any anatomical or pathological abnormality and comment on movement)

Subglottic area: (area immediately below vocal cords only)

TRACHEOSCOPY:-

Diagramatic Appearances of Larynx:

Opinion and Final Diagnosis:

ANTIBIOTIC DOSAGE

Benzyl penicillin	:	0,25 - 0,5 million units 6 hourly intramuscular
Phenoxymethyl penicillin	:	250 mg 6 hourly orally
Ampicillin	:	250 mg 6 hourly orally or intramuscular
Cloxacillin	:	250 mg 6 hourly orally or intramuscular
Carbenicillin	:	200 mg/kg/day in 4 divided doses intramuscular
Cephaloridine	:	80 mg/kg/day in 4 divided doses intramuscular
Chloramphenicol	:	80 mg/kg/day in 4 divided doses orally
Kanamycin I.M.I.	:	10 mg/kg/day in 2 divided doses intramuscular
Gentamycin I.M.I.	:	1 mg/kg/day in 2 divided doses later 3 - 5 mg/kg/day intramuscular

Electrolyte Solution : Half Concentrated Darrows contains:-

Sodium	61 MEq/L
Potassium	17 MEq/L
Chloride	51 MEq/L
Lactate	27 MEq/L
Dextrose	25 gms/L

WEIGHTS OF PATIENTS : BOSTON SCALE

Percentile	Number of Patients	
> 50th	8	
50th	1	
< 50th	5	
25th	0	
< 25th	13	
10th	2	
< 10th	8	
3rd	1	
< 3rd	25	(40%)
	63	

CASE SUMMARIES

Abbreviations Used.

A	Ampicillin
Ce	Cephaloridine
G	Gentamycin
Ca	Carbenicillin
Cl	Cloxacillin
P	Penicillin
Ch	Chloramphenicol
K	Kanamycin
INH	Isoniazide Hydrochloride
R.V.	Right ventricle
IT	Intubated
Ext	Extubated
T	Tracheostomy
F.C.T.	Failed conservative treatment
AE	Air entry
PR	Pulse rate
RR	Respiratory Rate
Mo	months
M	Male
F	Female
Rx	Treatment
CCF	Cardiac failure
D	Day
NTT	nasotracheal tube
ECG	electrocardiograph
PM	post-mortem
AR	assisted respiration

CASE SUMMARIES

SEVERE GROUP

R/N	Age	Sex	Indications for IT	Size Tube Days IT	Course	Culture/Antibiotics	CXR Grade O/A	Outcome
139	19 mo	F	Cyanosis	4 mm 4 days	Post Measles. Poor response to antibiotic. Died on D4 of blocked NTT. Autopsy: Bilateral pneumonia	Sterile Rx: Ch	2 Heart ↑	Died on D4
141	8 mo	M	Cyanosis Hypotonia Unaware	3,5 mm 3 days	"Viral". Dislodged NTT accidentally. Pneumonia took 18 days to clear. Hb 8,9 gm%	E.Coli, sens. to Cl and Ch. Staph pyogenes, sens. to P. Cl, A. Rx: Cl.	6	Alive
150	5 mo	F	Cyanosis	3 mm 9 days	Measles. Hb. 7 gm%. Severe pneumonia unresponsive to therapy delayed extubation. ECG: Left ventricular overload.	Sterile Rx: A + Cl.	6	Died on D9
234	2 yr	M	Cyanosis Unaware	3,5 mm 7 + 8 days	Measles. Ext. D7; return of recession with re-IT on D10 for 8 days. After second extubation pneumonia relapsed. No autopsy. ECG: R.V. overload. Hb 6,7 gm%.	Culture results lost. Initial Rx: Ch. Relapse Rx: Ce 2nd relapse Rx with Ch again	Lost	Died on D31
406	8 mo	F	Unaware PR 200/min RR 120/min	3,5 mm 7 + 6 days	Measles. Cardiac failure developed on D2. Ext. failed D7. Re-IT. Pneumonia uncontrolled. ECG normal. Autopsy refused.	E.Coli sens. to K, G. Pseudomonas sens. to K, G. Ca. Rx: A Then Cl + G	5	Died on D13
410	2 yr	F	Cyanosis Unaware	3,5 mm 2 days	Measles: cardiac arrest D2. Autopsy: Severe bilateral pneumonia, R.V. enlarged. ECG normal.	No culture Rx: A	Not Done	Died on D2
458	2 yr	F	Cyanosis	3,5 mm 7 days	Measles: hectic fever until antibiotic change. ECG: Leftward ĀQRS	B.proteus sens to G, Ca Pseudomonas sens to G, Ca. Rx: A then G.	3	Alive

SEVERE GROUP .. continued

R/N	Age	Sex	Indications for IT.	Size Tube Days IT	Course	Culture/Antibiotics	CXR Grade O/A	Outcome
469	15 mo	F	Cyanosis	3,5 mm 7 days	Measles. Pneumonia controlled early. Hb. 11,6 gm%	Sterile Rx: Ce + G.	3	Alive
527	2 yr	M	Cyanosis	3 mm 3 days	Measles. Hb 4,3 gm%; transfused. Diarrhoea. NTT occluded with secretions on D3. Autopsy: Extensive bilateral pneumonia. R.V. enlarged.	Sterile Rx: A + Cl.	0	Died on D3
530	2½ yr	M	Cyanosis	3,5 mm 7 NTT + 5 T days	Measles. Hyperpyrexial on admission. Relapse of pneumonia and ext. failed on D7. T then done. Control of pneumonia with antibiotic change. Hb 9,2 gm% Myocarditis diagnosed on D2. ECG: normal.	E Coli, sens. to G Rx: P then Ce + G.	7	Alive
534	18 mo	M	Cyanosis	3,5 mm 7 days	Measles. Pneumonia controlled early. Hb. 11,6 gm%	E Coli, sens. to G, Ce Rx: A + Cl then G.	4	Alive
567	2 yr	M	Cyanosed	4,5 mm 2 days	Post measles: Cardiac arrest D2. Autopsy refused.	No culture Rx: A	No CXR	Died on D2
581	2 yr	M	FCT. PR 200/min RR 60/min Hypotonia.	3,5 mm 7 days	Post measles: after 5 days of conservative treatment was intubated. After extubation his pneumonia took a further 2 months to clear. ECG: R.V. overload	1. Staph. pyogenes, sens to Cl, Ce. 2. E Coli, sens. to Ce. Pseudomonas sens. to Ca Rx: A then Ce + G, then G.	11	Alive
655	6 mo	M	Cyanosis	3,5 mm 7 + 4 days	Measles: Ext. D7: recession recurred and re-IT D11 for 4 days. Pneumonia took further 2 months to clear. Hb 10 gm%	1. Staph.pyogenes sens. to P, Cl. 2. E Coli sens. to G, Ca. Rx: A + Cl then G + Ce then Ca.	4	Alive

MODERATE INTUBATED GROUP

R/N	Age	Sex	Indications for IT	Size Tube Days IT	Course	Culture/Antibiotics	CXR Grade O/A	Outcome
140	3 yrs	M	Severe recession & reduction AE. No trial.	4 mm 7 days	"Viral". No problems HB 11 gm%	Culture: Sterile Rx: A	1	Alive
144	8 mo	F	FCT PR 200 Tone ↓ Recession ↑	3,5 mm 7 + 4 days	"Viral". Ext. failed D7. Re-IT. D8 put onto A.R. for clinically severe pneumonia. Poor response to antibiotic. ECG: biventricular overload. PM: Extensive pneumonia.	Culture: Sterile Rx: A + Cl.	5	Died on D9
166	16 mo	M	FCT PR ↑ RR ↑	4 mm 7 days	"Viral". No problems. Pneumonia controlled early. Hb 6,7 gm%	Culture: E Coli sens. to G, Ca. Rx: A	6	Alive
170	5 mo	M	FCT PR 200/min	3,5 mm IT 7 + 6 days	"Viral". Ext. failed D7; Re-IT and ext. failed on D13. Laryngoscopy: subglottic stricture. T on D13: After 28 days stricture regressed and ex-tubated. Pneumonia controlled early. Hb 11 gm%	Cultures lost. Rx: A	3	Alive
191	10 mo	M	FCT PR ↑ Restless ↑	4 mm 7 days	"Viral". Pneumonia controlled early. Hb 10,4 gm% ECG: R.V. overload.	Culture: E Coli sens. to Ch, G. Rx: A	6	Alive
202	2½ yr	M	FCT AE ↓ PR ↑ Recession ↑	4 mm IT 7 days then T	"Viral". Congenital papillomata of vocal cords seen at IT. T done and transferred for cautery. Hb 11 gm%	Culture: Sterile Rx: A	0	Alive

MODERATE INTUBATED GROUP .. Continued

R/N	Age	Sex	Indications for IT.	Size Tube Days IT	Course	Culture/Antibiotics	CXR Grade O/A	Outcome
225	10 mo	M	FCT PR 220/min RR 60/min	3,5 mm 8 days	Measles. On D3 developed CCF. ECG: AQRS + 10°. D4 A.R. Cardiac arrest D8. Pneumonia not responsive to therapy. Autopsy: Bilateral pneumonia. R.heart dilated.	Culture: E.Coli, sens. to Ce, G, Ca	7 Heart ↑	Died on D8
411	1 yr	F	FCT. Tone ↓ Pallor	3,5 mm IT 7 days T 1 day.	Measles: Ext. failed D7. T done. Pneumonia worsened from D4. Autopsy refused.	Culture: Staph pyogenes, sens to Ce. Pseudomonas Sens to G, Ca. Rx: A then G + Cl on D6	0	Died on D8
417	9 mo	M	FCT PR 200 RR 80	3,5 mm 6 days	Measles. Developed cardiac failure. Cardiac arrest D6. Pneumonia uncontrolled. Hb 8,3 gm%. Autopsy: Pneumonia and atelectasis. R.V. hypertrophied. ECG: Normal	Culture: Lost Rx: A then G + Cl on D4	10	Died on D6
497	11 mo	F	No trial. Severe recession and ↓AE	3,5 mm 7 days	Measles. Pneumonia slow to respond. Clinical myocarditis D17. ECG: Normal Hb 10,5 gm%	Culture: staph.pyogenes sens. to Ce, Cl, P. E.Coli sens. to G, K. Rx: A then G on D4	3	Alive
505	5 yr	M	FCT PR 180 RR 44	5 mm 7 days	Measles. Extremely restless but always good muscle tone. Very relieved by IT. Pneumonia not controlled until change of antibiotic. Hb 11,6 gm%	Culture: 1. E.Coli sens. to G. 2. E.Coli sens. to K, G. Rx: P then G	4	Alive
514	17 mo	F	FCT PR 180 RR 64	3,5 mm 7 days	Measles. High swinging fever controlled by Cephaloridine ECG: Myocarditis	Culture: Sterile Rx: A then Ce on D3	4	Alive

MODERATE INTUBATED GROUP .. Continued

R/N	Age	Sex	Indications for IT.	Size Tube Days IT	Course	Culture/Antibiotics	CXR Grade O/A	Outcome
519	11 mo	F	No trial Restless ++ Recession ++	3,5 mm 7 days	Measles. No problems. ECG: L.V. overload.	Culture: E.Coli sens to A, G. Staph.pyogenes sens to A, Ce, Cl.	6	Alive
529	16 mo	M	FCT Restless ↑ Tone ↓	3,5 mm 7 days	Measles. Swinging fever until change of antibiotic.	Culture: B.proteus sens to K, G. Rx: A then Ca + K on D6.	9	Alive
550	22 mo	M	FCT Triple rhythm RR↑	4 mm 10 days	Measles. Secretions purulent at IT. Severe pneumonia delayed ext. Hb 11 gm% ECG: R.V. overload and myocarditis.	Culture: E.Coli sens to K, G. B.proteus sens to K, G. Pseudomonas sens to Ca. Rx: A then G + Ce then Ca.	18	Alive
558	13 mo	F	FCT. Pale Tone ↓ Restless ↓	3,5 mm 6 days	Measles. No problems. Hb 10 gm%	Culture: E.Coli sens to Ce, G. Rx: A then Ca.	11	Alive
604	3 yr	M	FCT PR↑	4 mm 7 days	Post measles. Severe swinging fever until D17 when controlled by i.v.Ca. Ext. D7 Re-IT D12 for apnoea, AR for 6 days. Ext.D20. D27 developed acute pulm.oedema. Died D28. Autopsy refused. ECG: Myocarditis, later pulmonary hypertension.	Culture: 1. B.proteus sens to K, Ce, G 2. E.Coli sens K, G. Paracolon sens K. 3. B.proteus sens K, G. Ca. Rx: P then G + Ce then Ca.	12	Died on D28
632	2 yr	M	FCT Triple rhythm. RR↑	3,5 mm 6 + 4 days	Measles. Ext. D6 failed. Re-IT for 4 days. Pneumonia responded slowly. Clinical myocarditis. Hb 10 gm% ECG: L.V. overload.	Culture: Staph.pyogenes sens to P, Cl, Ce. Rx: P	9	Alive
705	8 mo	M	FCT PR↑ RR↑	3,5 mm 6 + 7 days	"Viral". Extubation D6 failed: Second Ext.D13. Cardiomegaly from initial X-ray (D2). Developed cardiac failure D8. ECG: Biventricular overload. Hb 9,4 gm%	Culture: E.Coli sens A, K, G, Ca. Rx: A, then G + Ca.	1 Heart↑	Alive

CASE SUMMARIES

MODERATE CONSERVATIVE GROUP

R/N	Age	Sex	Course	Antibiotic	CXR Grade O/A	Outcome
414	2 yr	F	Measles. AE improved on D3. Fever controlled when antibiotic changed. ECG: R.V. pressure overload	A then G	7	Alive
438	1 yr	M	Post Measles. AE improved on D3. Pneumonia was a problem. Hb 9 gm%	P then G + Cl	11	Alive
513	18 mo	F	Measles. AE improved on D2. Pneumonia controlled with antibiotic change. Hb 8 gm%	P then G + Ce	2	Alive
520	10 mo	M	Post Measles. AE improved on D2. Pneumonia never troublesome. Hb 7 gm%	Ch	6	Alive
540	4 yrs	M	Measles. AE improved on D5. Chest clear in two X-rays. Hb 12 gm%	A	0	Alive
552	14 mo	M	"Viral". History of stridor for 2 weeks before admission. AE fluctuated, finally normal on D7. Pneumonia never troublesome. Hb 12 gm%	A + Cl	4	Alive
557	4 yrs	M	"Viral" AE improved by D2. ECG: Lost.	A	Heart†	Alive
570	7 mo	M	"Viral" AE improved on D4. Pneumonia responded well. Hb 9 gm% ECG: Leftward AQRS.	A	8	Alive
571	3 yrs	M	Measles. AE improved on D2. Pneumonia slow to respond. Hb 10 gm%	P	2	Alive
592	19 mo	M	"Viral" Borderline for intubation for 24 hours. AE improved on D3. Pneumonia relapsed on D8; terminal CCF, died D13. Hb 12,8 gm% ECG not done. No autopsy.	P then G + Ce	2	Died on D13
628	9 mo	F	Measles. Struggled for 4 days. AE improved on D6. Stridor persisted for 26 days. Laryngoscopy: typical viral picture. Slow control of pneumonia. Hb 10 gm%	A K added D7	7	Alive
748	3 yrs	F	Measles. Borderline for intubation for 24 hours. AE was greatly reduced but improved on D6. Pneumonia responded after 3 days. Hb 11 gm%	A	Lost	Alive
920	18 mo	M	Post Measles. AE was markedly reduced; improved on D4. Pneumonia no problem. Hb 11 gm%	P	Lost	Alive

CASE SUMMARIES

MILD GROUP

R/N	Age	Sex	Course	Antibiotic	CXR Grade O/A	Outcome
200	5 mo	M	"Viral" Became moderate severity on D2-D3. Developed CCF. ECG: Normal. Hb 12 gm%. Pneumonia slow to be controlled.	A + Cl	6	Alive
216	1 yr	F	Post Measles. Developed CCF D4. ECG: Myocarditis. Pneumonia poorly controlled until D17. Hb 10 gm%	A + Cl INH	10	Alive
224	10 mo	F	Measles. No problems	A	16	Alive
233	2 yr	M	Measles. No problems Hb 10 gm%	A	7	Alive
248	18 mo	M	"Viral". Hb 6 gm% (Hypochromic microcytic) Blood transfusion	A	5	Alive
416	2 yr	F	"Viral". No problems	A	7	Alive
463	13 mo	M	Measles. Became moderate severity D3-D4. Slow response of pneumonia. Hb 10 gm%	A	9	Alive
466	9 mo	M	Measles. No problems. Hb 10 gm%	P	8	Alive
468	5 yr	M	Measles. Prompt response of fever to antibiotic change. Hb 13 gm%	Ch then Ce	3	Alive
496	9 mo	M	Measles. Developed CCF on D3. ECG: Myocarditis. Hb 10 gm%	A then Ce	Lost	Alive
532	1 yr	M	Measles. Became moderate severity D2-D3. Hb 11 gm%	A	6	Alive
547	20 mo	M	Measles. No problems. Hb 14 gm%	A	4	Alive
577	17 mo	M	"Viral". No problems. Hb 10,5 gm%	Ch	1	Alive
590	6 mo	F	Measles. No problems. Hb 10 gm%	P	7	Alive
603	7 mo	M	Measles. Became moderate severity D3-D5. Hb 10 gm% ECG: R.V. pressure overload.	P	5	Alive
629	16 mo	M	Measles. No problems.	A	4	Alive
639	3 yr	M	Measles. Became moderate severity D2-D3	P then K	5	Alive

NORMAL CONTROL VALUES

BLOOD GASES AND ACID BASE OF HEALTHY AFRICAN CHILDREN

Age in months	pH	$PaCO_2$ mm.Hg.	Base Excess m.Eq/L	$Pa0_2$ mm.Hg.	$[\Delta Aa0_2]$ Vols. %
42	7,465	33	+ 1,0	91	0,28
9	7,445	33	- 0,5	84	0,32
36	7,442	37	+ 2,0	87	0,16
24	7,450	29	- 3,0	94	0,22
17	7,485	32	+ 2,0	100	0,21
36	7,470	30	- 1,0	87	0,34
12	7,400	33	- 1,0	95	0,21
17	7,385	35	- 3,0	86	0,30
36	7,400	43	+ 1,0	85	0,25
48	7,380	41	- 1,1	83	0,35
24	7,440	39	+ 2,3	86	0,30
8	7,350	41	- 3,0	89	0,22
12	7,370	39	- 2,1	90	0,22
5	7,440	33	- 0,6	87	0,30
12	7,390	39	- 1,0	90	0,22
20	7,410	41	+ 1,0	98	0,13
12	7,480	33	+ 2,9	92	0,26
13	7,510	30	+ 4,0	90	0,30
24	7,380	41	+ 0,9	89	0,22
25	7,425	37	+ 0,8	88	0,30
-	7,430	36	+ 0,6	86	0,34
14	7,440	42	- 3,2	79	0,40
12	7,340	37	- 5,0	81	0,44
-	7,387	37	- 2,0	80	0,44
6	7,420	35	- 1,0	79	0,44
36	7,405	37	- 0,8	82	0,44
24	7,420	35	- 0,7	82	0,44
24	7,417	36	- 0,5	79	0,44
-	7,350	40	- 4,5	88	0,22
-	7,400	42	+ 0,8	80	0,40
-	7,445	36	+ 2,0	86	0,34
n	31	31	31	31	31
Mean	7,415	37	- 0,4	87	0,30
S.D.	0,043	4	2	5	0,10

CALCULATION OF ALVEOLAR TO ARTERIAL OXYGEN GRADIENT

The alveolar oxygen tension is calculated from a simplified version of the alveolar air equation of Rahn and Fenn (1955):

$$PA0_2 = PI0_2 - \frac{PaC0_2}{R}$$

$PI0_2$ is calculated as 21% of barometric pressure less 47 mm.Hg. (pressure of water vapour at the carina).

$PaC0_2$ is measured.

R is assumed to be equal to 1.

The gradient is obtained by subtracting the measured arterial oxygen tension from the calculated alveolar oxygen tension.

If the gradient is required to be expressed in content the $PA0_2$ and $Pa0_2$ are converted to content using a set of tables (Kelman and Nunn, 1968) which take into account the effect of acid base and body temperature in the oxyhaemaglobin dissociation curve.

BLOOD GASES AND CLINICAL FEATURES AT ASSESSMENT

SEVERE GROUP

R/N	PaO_2 mm.Hg	$PaCO_2$ mm.Hg	pH	Pulse Rate per min.	Respiratory Rate per min.	Cyanosis	Tone Reduced	Reduced Air-Entry	Aware/ Unaware	Restless	Result
139	48	65	7,375	186	46	C	II	III	Unaware	+	Died
141	63	34	7,328	168	46	C	II	II	Aware	0	Survived
150	56	30	7,320	180	56	0	I	II	Aware	0	Died
234	30	56	7,270	180	60	C	II	III	Unaware	0	Died
406	59	45	7,425	200	120	0	I	II	Unaware	0	Died
410	39	26	7,460	160	48	C	II	III	Unaware	0	Died
458	50	51	7,340	200	52	C	N	I	Aware	+	Survived
469	62	19	7,430	130	60	C	N	II	Aware	0	Survived
527	52	37	7,280	170	40	C	I	III	Unaware	0	Died
530	44	41	7,050	200	60	C	II	III	Unaware	0	Survived
534	51	48	7,275	200	60	C	N	II	Unaware	+	Survived
567	49	37	7,300	200	70	C	N	I	Aware	+	Died
665	56	47	7,340	150	60	C	II	II	Unaware	0	Survived

BLOOD GASES AND CLINICAL FEATURES AT ASSESSMENT

MODERATE INTUBATED GROUP

R/N	$Pa0_2$ mm.Hg	$PaC0_2$ mm.Hg	pH	Pulse Rate per min.	Respiratory Rate per min.	Pallor or Cyanosis	Tone Reduced	Reduced Air-Entry	Aware/ Unaware	Restless	Result
140	63	52	7,437	140	28	0	I	II	Aware	0	Survived
166	79	24	7,375	200	50	0	N	II	Aware	0	Survived
170	74	46	7,370	200	60	Pallor	N	II	Aware	+	Survived
191	60	39	7,380	170	50	0	N	II	Aware	+	Survived
202	84	55	7,355	160	40	0	N	III	Aware	0	Survived
225	67	48	7,325	200	66	0	N	I	Aware	+	Died
411	69	40	7,380	180	?	Pallor	I	II	Unaware	+	Died
417	62	31	7,400	200	80	0	I	0	Aware	0	Died
497	76	36	7,370	160	40	0	N	II	Aware	+	Survived
505	62	43	7,340	180	44	0	N	II	Aware	++	Survived
550	60	14	7,540	180	66	0	I	I	Aware	+	Survived
558	53	48	7,340	170	60	Pallor	I	II	Aware	0	Survived
604	48	37	7,400	200	60	Pallor	I	II	Aware	++	Died
632	60	39	7,400	170	50	0	I	I	Aware	0	Survived
705	82	35	7,385	160	48	0	N	II	Aware	+	Survived

BLOOD GASES AND CLINICAL FEATURES AT ASSESSMENT

MODERATE CONSERVATIVE GROUP

R/N	$Pa0_2$ mm.Hg	$PaC0_2$ mm.Hg	pH	Pulse Rate per min.	Respiratory Rate per min.	Pallor or Cyanosis	Tone Reduced	Reduced Air-Entry	Aware/ Unaware	Restless	Result
414	94	25	7,520	150	40	0	N	I	Aware	+	Survived
438	66	51	7,300	130	46	0	N	I	Aware	0	Survived
513	90	30	7,440	160	40	0	N	I	Aware	+	Survived
520	62	42	7,385	160	44	0	N	I	Aware	0	Survived
540	56	40	7,370	180	46	0	N	III	Aware	+	Survived
552	50	41	7,460	144	48	0	I	I	Aware	+	Survived
557	59	42	7,300	130	40	0	N	I	Aware	+	Survived
570	66	51	7,340	180	50	Pallor	N	II	Aware	+	Survived
571	62	40	7,420	164	34	0	N	I	Aware	0	Survived
592	66	30	7,432	160	60	0	I	II	Aware	0	Died
628	60	37	7,350	170	58	0	N	I	Aware	+	Survived
748	83	36	7,344	135	40	0	N	II	Aware	+	Survived
920	76	33	7,321	160	60	0	N	III	Aware	+	Survived

BLOOD GASES AND CLINICAL FEATURES AT ASSESSMENT

MILD GROUP

R/N	$Pa0_2$ mm.Hg	$PaC0_2$ mm.Hg	pH	Pulse Rate per min.	Respiratory Rate per min.	Pallor or Cyanosis	Tone Reduced	Reduced Air-Entry	Aware/ Unaware	Restless	Result
200	89	39	7,390	130	36	0	N	0	Aware	0	Survived
216	44	31	7,425	180	54	0	N	0	Aware	0	Survived
224	97	19	7,450	160	48	0	N	0	Aware	0	Survived
233	86	34	7,420	160	52	0	N	0	Aware	0	Survived
248	82	37	7,435	160	32	0	N	0	Aware	0	Survived
416	90	19	7,490	140	40	0	N	0	Aware	0	Survived
463	59	30	7,560	160	50	0	N	0	Aware	0	Survived
466	62	35	7,490	160	54	0	N	0	Aware	+	Survived
468	73	29	7,480	152	30	0	N	0	Aware	+	Survived
496	60	35	7,400	180	?	0	N	0	Aware	+	Survived
532	74	31	7,490	168	76	0	N	0	Aware	+	Survived
547	74	35	7,400	140	30	0	N	0	Aware	0	Survived
577	86	37	7,350	130	45	0	N	0	Aware	0	Survived
590	82	33	7,360	120	50	0	N	0	Aware	+	Survived
603	80	37	7,350	170	40	0	N	0	Aware	0	Survived
629	88	27	7,430	140	40	0	N	0	Aware	0	Survived
639	75	29	7,360	160	36	0	N	0	Aware	0	Survived

ARTERIAL OXYGEN TENSION AND AWARENESS

IN INTUBATED CASES

AWARE		UNAWARE	
R/N	PaO_2 mm.Hg	R/N	PaO_2 mm.Hg
140	63	234	30
141	63	406	59
150	56	410	39
166	79	527	52
170	74	530	44
191	60	534	51
202	84	139	48
225	67	655	56
411	69		
417	62		
458	50		
469	62		
497	76		
505	62		
550	60		
567	49		
558	53		
604	68		
632	60		
705	82		
n.20		n. 8	
Mean 65		Mean 49	
SD 10		SD 11	

Means different $p < 0,01$

ARTERIAL OXYGEN TENSION AND ALVEOLAR TO ARTERIAL OXYGEN GRADIENT IN CONTENT MEASURED ON OXYGEN BREATHING

	SEVERE GROUP		MODERATE INTUBATED GROUP		
R/N	$Pa0_2$ mm.Hg	$[\Delta Aa0_2]$ vols %	R/N	$Pa0_2$ mm.Hg	$[\Delta Aa0_2]$ vols %
139	300	1,07	140	273	0,76
141	390	1,48	166	375	0,96
150	270	1,27	202	300	1,11
234	200	1,43	417	350	1,06
406	410	2,24	497	460	0,69
410	152	1,77	550	370	1,14
527	285	1,34	558	410	0,85
530	425	0,80	632	510	0,53
534	530	0,47			
n	9	9		8	8
Mean	329	1,32		381	0,89
SD	$\pm$ 119,44	$\pm$ 0,52		$\pm$ 78,44	$\pm$ 0,22

Mean $Pa0_2$ not significantly different

Mean $[\Delta Aa0_2]$ different $p < 0,05$

PULSE AND RESPIRATORY RATES : ALVEOLAR TO ARTERIAL OXYGEN GRADIENTS BEFORE AND AFTER INTUBATION

	R/N	Δ Pulse Rate per minute	Δ Respiratory Rate per minute	$\Delta[\Delta Aa0_2]$ vols %
SEVERE	139	- 46	- 14	- 0,18
	141	+ 32	+ 2	- 0,2
	150	- 20	- 16	+ 0,82
	234	- 44	?	+ 0,99
	406	- 15	?	+ 6,67
	410	- 4	- 8	+ 0,1
	458	- 10	?	- 2,53
	527	- 34	- 4	+ 0,92
	530	-100	- 16	- 3,52
	534	- 40	- 4	- 0,58
MODERATE INTUBATED	140	+ 36	?	+ 1,2
	166	- 40	- 2	+ 0,32
	170	- 40	?	+ 1,54
	202	0	- 20	- 0,5
	632	- 70	- 10	+ 0,1
	417	- 30	- 5	- 0,18
	497	0	0	+ 0,62
	550	+ 10	- 6	+ 1,11
	558	0	0	+ 1,27

ALVEOLAR TO ARTERIAL OXYGEN GRADIENT ON AIR AND CHEST RADIOGRAPH GRADING:

STEADY STATE

R/N	Day	$\Delta Aa0_2$ mm.Hg	CXR Grade	R/N	Day	$\Delta Aa0_2$ mm.Hg	CXR Grade
140	5	69	1	530	9	52	7
141	4	47	6	532	2	27	6
144	4	52	5	534	11	56	1
216	1	75	10	550	15	38	18
224	3	31	16	552	4	45	5
248	2	29	5	557	3	29	0
406	3	53	5	558	4	43	11
414	2	32	7	570	2	33	8
416	3	29	7	581	3	53	4
463	3	51	9	590	3	48	7
466	2	58	8	592	2	54	2
468	2	48	3	592	9	61	8
469	3	40	3	604	12	55	12
497	4	36	3	629	5	45	4
513	2	30	2	632	2	59	9
514	10	56	8	632	16	48	2
519	6	55	6	639	5	46	5
520	7	28	6	705	2	48	1
529	7	33	9				

Thirty-seven observations on 35 patients.

MORTALITY RATE AND HAEMOGLOBIN

INTUBATED PATIENTS

SURVIVED		DIED	
R/N	Hb. Gm.%	R/N	Hb. Gm.%
140	11	150	7
141	8,7	225	8,5
166	7,8	234	6,7
170	11	406	10
191	10,4	411	7
202	11	417	8,3
458	10,3	527	6,4
469	11,6	604	10,5
497	10,5		
505	11,6		
529	9,2		
534	11,6		
550	11		
558	10		
632	10		
655	10		
705	9,4		

n 17	n 8
Mean 10,3	Mean 8
SD 1,1	SD 1,5

Means different $p < 0,01$

ARTERIAL OXYGEN TENSION AND ALVEOLAR TO ARTERIAL OXYGEN GRADIENT IN CONTENT, MEASURED ON OXYGEN BREATHING

INTUBATED PATIENTS

SURVIVED			DIED		
R/N	$Pa0_2$ mm.Hg	$[\Delta Aa0_2]$ vols %	R/N	$Pa0_2$ mm.Hg	$[\Delta Aa0_2]$ vols %
140	273	0,76	139	300	1,07
141	390	1,48	150	270	1,27
166	375	0,96	234	200	1,43
202	300	1,11	406	410	2,24
497	460	0,69	410	152	1,77
530	425	0,80	417	350	1,06
534	530	0,47	527	285	1,34
550	370	1,14			
558	410	0,85			
632	510	0,53			
n	10	10		7	7
Mean	404	0,88		277	1,46
SD	$\pm$ 82	$\pm$ 0,30		87	$\pm$ 0,42

Mean $Pa0_2$ different $p < 0,05$

Mean $[\Delta Aa0_2]$ different $p < 0,05$

THE EFFECT OF INTUBATION ON ACID BASE

Summary of Means

	SEVERE		MODERATE INTUBATED	
pH				
Before IT	7,323 ± 0,102		7,390 ± 0,057	
After IT (A1)	7,386 ± 0,079		7,419 ± 0,041	
Mean of differences	+ 0,063 ± 0,071	<0,01	+ 0,021 ± 0,052	N.S
n	13		11	
$PaCO_2$ mm.Hg				
Before IT	41 ± 12		38 ± 12	
A1	33 ± 10		33 ± 9	
Mean of differences	- 8 ± 10	<0,05	- 5 ± 7	<0,05
n	13		11	
Base Excess				
Before IT	- 4,4 ± 7		- 1,5 ± 3,4	
A1	- 3,9 ± 7		- 2,2 ± 5	
Mean of differences	+ 1,1 ± 3,6	N.S.	0,66 ± 1,8	N.S.
n	13		11	

THE EFFECT OF INTUBATION ON OXYGEN

Summary of Means

	SEVERE		MODERATE INTUBATED	
$Pa0_2$ mm.Hg.				
Before IT	51 ± 9		68 ± 11	
After IT (A1)	54 ± 21		59 ± 10	
Mean of differences	+ 3 ± 12	N.S.	- 9 ± 7	<0,01
n	13		11	
$[a0_2]$ vols %.				
Before IT	9,7 ± 2,7		12,97 ± 1,78	
A1	9,9 ± 3,5		12,46 ± 1,66	
Mean of differences	+ 0,15 ± 2,5	N.S.	- 0,47 ± 0,65	<0,05
n	13		11	
$[\Delta Aa0_2]$ vols %.				
Before IT	2,9 ± 1,5		1 ± 0,5	
A1	2,99 ± 2,1		1,5 ± 0,8	
Mean of differences	+ 0,14 ± 2,4	N.S.	+ 0,49 ± 0,64	N.S.
n	12		11	
$[\Delta Aa0_2]$ vols %.				
A1 (air)	2,9 ± 2,1		1,5 ± 0,8	
On 100% 0_2	1,3 ± 0,5		0,89 ± 0,22	
Mean of differences	- 2,0 ± 2,0	<0,05	- 0,62 ± 0,79	N.S.
n	9		8	

EFFECT OF INTUBATION

SEVERE GROUP

	pH			$PaCO_2$		
R/N	Before	After	Δ	Before	After	Δ
139	7,375	7,535	+ 0,160	65	48	- 17
141	7,328	7,405	+ 0,077	34	29	- 5
150	7,320	7,340	+ 0,020	30	40	+ 10
234	7,270	7,285	+ 0,015	56	53	- 3
406	7,425	7,355	- 0,070	45	35	- 10
410	7,460	7,417	- 0,043	26	31	+ 5
458	7,340	7,460	+ 0,120	51	17	- 34
469	7,430	7,495	+ 0,065	19	25	+ 6
527	7,280	7,300	+ 0,020	37	31	- 6
530	7,050	7,310	+ 0,260	41	25	- 16
534	7,275	7,340	+ 0,065	48	29	- 19
567	7,300	7,330	+ 0,030	37	35	- 2
655	7,340	7,440	+ 0,100	47	30	- 17
n	13	13	13	13	13	13
Mean	7,322	7,388	+ 0,633	41	33	- 8
S.D.	0,102	0,079	0,071	12	10	10
			$p < 0,01$			$p < 0,05$

EFFECT OF INTUBATION

BASE EXCESS

SEVERE GROUP				MODERATE INTUBATED GROUP			
R/N	Before	After	Δ	R/N	Before	After	Δ
139	+ 7	+ 13	+ 6	140	+ 6	+ 5	- 1
141	- 7	- 4,7	+ 2,3	166	- 6	- 10	- 4
150	- 9	- 5,5	+ 3,5	170	0	+ 1	+ 1
232	- 1	- 2,4	+ 1,4	191	- 2	- 1	+ 1
406	+ 3	- 5	- 2	202	+ 2	- 3	+ 1
410	+ 1	+ 4	+ 3	417	- 4,5	- 4	+ 0,5
458	0	- 8	- 8	497	- 5	- 9	- 4
469	- 2	+ 2	+ 4	550	- 2,4	- 2	+ 0,4
527	- 10	- 10	0	558	- 1	- 1	0
530	- 23	- 18	+ 5	632	- 1	- 2	- 1
534	- 6,5	- 8	- 1	705	- 2,8	- 4	- 1,2
567	- 7	- 7	0				
655	- 3	- 2	+ 1				
n	13	13	13	n	11	11	11
Mean	- 4,4	- 3,9	+ 1,1	Mean	- 1,5	- 2,2	- 0,7
S.D.	7,4	7,5	3,6	S.D.	3,4	4,5	1,83
		N.S.					N.S.

EFFECT OF INTUBATION

MODERATE INTUBATED GROUP

	pH			$PaCO_2$		
R/N	Before	After	Δ	Before	After	Δ
140	7,437	7,440	+ 0,003	52	47	- 4
166	7,375	7,350	- 0,025	24	21	- 3
170	7,370	7,370	0	46	48	+ 2
191	7,380	7,440	+ 0,060	39	32	- 7
202	7,355	7,480	+ 0,125	55	33	- 22
417	7,340	7,430	+ 0,090	31	21	- 10
497	7,370	7,300	- 0,070	36	34	- 2
550	7,540	7,470	- 0,070	14	29	+ 15
558	7,340	7,420	+ 0,080	48	35	- 13
632	7,400	7,440	+ 0,040	39	30	- 9
705	7,385	7,377	- 0,008	35	33	- 2
n	11	11	11	11	11	11
Mean	7,390	7,419	+ 0,021	38	33	- 5
S.D.	0,057	0,041	0,052	12	9	7

N.S.

$p < 0,05$

EFFECT OF INTUBATION ON OXYGEN TENSION AND CONTENT

MEAN OF DIFFERENCES

	SEVERE GROUP			MODERATE INTUBATED GROUP	
R/N	$\Delta Pa0_2$ mm.Hg	$\Delta[a0_2]$ vols %	R/N	$\Delta Pa0_2$ mm.Hg	$\Delta[a0_2]$ vols %
139	- 4	+ 0,45	140	- 5	+ 0,43
141	+ 6	+ 0,24	166	- 8	+ 0,29
150	- 9	- 0,92	170	- 24	- 1,59
234	- 4	- 0,96	191	- 4	- 0,17
406	- 28	- 6,69	202	- 4	+ 0,04
410	0	+ 0,02	417	- 2	+ 0,32
458	+ 20	+ 3,09	497	- 13	- 0,74
469	+ 44	+ 1,09	550	- 9	- 1,25
527	- 7	- 0,83	558	- 8	- 1,11
530	+ 8	+ 3,9	632	- 2	0
534	- 2	+ 0,99	705	- 21	- 0,8
567	+ 4	+ 0,33			
655	- 1	+ 1,23			
n	13	13	n	11	11
Mean	+ 3	+ 0,15	Mean	- 9	- 0,47
S.D.	12	2,51	S.D.	7	0,65
	N.S.	N.S.		p <0,01	p <0,05

EFFECT OF INTUBATION

ALVEOLAR TO ARTERIAL OXYGEN GRADIENTS BREATHING AIR

mm.Hg

SEVERE GROUP		MODERATE INTUBATED GROUP	
R/N	Change in Alveolar to arterial oxygen gradient	R/N	Change in Alveolar to arterial oxygen gradient
139	+ 21	140	+ 10
141	- 1	166	+ 12
150	- 1	170	+ 23
234	+ 7	191	+ 4
406	+ 38	202	+ 26
410	- 5	417	+ 12
458	+ 14	497	+ 15
527	+ 13	550	- 6
530	- 2	558	+ 21
534	+ 21	632	+ 11
567	- 2	705	+ 23
655	+ 18		
n	12		11
Mean	+ 10		+ 14
S.D.	13		9
	N.S.		N.S.

Method of calculation of Alveolar to arterial oxygen gradient ($\Delta PAa0_2$) :-

$$\Delta PAa0_2 = - \frac{\Delta PaC0_2}{K} - \Delta Pa0_2$$

Where K varies from 1,15 (R = 1,2) to 0,91 (R = 0,8)

If R = 1, K = 1

R is assumed to be equal to one.

(Holloway et al, Thorax (1969) 24, 421)

ALVEOLAR TO ARTERIAL OXYGEN GRADIENTS ON AIR BEFORE INTUBATION, AFTER INTUBATION, AND ON OXYGEN BREATHING, IN CONTENTS

SEVERE GROUP

vols %

R/N	Before IT	A1 +	Δ A1/Bef. *	0_2 Breathing	Δ 0_2/A1
139	1,81	1,63	- 0,18	1,07	- 0,56
141	1,06	0,86	- 0,20	1,48	+ 0,62
150	1,30	2,12	+ 0,82	1,27	- 0,85
234	5,22	6,21	+ 0,99	1,43	- 4,78
406	1,06	7,68	+ 6,62	2,24	- 5,44
410	4,02	4,57	+ 0,10	1,77	- 2,80
458	3,59	1,06	- 2,33	-	-
527	1,48	2,40	+ 0,92	1,34	- 1,06
530	5,16	1,64	- 3,52	0,80	- 0,84
534	3,59	3,01	- 0,58	0,47	- 2,54
567	2,87	2,73	- 0,14	-	-
655	2,84	2,02	- 0,82	-	-
n	12	12	12	9	9
Mean	2,85	2,99	+ 0,14	1,32	- 2,03
S.D.	± 1,54	± 2,11	± 2,43	± 0,52	± 2,03
			N.S.	**	p <0,05

** $[\Delta Aa0_2]$ of severe group and moderate intubated group significantly different (p <0,05)

* Bef. = Before intubation

\+ A1 = After intubation

ALVEOLAR TO ARTERIAL OXYGEN GRADIENTS ON AIR BEFORE INTUBATION, AFTER INTUBATION, AND ON OXYGEN BREATHING, IN CONTENTS

MODERATE INTUBATED GROUP

vols %

R/N	Before IT	$A1^+$	$\Delta A1/Bef.^*$	0_2 Breathing	$\Delta 0_2/A1$
140	1,07	1,19	+ 0,12	0,76	- 0,43
166	0,53	0,85	+ 0,33	0,96	+ 0,11
170	0,05	2,04	+ 1,54	-	-
191	1,34	1,54	+ 0,2	-	-
202	1,07	0,57	- 0,5	1,11	+ 0,54
417	1,53	1,35	- 0,18	1,06	- 0,29
497	0,59	1,21	+ 0,62	0,69	- 0,52
550	1,11	2,22	+ 1,11	1,14	- 1,08
558	2,12	3,39	+ 1,27	0,85	- 2,54
632	1,11	1,21	+ 0,1	0,53	- 0,68
705	0,39	1,2	+ 0,81	-	-
n	11	11	11	8	8
Mean	1,024	1,525	+ 0,492	0,8875	- 0,616
S.D.	± 0,509	± 0,777	± 0,637	± 0,2179	± 0,787
			N.S.	**	N.S.

** $[\Delta Aa0_2]$ of severe group and moderate intubated group significantly different ($p < 0,05$)

* Bef. = Before intubation

\+ A1 = After intubation

THE EFFECT OF INTUBATION

ALL PATIENTS

PULSE AND RESPIRATORY RATES

	PULSE RATE			RESPIRATORY RATE		
R/N	Before Intubation	After Intubation	Difference	Before Intubation	After Intubation	Difference
141	160	200	+ 40			
234	180	180	0	60	60	0
410	160	156	- 4	48	40	- 8
458	200	190	- 10			
469				60	40	- 20
519	160	160	0	48	56	+ 8
527	170	136	- 34	40	36	- 4
530	200	100	- 100	60	44	- 16
534	200	160	- 40	60	56	- 4
567	200	164	- 36	70	60	- 10
665	150	160	+ 10	60	60	0
166	200	160	- 40	50	48	- 2
170	200	160	- 40	60	70	+ 10
202	160	160	0	40	20	- 20
225	200	200	0	66	34	- 32
417	200	170	- 30	80	76	- 4
497	160	160	0	40	40	0
515				64	40	- 26
550	180	200	+ 20	66	60	- 6
558	170	160	- 10	60	60	0
604	200	150	- 50	60	44	- 16
632	170	80	- 90	50	40	- 10
529	160	168	+ 8	60	68	+ 8
581	200	156	- 44			
		n	22		n	21
		Mean	- 20		Mean	- 7
		S.D.	34		S.D.	11
			p <0,02			p <0,01

EFFECT OF INTUBATION

ALVEOLAR OXYGEN CONTENT ON AIR.

vols %

R/N	$\Delta[AO_2]$
139	+ 0,27
140	+ 0,16
141	+ 0,04
150	- 0,01
166	+ 0,03
202	- 0,46
234	+ 0,03
406	+ 0,10
410	- 0,07
417	+ 0,12
497	+ 0,14
527	- 0,12
530	+ 0,09
534	+ 0,38
550	+ 0,41
558	- 0,14
632	- 1,11
n	17
Mean	- 0,01
S.D.	$\pm$ 0,35

Not significant

CALCULATION OF $P\bar{V}0_2$

To test the hypothesis that the increase in alveolar to arterial oxygen gradient ($[\Delta Aa0_2]$) after intubation could be accounted for by a fall in cardiac output.

The size of the shunt that was present before intubation was calculated using the shunt equation (Page 48, Chapter VI), the calculated $[\Delta Aa0_2]$ and an assumed arterio-venous oxygen difference ($[\Delta a\bar{v}0_2]$) of 4 vols %.

With the shunt held at pre-intubation level, and using the calculated post-intubation $[\Delta Aa0_2]$ the $[\Delta a\bar{v}0_2]$ was obtained from the graph on page a39, Appendix. This $[\Delta a\bar{v}0_2]$ was subtracted from the measured post-intubation arterial oxygen content, to give the mixed venous oxygen content. This was then converted to tension ($P\bar{v}0_2$) via saturation and the Severinghaus Oxyhaemaglobin Dissociation Slide Rule.

If the $P\bar{v}0_2$ was above 20 mm.Hg. it was possible that the increase in the $[\Delta Aa0_2]$ that occurred after intubation could have been due to a fall in cardiac output. If the $P\bar{v}0_2$ was impossibly high or less than 20 mm.Hg., the increase in $[\Delta Aa0_2]$ could not have been entirely due to a fall in cardiac output.

The results of this exercise appear on page a38 of Appendix.

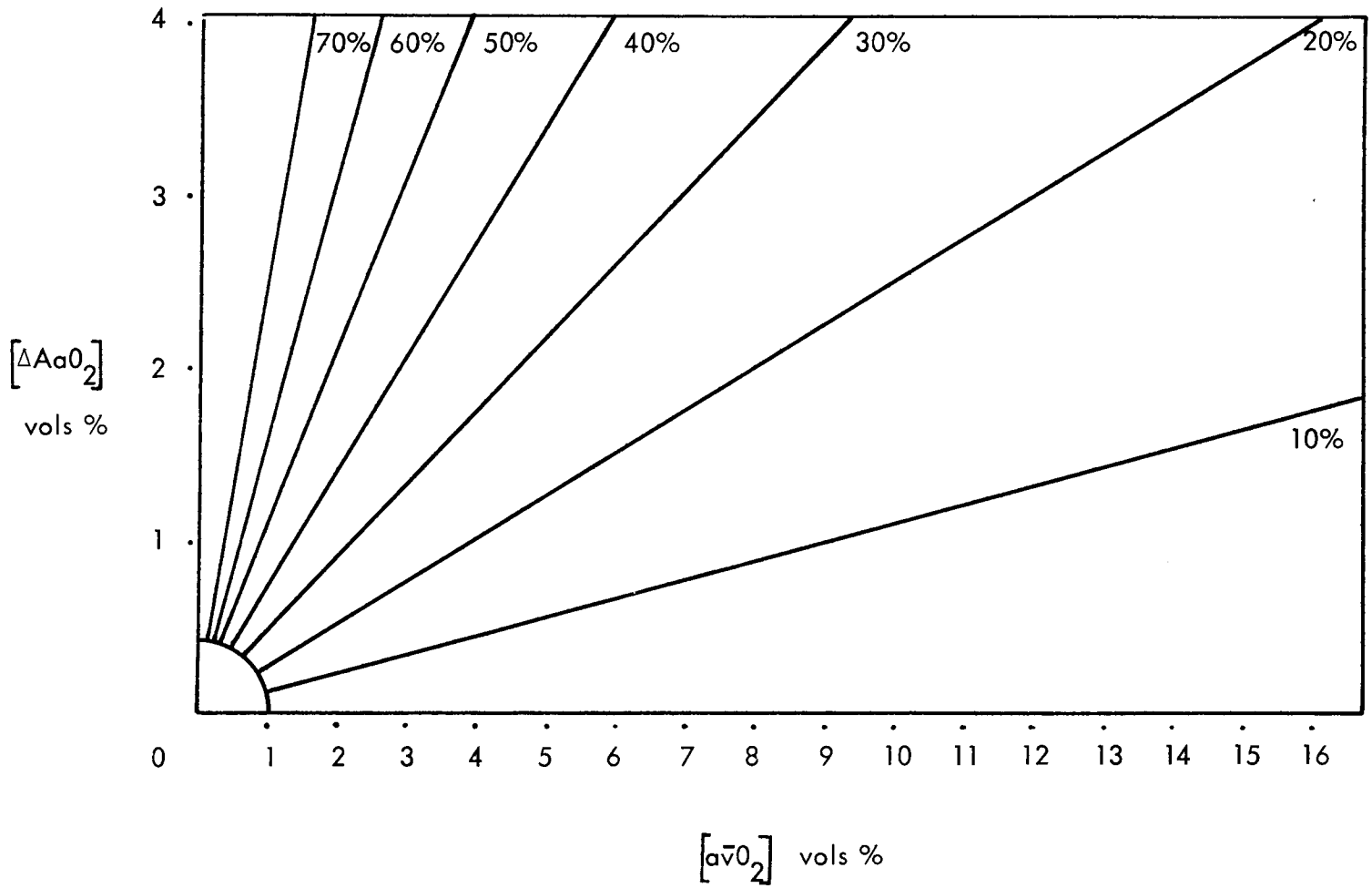
The derivation of the equation of the graph used in this calculation is on page a40 of Appendix.

$P\bar{v}O_2$

Calculated in those patients whose $[\Delta AaO_2]$ increased after Intubation

R/N	Before Intubation		After Intubation				
	$[\Delta AaO_2]$ Vols %	Shunt	$[\Delta AaO_2]$ Vols %	$[aO_2]$ Vols %	$[\Delta a\bar{v}O_2]$ Vols %	$[\bar{v}O_2]$ Vols %	$P\bar{v}O_2$ mm. Hg.
150	1,30	25 %	2,12	7,69	6,5	1,19	12,5
166	0,53	12 %	0,85	10,46	6	4,46	27
406	1,06	21 %	7,68	6,15	Incalculable		
491	0,59	13 %	1,21	14,02	9,5	4,52	19,6
527	1,48	27 %	2,40	6,10	8,00	Incalculable	
550	1,11	22 %	2,22	13,17	7,5	5,67	23
558	2,12	35 %	3,39	10,53	6,5	4,03	22

GRAPH OF THE EQUATION $\Delta Aa0_2 = \dfrac{a\bar{v}0_2 . QS/QT}{1 - QS/QT}$



THE DERIVATION OF THE EQUATION

$$\Delta Aa0_2 = \frac{a\bar{v}0_2 \; QS/QT}{1 - QS/QT}$$

$$QS/QT = \frac{C'0_2 - a0_2}{(C'0 - a0_2)+(a0 - \bar{v}0_2}$$

Where $C'0_2$ = end pulmonary arterial oxygen content

$a0_2$ = arterial oxygen content

$\bar{v}0_2$ = mixed venous oxygen content

QS = proportion of total cardiac output by-passing gas exchange surface

QT = total cardiac output

$$QS/QT = \frac{A0_2 - a0_2}{(A0-a0_2)+(a0_2-\bar{v}0_2)}$$

Where $A0_2$ is the alveolar oxygen content and a diffusion defect is assumed to be absent so that $A0_2$ is equal to $C'0_2$.

By re-arrangement : $$\Delta Aa0_2 = \frac{\Delta a\bar{v}0_2 \; QS/QT}{1 - QS/QT}$$

Where $A0_2-a0_2$ is written as $\Delta Aa0_2$

and $a0_2-\bar{v}0_2$ is written as $\Delta a\bar{v}0_2$

On the preceeding page the graph of the equation is shown where

$$y = \Delta Aa0_2 \qquad m = \frac{QS/QT}{1 - QS/QT} \qquad x = \Delta a\bar{v}0_2$$

QS/QT isopleths have been drawn. For convenience, each shunt has been converted to percentage : for example, QS/QT of 0,1 = 10%.

The isopleths have been labelled according to the QS/QT each represents.

VENTILATION WITH CARBON DIOXIDE CHALLENGE

R/N	Pre ΔCO_2 % I	Pre ΔCO_2 % II	Mean Pre ΔCO_2 %	Pre Δ VE Litres I	Pre Δ VE Litres II	Mean Pre ΔVE Litres	Post ΔCO_2 % I	Post ΔCO_2 % II	Mean Post ΔCO_2 %	Post Δ VE Litres I	Post Δ VE Litres II	Mean Post Δ VE Litres	$\frac{\text{Pre } \Delta VE}{\text{Pre } \Delta CO_2}$ L/% CO_2	$\frac{\text{Post } \Delta VE}{\text{Post } \Delta CO_2}$ L/% CO_2
33	8,8	7,8	8,4	13,09	6,68	9,8	6,8	7,2	7,0	8,63	8,91	8,77	1,166	1,252
140	9,0	5,0	7,0	11,56	8,46	10,01	6,4	7,0	6,7	9,31	9,87	9,59	1,428	1,431
150	7,6	6,2	6,9	5,01	7,78	6,4	8,4	7,6	8,0	7,8	5,30	6,55	0,927	0,818
166	4,7	7,8	6,25	10,68	16,58	13,63	4,2	5,6	4,9	19,11	26,89	23,0	2,180	4,693
170	6,4	7,0	6,7	3,34	3,34	3,34	8,4	6,4	7,4	9,75	5,85	7,8	0,498	1,054
191	4,0	5,6	4,8	4,94	6,54	5,78	8,4	8,4	8,4	12,71	11,87	12,29	1,204	1,463
202	1,2	8,4	7,8	6,54	8,18	7,36	8,8	-	8,8	2,26	-	21,26	0,943	2,415
234	6,6	7,6	7,1	2,79	2,79	2,79	7,4	-	7,4	5,57	-	5,57	0,392	0,752
451	4,4	3,0	3,7	3,63	1,82	2,7	2,4	2,8	2,6	5,6	4,7	5,15	0,729	1,980
497	6,6	6,8	6,7	7,5	6,95	7,2	6,2	6,4	6,3	6,67	7,5	7,08	1,074	1,123
540	5,0	-	5,0	8,9	-	8,9	4,2	4,0	4,1	13,6	18,6	16,1	1,78	3,926
558	4,7	4,4	4,6	6,98	6,15	6,6	4,8	4,6	4,7	8,95	10,2	9,6	1,434	2,042

Δ = Difference between end and beginning of experiment

Pre = Before Intubation

Post = After Intubation and physiotherapy

I and II = First and second experiment

ACID BASE AND BLOOD GASES

DAILY MEAN VALUES

pH

GROUP	Before IT or Day 1	A1	A2	D2	D3	D4	D5	D6	D7 -
Severe	7,322	7,385	7,414	7,443	7,441	7,443	7,478	7,441	7,443
	±,102	±,079	±,076	±,071	±,041	±,050	±,028	±,043	±,022
n	13	13	7	9	4	8	5	3	7
M.IT	7,386	7,419	7,412	7,448	7,445	7,435	7,452	7,427	7,456
	±,051	±,041	±,070	±,048	±,051	±,064	±,047	±,075	±,048
n	15	11	4	16	11	9	6	7	10
M.C.	7,379	-	-	7,451	7,448	7,439	7,449	7,435	7,378
	±,068			±,037	±,065	±,028	±,054	±,022	±,056
n	12			11	11	6	5	5	5
Mild	7,426	-	-	7,431	7,464	7,437	7,411	7,451	7,406
	±,057			±,052	±,036	±,048	±,059	±,027	±,064
n	14			13	12	3	6	3	4

D = day

A1 = 30 minutes after intubation

A2 = 4 hours after intubation

ACID BASE AND BLOOD GASES

DAILY MEAN VALUES

$\frac{PaCO_2}{mm.Hg.}$

GROUP	Before IT or Day 1	A1	A2	D2	D3	D4	D5	D6	D7
Severe	41	33	31	32	36	32	33	32	31
	±12	±10	± 8	± 5	±10	± 3	± 2	± 6	± 7
n	13	13	7	9	4	8	5	3	7
M.IT	39	30	38	32	30	35	30	33	35
	±11	± 8	± 7	± 5	± 6	± 7	± 4	± 5	± 4
n	15	11	4	16	11	8	6	7	9
M.C.	39	-	-	39	37	37	33	34	37
	± 8			± 7	± 6	± 4	± 4	± 5	± 6
n	12			11	11	6	5	5	5
Mild	32	-	-	34	32	33	35	33	37
	± 6			± 7	± 5	± 3	± 6	± 5	± 5
n	14			13	12	3	6	3	4

D = day

A1 = 30 minutes after intubation

A2 = 4 hours after intubation

ACID BASE AND BLOOD GASES

DAILY MEAN VALUES

BASE EXCESS

m.Eq/L

GROUP	Before IT or Day 1	A1	A2	D2	D3	D4	D5	D6	D7
Severe	- 4,4	- 3,9	- 4,4	+ 1,3	+ 1	- 0,3	+ 2,6	- 1,9	- 0,4
	± 7,5	± 7,5	± 2,7	± 2,6	± 2,7	± 3,3	± 2,3	± 2,6	± 3,1
n	13	13	7	9	4	8	5	3	7
M.IT	- 1,8	- 2,2	- 0,8	0	- 0,8	+ 0,2	- 1,1	- 0,1	+ 0,1
	± 3,1	± 4,5	± 4,3	± 5,5	± 3	± 4,5	± 3,4	± 4,4	± 3,4
n	14	1	4	16	11	8	6	7	9
M.C.	- 1,8	-	-	+ 2,6	+ 2,6	+ 1,6	+ 1,5	- 0,5	- 3,6
	± 4,3			± 2,5	± 4,5	± 1,7	± 2,3	± 2,7	± 2,9
n	11			11	11	6	5	5	5
Mild	- 1,6	-	-	- 0,2	+ 0,4	+ 1,9	- 1,1	+ 0,8	- 0,5
	± 4,6			± 2,3	± 2,9	± 1,9	± 3,2	± 0,5	± 2,3
n	15			13	11	3	6	3	4

D = day

A1 = 30 minutes after intubation

A2 = 4 hours after intubation

ACID BASE AND BLOOD GASES

DAILY MEAN VALUES

$\frac{PaO_2}{mm.Hg.}$

GROUP	Before IT or Day 1	A1	A2	D2	D3	D4	D5	D6	D7
Severe	51	54	51	68	69	73	72	75	76
	± 9	±21	±29	±13	± 8	± 8	±12	±12	± 9
n	13	13	7	9	4	8	5	3	7
M.IT	68	59	70	69	61	64	62	68	72
	± 9	±10	± 8	±18	± 8	± 7	± 4	±11	±12
n	15	11	4	15	11	9	6	7	10
M.C.	69	-	-	65	71	66	70	71	78
	±14			± 9	±12	±14	±20	±14	±14
n	12			11	11	6	5	5	5
Mild	79	-	-	75	74	79	75	71	79
	±13			±13	±16	±11	±13	±17	±11
n	14			13	12	3	6	3	4

D = day

A1 = 30 minutes after intubation

A2 = 4 hours after intubation

ACID BASE AND BLOOD GASES

DAILY MEAN VALUES

ALVEOLAR TO ARTERIAL OXYGEN GRADIENT

vols %

GROUP	Before IT or Day 1	A1	A2	D2	D3	D7
Severe	2,71	2,77	1,93	0,98	0,64	0,59
	± 1,51	± 2,16	± 2,07	± 0,89	± 0,24	± 0,38
n	13	13	7	9	8	7
M.IT	1,05	1,49	-	1,06	1,27	0,75
	± 0,49	± 0,80		± 0,74	± 0,68	± 0,61
n	14	11		14	11	9
M.C.	1,19	-	-	0,82	0,74	0,59
	± 0,83			± 0,39	± 0,42	± 0,39
n	11			11	11	5
Mild	0,69	-	-	0,65	0,70	0,41
	± 0,80			± 0,37	± 0,65	± 0,34
n	15			13	11	4

D = day

A1 = 30 minutes after intubation

A2 = 4 hours after intubation

DAILY BLOOD GASES AND ACID BASE

SEVERE GROUP

pH

R/N	Before IT	A1	A2	D2	D3	D4	D5	D6	D7
139	7,375	7,535	7,520	7,435					
141	7,328	7,405	7,430			7,410	7,480		
150	7,320	7,340		7,390					
234	7,270	7,285		7,440					
406	7,425	7,355	7,310	7,515	7,485	7,460			7,472
410	7,460	7,417	7,390						
458	7,340	7,460	7,500	7,540	7,460	7,490			7,460
469	7,430	7,495		7,495	7,430	7,400			7,410
527	7,280	7,300	7,350						
530	7,050	7,310				7,370	7,450	7,395	7,440
534	7,275	7,340		7,445		7,500	7,500	7,480	7,450
567	7,300	7,330							
581				7,430		7,420	7,450		7,420
655	7,340	7,440	7,400	7,300	7,390	7,500	7,510	7,452	7,450
n	13	13	7	9	4	8	5	3	7
Mean	7,322	7,385	7,414	7,443	7,441	7,443	7,478	7,441	7,443
S.D.	0,102	0,079	0,076	0,071	0,041	0,050	0,028	0,043	0,022

DAILY BLOOD GASES AND ACID BASE

SEVERE GROUP

$PaCO_2$

mm.Hg.

R/N	Before IT	A1	A2	D2	D3	D4	D5	D6	D7
139	65	48	31	31					
141	34	29	25			29	35		
150	30	40		41					
234	56	53		39					
406	45	35	45	33	27	29			25
410	26	31	19						
458	51	17	29	25	33	35			37
469	19	25		25	35	34			35
527	37	31	31						
530	41	25				37	35	37	36
534	48	29		33		31	34	25	21
567	37	35							
581				33		33	31		37
655	47	30	37	31	50	29	31	35	27
n	13	13	7	9	4	8	5	3	7
Mean	41	33	31	32	36	32	33	32	31
S.D.	12,12	9,6	8,3	5,4	9,8	3,1	2,0	6,4	6,6

DAILY BLOOD GASES AND ACID BASE

SEVERE GROUP

BASE EXCESS

m.Eq/L

R/N	Before IT	A1	A2	A3	D3	D4	D5	D6	D7
139	+7	+13	+2	-1,6					
141	-7	-4,7	-5			-4	+5		
150	-9	-4,5		0					
234	-1	-2,4		+2					
406	+3	-5	-5	+5	+2,7	-2,5			-3
410	+1	+4	-8						
458	0	-8	-7	+6	+3	+5			6,6
469	2	+2		+1	-3	-2			0
527	-10	-10	-7						
530	-23	-18				-3	+1,4	+1	-1
534	-6,5	-8		-2		+4	+5	-4	-1
567	-7	-7							
581				+1,5		-1	+0,3		+1
655	-3	-2	-1	0	+1,4	+0,8	+1,2	+2,8	+0,2
n	13	13	7	9	4	8	5	3	7
Mean	-4,4	-4,0	-4,4	+1,3	+1	-0,3	+2,6	-1,9	+0,4
S.D.	7,5	7,5	2,7	2,6	2,8	3,3	2,3	2,6	3,1

DAILY BLOOD GASES AND ACID BASE

SEVERE GROUP

$Pa0_2$

mm.Hg

R/N	Before IT	A1	A2	D2	D3	D4	D5	D6	D7
139	48	44	80	80					
141	64	70	83			74	86		
150	56	47		60					
234	30	26		40					
406	59	31	37	70	70	70			84
410	39	39	40						
458	50	70	84	73	65	69			84
469	62	106		81	79	90			84
527	52	45	58						
530	45	63				67	82	83	81
534	51	49		81		80	65	82	65
567	49	53							
581				64		68	70		72
655	56	55	61	65	60	64	58	61	64
n	13	13	7	9	4	8	5	3	7
Mean	51	54	51	68	69	73	72	75	76
S.D.	9	21	29	13	8	8	12	12	9

DAILY ALVEOLAR TO ARTERIAL OXYGEN GRADIENTS AND ARTERIAL OXYGEN EXPRESSED AS CONTENT

vols %

SEVERE GROUP

R/N	Pre-Intubation		After Intubation (A1+)		After Intubation (A2*)		Day 2		Day 4		Day 7	
	$\Delta Aa0_2$	$a0_2$	$\Delta Aa0_2$	$a0_2$	$\Delta Aa0_2$	$a0_2$	$\Delta Aa0_2$	$a0_2$	$\Delta Aa0_2$	$a0_2$	$\Delta Aa0_2$	$a0_2$
139	1,81	10,50	1,63	10,95	0,34	12,37	0,40	12,28				
141	1,06	11,50	0,86	11,74	0,47	12,20			0,49	12,19		
150	1,30	8,61	2,12	7,69			1,07	8,74				
234	5,22	4,33	6,21	3,37			3,08	6,73				
406	1,06	12,84	7,68	6,15	5,28	8,49	0,70	13,29	0,83	13,17	0,34	13,75
410	4,02	8,16	4,57	8,18	4,47	8,18						
458	3,59	9,93	1,06	13,02	0,41	13,59	0,69	13,37	0,62	13,39	0,22	13,71
469	1,30	15,53	0,18	16,62			0,44	16,42	0,26	16,48	0,34	16,40
527	1,48	6,93	2,40	6,10	1,00	7,54						
530	5,16	8,43	1,64	12,33					0,80	12,18	0,39	13,62
534	3,59	9,93	3,01	10,92			0,39	13,63	0,38	13,68	0,80	13,32
567	2,82	9,42	2,73	9,75								
581							0,41	13,59	0,79	13,19	0,73	13,29
655	2,84	10,71	2,02	11,94	1,51	12,41	1,64	12,24	0,92	13,10	1,31	12,65
n	13	13	13	13	7	7	9	9	8	8	7	7
Mean	2,71	9,27	2,77	9,35	1,93	12,61	0,98	12,25	0,64	13,55	0,59	13,82
S.D.	1,51	2,23	2,16	3,03	2,07	1,90	0,89	2,88	0,24	1,26	0,38	1,20

* A1 = 30 minutes after intubation. + A2 = 4 hours after intubation

DAILY BLOOD GASES AND ACID BASE

MODERATE INTUBATED GROUP

pH

R/N	Before IT	A1	A2	D2	D3	D4	D5	D6	D7
140	7,437	7,440		7,470			7,486	7,460	
144			7,500	7,485	7,470	7,470	7,455		
166	7,375	7,350		7,480					7,455
170	7,370	7,370							
191	7,380	7,440		7,510					7,435
202	7,355	7,480	7,435	7,450					
225	7,325			7,460	7,390				
411	7,380			7,470				7,540	
417	7,400	7,430				7,470			
497	7,370	7,400	7,343	7,370	7,465	7,390		7,450	7,470
505	7,340			7,410	7,460	7,460			7,475
514				7,495		7,500	7,495		7,495
519				7,360	7,500			7,340	7,350
529					7,420			7,360	7,490
550	7,540	7,470		7,440	7,465	7,500			7,400
558	7,340	7,420	7,370	7,490	7,530	7,430	7,480	7,480	
604	7,400			7,480	7,350	7,300	7,370		7,490
632	7,400	7,440		7,430	7,430				7,50
705	7,385	7,377		7,370	7,415	7,400	7,430	7,360	
n	15	11	4	16	11	9	6	7	10
Mean	7,386	7,419	7,412	7,448	7,445	7,435	7,452	7,427	7,456
S.D.	0,051	0,041	0,07	0,048	0,051	0,064	0,047	0,075	0,048

DAILY BLOOD GASES AND ACID BASE

MODERATE INTUBATED GROUP

$PaCO_2$

mm.Hg.

R/N	Before IT	A1	A2	D2	D3	D4	D5	D6	D7
140	52	47		34			23	30	
144			29	29	25	26	27		
166	24	21		19					33
170	46	48							
191	39	32		29					34
202	55	33	46	42					
225	48			36	32				
411	40			33				32	
417	31	21				37			
497	36	34	42	35	23	39		24	36
505	43			27	33	31			33
514				31			29		
519				33	23			37	39
529					34			33	29
550	14	29		34	33	37			44
558	48	35	35	33	25	46	33	38	
604	37			30	29	38	33		31
632	39	30		31	37				32
705	35	33		39	40	27	33	37	
n	15	11	4	16	11	8	6	7	9
Mean	39	30	38	32	30	35	30	33	35
S.D.	11	8	7	5	6	7	4	5	5

DAILY BLOOD GASES AND ACID BASE

MODERATE INTUBATED GROUP

BASE EXCESS

m.Eq/L

R/N	Before IT	A1	A2	A3	D3	D4	D5	D6	D7
140	+6	+5		+3			-3	-2,4	
144			+1,5	+0,9	-2,7	-2	-2,4		
166	-6	-10		-2					+2
170	0	+1							
191	-2	-1		+2					0
202	+2	+3	+4,5	+4					
225	-3			+3	-3				
411				+3				+8	
417	-4,5	-4				+4,6			
497	-5	-9	-5	-6	-3	-1		+4	-5
505	-5			-4	+2	+3			+4
514				+4			+5		
519				-8	+1			-5	-4
529					-1,5			-6	+3
550	-2,4	-2		0	+1	+6			+2,5
558	-1	-1	-4	+5	+1	+4	+3,2	+5	
604	-1			+5	-8	-7	-5		+3
632	-1	-2		-3	+0,6				+3
705	-2,8	-4		-3	+0,3	-6	+0,2	-4	
n	14	11	4	16	11	8	6	7	9
Mean	-1,8	-2,2	-0,7	0	-0,6	+0,2	-1,1	-0,1	+0,1
S.D.	3,1	4,5	4,3	5,5	2,9	4,5	3,4	4,4	3,4

DAILY BLOOD GASES AND ACID BASE

MODERATE INTUBATED GROUP

$Pa0_2$

mm.Hg.

R/N	Before IT	A1	A2	D2	D3	D4	D5	D6	D7
140	63	58		104			58	80	
144			70	71	70	72	70		
166	79	71		110					82
170	74	50							
191	60	56		64					75
202	84	80	80						
275	67			66	60				
411	69			54				56	
417	62	60				68			
497	76	63	70	89	73	75		76	78
505	62			68	60	62			70
514				53		64	61		75
519				57	60			58	87
529					55			84	84
550	60	51		49	45	49			49
558	53	45	61	62	59	61	60	60	
604	68			66	69	63	61		60
632	60	58		60	60				61
705	82	61		63	66	60	62	63	
n	15	11	4	15	11	9	6	7	10
Mean	68	59	70	69	61	64	62	68	72
S.D.	9	10	8	18	8	8	4	11	12

DAILY ALVEOLAR TO ARTERIAL OXYGEN GRADIENTS AND ARTERIAL OXYGEN EXPRESSED AS CONTENT

vols %

MODERATE INTUBATED GROUP

	Pre IT		Post IT(A1 *)		Day 2		Day 3		Day 7	
R/N	$[\Delta Aa0_2]$	$[a0_2]$	$[\Delta Aa0_2]$	$[a0_2]$	$[\Delta Aa0_2]$	$[a0_2]$	$[\Delta Aa0_2]$	$[a0_2]$	$[\Delta Aa0_2]$	$[a0_2]$
140	1,07	14,06	0,80	14,49	0,09	15,26				
144							0,55	12,14		
166	0,53	10,75	0,85	10,46	0,13	11,22			0,27	11,02
170	0,50	14,76	2,04	13,17						
191	1,26	12,65	1,54	12,48	0,83	13,22			0,49	13,52
202	1,07	14,92	0,57	14,96						
225	0,79	11,62			1,44	11,04	1,64	10,93		
411					1,24	10,02				
417	1,53	9,64	1,35	9,96						
497	0,59	14,76	1,21	14,02	0,21	15,01	0,70	14,78	0,52	14,87
519					2,02	11,86	1,00	13,12	0,26	13,69
505	1,70	14,75			1,08	15,64	1,78	14,86	0,59	16,20
514					1,31	10,00				
550	1,11	14,42	2,22	13,17	2,84	12,44	2,92	12,43	2,09	13,17
529							1,56	11,03	0,29	12,40
558	2,12	11,64	3,39	10,53	0,90	13,11	0,97	13,12		
604	0,87	14,35			0,80	14,63	1,18	14,10	1,29	14,10
632	1,11	12,84	1,21	12,84	1,06	12,99	1,02	12,99	0,94	13,12
705	0,39	12,20	1,20	11,40	0,89	11,69	0,68	13,32		
n	14	14	11	11	14	14	11	11	9	9
Mean	1,05	13,10	1,49	12,46	1,06	12,72	1,27	12,98	0,75	13,57
S.D.	0,49	1,73	0,80	1,66	0,74	1,88	0,68	1,31	0,61	1,46

* A1 = 30 minutes after intubation

DAILY BLOOD GASES AND ACID BASE

MODERATE CONSERVATIVE GROUP

pH

R/N	D1	D2	D3	D4	D5	D6	D7
414	7,520	7,495	7,570				
438	7,300	7,381	7,470			7,400	
513	7,440	7,455	7,450		7,450		
520	7,385	7,470	7,370	7,430	7,390		7,360
540	7,370	7,495	7,480		7,535		
552	7,460		7,360	7,395			7,320
557	7,300		7,430				
570	7,340	7,420	7,410				
571	7,420	7,470	7,450	7,480		7,450	
592		7,430	7,400	7,430	7,450		
628	7,350	7,410				7,450	7,360
748	7,341	7,450		7,440	7,420	7,430	7,470
920	7,231	7,490	7,541	7,460		7,445	7,380
n	12	11	11	6	5	5	5
Mean	7,379	7,451	7,448	7,439	7,449	7,435	7,378
S.D.	0,685	0,037	0,065	0,028	0,054	0,022	0,056

DAILY BLOOD GASES AND ACID BASE

MODERATE CONSERVATIVE GROUP

$\frac{PaCO_2}{mm.Hg}$

R/N	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
414	25	41	31				
438	51	56	45			41	
513	30	33	33		35		
520	42	37	33	37	39		33
540	40	35	35		29		
552	41		50	45			39
557	42		38				
570	51	37	37				
571	40	39	42	34		33	
592		30	32	37	33		
628	37	38				31	47
748	36	35		33	31	28	31
920	33	47	35	38		38	37
n	12	11	11	6	5	5	5
Mean	39	39	37	37	33	34	37
S.D.	8	7	6	4	4	5	6

DAILY BLOOD GASES AND ACID BASE

MODERATE CONSERVATIVE GROUP

BASE EXCESS

m.Eq/L

R/N	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
414	+3	+8	+9				
438	-6	+3	+7			0	
513	-3	+1	-2		+2		
520	0	+5	-6	+1	-1		-6,4
540	+2	+4	-4		+5		
552	+5		+1,2	+2			-5,6
557	-5		-0,6				
570	+1	+0,4	+1,6				
571	+1	+5	+4,4	+2,7		+8	
592		-1	+2,2	+1	+0,3		
628	-5	0				-0,5	-4,2
748	-6	+1		-1	+1,2	-5	+1
920	-9	+2	+8	+4		+2	-3
n	12	11	11	6	5	5	5
Mean	-1,8	-2,6	+2,6	+1,6	+1,5	-0,5	-3,6
S.D.	4,3	2,5	4,5	1,7	2,3	2,7	2,9

DAILY BLOOD GASES AND ACID BASE

MODERATE CONSERVATIVE GROUP

$Pa0_2$

mm.Hg.

R/N	D1	D2	D3	D4	D5	D6	D7
414	94	77	70				
438	66	55	74			55	
513	90	54	60		74		
520	62	37	80	82	86		89
540	56	35	60		90		
552	50		54	60			68
557	59		88				
570	66	70	88				
571	62	76	68	81		80	
592		66	68	62	61		
628	60	60				63	61
748	83	59		45	40	90	94
920	76	59	62	65		67	78
n	12	11	11	6	5	5	5
Mean	69	65	71	66	70	71	78
S.D.	14	9	12	14	20	14	14

DAILY ALVEOLAR TO ARTERIAL OXYGEN GRADIENTS AND ARTERIAL OXYGEN EXPRESSED AS CONTENT

vols. %

MODERATE CONSERVATIVE GROUP

R/N	Day 1		Day 2		Day 3		Day 7	
	$[\Delta Aa0_2]$	$[a0_2]$	$[\Delta Aa0_2]$	$[a0_2]$	$[\Delta Aa0_2]$	$[a0_2]$	$[\Delta Aa0_2]$	$[a0_2]$
414	0,27	12,40	0,34	12,29	0,68	11,98		
438	1,06	11,35	1,58	10,77	0,63	11,79		
513	0,24	11,07	0,98	10,31	0,85	10,43		
520	0,63	9,14	0,50	9,31	0,26	9,63	0,20	9,69
540	3,06	13,39	0,35	16,46	1,18	15,56		
552	1,80	14,93			1,62	14,94	0,99	15,64
557	1,85	13,32			0,29	15,09		
570	1,06	11,30	0,67	11,88	0,22	12,39		
571	1,11	12,80	0,45	13,52	0,66	13,31		
592			1,02	17,13	0,91	17,24		
628	1,46	12,41	0,98	12,99			1,01	12,84
748	0,59	14,64	1,10	14,28			0,24	15,15
920			1,11	14,10	0,87	14,52	0,53	14,82
n	11	11	11	11	11	11	5	5
Mean	1,19	12,43	0,82	13,00	0,74	13,35	0,59	13,69
S.D.	0,83	1,68	0,39	2,44	0,42	2,33	0,39	2,34

DAILY BLOOD GASES AND ACID BASE

MILD GROUP

pH

R/N	D1	D2	D3	D4	D5	D6	D7
200	7,390	7,400					
216	7,425		7,489			7,425	
224	7,450	7,520	7,485				
233	7,420	7,420					
248	7,350	7,450	7,440			7,450	
416	7,490	7,400	7,500				
463			7,560			7,480	7,485
466	7,490	7,500	7,450	7,490	7,320		
468		7,480	7,520				
496		7,400	7,420				7,330
532	7,490	7,400	7,470	7,420			
547	7,520		7,400		7,470		
577	7,350	7,460					
590	7,360	7,450	7,460	7,400	7,390		
603	7,350	7,330	7,430		7,480		7,390
629	7,430				7,390		
639	7,360	7,400			7,420		7,420
n	14	13	12	3	6	3	4
Mean	7,426	7,431	7,464	7,437	7,411	7,451	7,406
S.D.	0,057	0,052	0,036	0,048	0,059	0,027	0,064

DAILY BLOOD GASES AND ACID BASE

MILD GROUP

$\frac{PaCO_2}{mm.Hg}$

R/N	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
200	39	37					
216	31	26	41			36	
224	19	23	29				
233	34	37					
248	37	37	41			35	
416	19	43	27				
463			40			27	33
466	35	28	35	30	44		
468		29	30				
496		35	33				43
532	31	41	31	37			
547	35		37		31		
577	37	22					
590	33	31	33	33	38		
603	37	42	24		31		37
629	27				30		
639	29	38			39		34
n	14	13	12	3	6	3	4
Mean	32	34	32	33	35	33	37
S.D.	6	7	5	3	6	5	5

DAILY BLOOD GASES AND ACID BASE

MILD GROUP

BASE EXCESS

m.Eq/L

R/N	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
200	-1	-1					
216	-2,6		-1,8			0	
224	-6,7	+1	+1,8				
233	-1,3	+0,4					
248	+1	+2	+3			+1,5	
416	-6,5	+1	+1,2				
463	+7					+1	+5
466	+5,6	+3	+1,3	+1,3	-5		
468		+1	+5				
496		-2	-3				-4
532	+1	+1	+1	+0,3			
547	+6		-1		+0,7		
577	-4	-5					
590	-6	-0,5	+2	+4	-1,2		
603	-5	-4	-5		+2,5		-2
629	-3				-5		
639	-8	-0,6			+1,2		-1
n	15	13	11	3	6	3	4
Mean	-1,6	-0,2	+0,4	+1,9	-1,1	+0,8	-0,5
S.D.	4,6	2,3	2,9	1,9	3,2	0,5	2,3

DAILY BLOOD GASES AND ACID BASE

MILD GROUP

$\frac{Pa0_2}{mm.Hg.}$

R/N	D1	D2	D3	D4	D5	D6	D7
200	89	68					
216	44		47			52	
224	97	97	90				
233	86	73					
248	82	84	80			82	
416	90	98	94				
463			59			80	85
466	62	64	70	86	90		
468		73	105				
496		60	60				90
532	74	84	76	86			
547	74		73		92		
577	86	84					
590	82	64	69	66	62		
603	80	65	66		67		71
629	88				75		
639	75	64			65		68
n	14	13	12	3	6	3	4
Mean	79	75	74	79	75	71	79
S.D.	13	13	16	12	13	17	11

DAILY ALVEOLAR TO ARTERIAL OXYGEN GRADIENTS AND ARTERIAL OXYGEN EXPRESSED AS CONTENT

vols. %

MILD GROUP

	Day 1		Day 2		Day 3		Day 7	
R/N	$[\Delta Aa0_2]$	$[a0_2]$	$[\Delta Aa0_2]$	$[a0_2]$	$[\Delta Aa0_2]$	$[a0_2]$	$[\Delta Aa0_2]$	$[a0_2]$
200	0,28	16,35	1,15	15,43				
216	3,43	10,53			2,40	11,65		
224	0,25	12,47	0,22	12,53	0,28	12,38		
233	0,33	13,65	0,52	13,45				
248	0,22	8,30	0,19	8,33	0,27	8,23		
416	0,29	12,46	0,12	12,43	0,18	12,51		
463	1,11	12,84					0,46	13,50
469							0,27	13,60
466	0,81	13,22	0,67	13,41	0,31	13,75		
468			1,06	16,99	0,17	17,92		
532	0,56	14,85	0,35	14,92	0,56	14,85		
496			1,14	12,84	1,06	12,99		
547	0,63	18,84			0,88	18,47		
577	0,40	14,83	0,43	15,05	0,66	13,39		
590	0,48	14,44	0,92	13,10				
630	0,49	13,38	0,85	13,10	0,95	13,10	0,74	13,17
629	0,32	12,34						
639	0,68	11,92	0,88	11,67			0,65	11,99
n	15	15	13	13	11	11	4	4
Mean	0,69	13,36	0,65	13,33	0,70	13,57	0,41	13,07
S.D.	0,79	2,44	0,37	2,10	0,65	2,83	0,34	0,74

HYPERVENTILATION

Relationship of $PaCO_2$ and base excess

Pre-Intubation or Day 1						Day 2					
$PaCO_2$ <32 mm.Hg.			$PaCO_2$ 32-42 mm.Hg			$PaCO_2$ <32 mm.Hg.			$PaCO_2$ 32-42 mm.Hg.		
R/N	$PaCO_2$	B.E.	R/N	$PaCO_2$	B.E.	R/N	$PaCO_2$	B.E.	R/N	$PaCO_2$	B.E.
150	30	-9,0	141	34	-7,0	139	31	-1,6	140	34	+3,0
166	24	-6,0	191	39	-2,0	144	29	+0,9	150	41	-
216	31	-2,6	200	39	-1,0	166	19	-2,0	200	37	-1,0
224	19	-6,7	233	34	-1,3	191	29	+2,0	225	36	+3,0
410	26	+1,0	248	37	+1,0	224	33	+1,0	233	37	+0,4
414	25	+3,0	411	40	-2,5	458	25	+6,0	234	39	+2,0
416	19	-6,5	466	35	+5,6	466	28	+3,0	248	37	+2,0
417	31	-4,5	497	36	-5,0	468	24	+1,0	406	33	+5,0
469	19	-2,0	520	42	-	469	25	+1,0	411	33	+3,0
513	31	-3,0	527	37	-10,0	505	27	-4,0	414	41	+8,0
532	31	+1,0	530	41	-23,0	514	31	+4,0	496	35	-2,0
550	14	-2,4	540	40	+2,0	577	22	-5,0	497	35	-6,0
629	27	-3,0	547	35	+6,0	590	31	-0,5	519	33	-8,0
639	29	-8,0	552	41	+5,0	592	30	-1,0	520	37	+5,0
			557	42	-5,0	604	30	+0,5	532	41	+1,0
			567	37	-7,0	632	31	-3,0	534	33	-2,0
			571	40	+1,0	655	31	-	540	35	+4,0
			577	37	-4,0				550	34	-
			590	33	-6,0				558	33	+5,0
			603	37	-5,0				571	39	+5,0
			604	37	-1,0				581	33	-1,0
			628	37	-5,0				603	42	-4,0
			632	39	-1,0				628	38	-
			705	35	-2,8				639	38	-0,6
			748	36	-6,0				705	39	-3,0
									748	35	+1,0
n		14			25			17			26
Mean		-3,5			-3,1			+0,1			+0,8
S.D.		3,6 *			5,7 *			2,8 **			3,7 **

* Not significant

** Not significant

HYPERVENTILATION

$PaCO_2$ related to Chest Radiograph Grading

R/N	$PaCO_2$ < 31 mm.Hg. $PaCO_2$ mm.Hg	X-Ray Grade
140	23	1
141	29	6
144	26	5
216	31	10
224	29	16
406	27	5
411	27	0
416	27	7
466	28	8
468	29	3
513	30	2
514	22	4
514	29	8
529	31	9
592	30	2
592	30	8
604	30	12
629	30	4
632	31	9
705	27	1
705	29	3
n	21	
Mean	6	
S.D.	4	

R/N	$PaCO_2$ > 32 mm.Hg. $PaCO_2$ mm.Hg	X-Ray Grade
144	38	5
233	34	7
248	37	5
414	41	7
463	40	9
469	35	3
497	39	3
519	37	6
520	33	6
530	43	7
532	37	6
534	34	1
547	35	4
550	40	18
550	35	18
552	41	4
552	45	5
557	33	0
558	46	11
570	51	8
571	40	2
577	37	1
581	33	4
590	33	7
603	37	5
628	37	7
632	33	2
639	39	5
705	39	1
705	33	3
n	30	
Mean	6	
S.D.	4	

51 observations on 45 patients: pre-intubation state excluded.

HYPERVENTILATION

Relationship of $PaCO_2$ and PaO_2

Pre-Intubation or Day 1						Day 2					
$PaCO_2$ <32 mm.Hg			$PaCO_2$ 32-42 mm.Hg			$PaCO_2$ <32 mm.Hg			$PaCO_2$ 32-42 mm.Hg		
R/N	$PaCO_2$	PaO_2	R/N	$PaCO_2$	PaO_2	R/N	$PaCO_2$	PaO_2	R/N	$PaCO_2$	PaO_2
150	30	56	141	34	64	144	29	71	150	41	60
166	24	79	191	39	60	191	29	64	200	37	68
216	31	44	200	39	89	224	23	97	225	36	66
224	19	97	233	34	86	458	25	73	233	37	73
410	26	39	248	37	82	466	28	64	234	39	40
414	25	94	411	40	69	468	29	73	248	37	84
416	19	90	466	35	62	469	25	81	406	33	70
417	31	62	497	36	76	505	27	68	411	33	54
469	19	62	520	42	62	514	31	53	414	41	77
513	31	92	527	37	52	577	22	84	496	35	60
532	31	74	530	41	45	590	31	64	497	35	89
550	14	60	540	40	56	592	30	66	519	33	57
629	27	88	547	35	74	604	30	66	520	37	64
639	29	75	552	41	50	632	31	60	532	41	84
			557	42	59	655	31	65	534	33	81
			567	37	49				540	35	80
			571	40	62				550	34	49
			577	37	86				558	33	62
			590	33	82				571	39	76
			603	37	80				581	33	64
			604	37	68				603	42	65
			628	37	60				628	38	60
			632	39	60				639	38	64
			705	35	82				705	39	63
			748	36	83				748	35	59
			920	33	76						
n		14			26			15			25
Mean		71			68			70			67
S.D.		18			13			11			12
		*			*			**			**

* Not significant

** Not significant

ABNORMAL ELECTROCARDIOGRAPHS

OF PATIENTS DISCUSSED IN CHAPTER IX

ABBREVIATIONS

S.R.	:	Sinus rhythm
S.T.	:	Sinus tachycardia
$\overset{\circ}{A}P$	:	Mean P wave axis
$\overset{\circ}{A}QRS$	:	Mean QRS axis
$\overset{\circ}{A}T$	:	Mean T wave axis
Indet.	:	Indeterminate axis
Heart ↑	:	Heart enlarged on X-Ray
CXR	:	Chest X-Ray
N.D.	:	Not done
Deg	:	degrees

ABNORMAL ELECTROCARDIOGRAPHS

R/N	Age	Day	Rhythm	ÅP deg	PR secs	ÅQRS deg	ÅT deg	R/S VI m.v.	R/S V5 m.v.	T, ST, etc.	X-Ray Score	Hb. Gm%	Blood pH	Gases $Pa0_2$	Interpretation
144	8/12	D3	SR	+60	0,09	+100	+50	6/3	12/2	TV↓;Q in II,III, aVF.	5	9	7,470	70	Biventricular overload.
150	5/12	D1	SR	+50	0,09	+15	+30	4/2	19/0	T↓VI-V4, flat TV5-V6.	6	7	7,320	56	Left ventricular volume overload.
		D2	SR	+40	0,08	+10	+30	7/4	17/0	As above.			7,390	60	
191	10/12	D2	SR	+60	0,12	+150	+10	3/3	2/9	TVI↓	0	10	7,510	64	Right ventricular pressure overload.
216	1 yr	D2	ST	+50	0,10	+60	+50	12/10	12/2	TVI↓	10	10	7,425	44	Left ventricular strain due to ? Myocarditis or ? hypoxia.
		D15	ST	+60	0,12	+40	+45	8/10	18/2	TVI-4 inverted. Depressed ST. TV5-V7 flat. Voltage normal.	7		7,425	52	
225	10/12	D1	ST	+30	0,10	+10	+45	7/18	22/2	TVI↓	7 Heart	9	7,325	67	Leftward QRS axis.
		D3	ST	+30	0,09	+10	+30	7/19	22/16	TVI↓			7,390	60	
234	2 yr	D1	ST	+60	0,10	+45	+20	7/3	12/2	TVI↑	N.D.	7	7,270	30	Right ventricular pressure overload.
414	2 yr	D3	ST	+60	0,12	+120	+50	5/2	24/3	TVI↓	7	9	7,570	70	Right ventricular pressure overload.
458	2 yr	D2	ST	+45	0,14	0	+45	9/8	14/0	TVI↓	11	10	7,540	73	Leftward QRS axis.
		D4	SR	+60	0,12	0	+70	7/6	14/0	TVI↓			7,490	69	

ABNORMAL ELECTROCARDIOGRAPHS .. Continued

R/N	Age	Day	Rhythm	∠P deg	PR secs	∠QRS deg	∠T deg	R/S VI m.v.	R/S V5	T, ST, etc.	X-Ray Score	Hb. Gm%	Blood pH	Gases $Pa0_2$	Interpretation
496	9/12	D3	ST	+90	0,12	-10	+90	2/3	17/4	TVI↓ Small complexes limb leads.	Lost	10	7,420	60	Left ventricular strain due to ? Myocarditis.
		D5	SR	+60	0,12	-10	+60	3/7	8/6	TVI↓ Limb complexes improved. Flat with coning.	TV3-V7		7,330	90	
		D8	SR	+60	0,14	0	+60	3/8	20/8	As above.					
514	17/12	D1	ST	+60	0,12	+60	+50	2/2	5/0	TVI↓ Low voltage throughout.	4	8	7,520	66	
		D5	SR	+50	0,13	+45	+30	5/8	9/0	TVI↓			7,495	61	Myocarditis.
		D7	SR	+60	0,12	+65	+35	5/8	11/0	TVI flat. Voltage improved.			7,495	75	
		D9	SR	+45	0,13	+60	+35	5/12	11/0	As above.	8		7,450	65	
519	11/12	D3	SR	+60	0,12	+10	+50	6/5	25/0	TVI↓	6	10	7,500	60	Left ventricular volume overload.
		D8	SR	+55	0,12	+45	+40	7/6	17/0	TVI↓ QIII.			7,350	84	
		D13	SR	+30	0,12	+40	+10	13/15	10/0	TVI↓ Q gone.					
530	$2\frac{1}{2}$ yr	D2	SR	+45	0,12	+80	+40	7/5	20/0	TVI↓ ST elevation II, V4 V5 V6.	7	10			
		D4	SR	+40	0,10	+40	+30	6/5	9/0	TVI↓ Voltage limb leads small; ST elevation as before.			7,370	67	Myocarditis.
		D6	SR	+20	0,10	+10	+20	9/7	10/0	TVI↓ ST elevation less. Voltage as before.			7,395	83	
		D11	SR	+30	0,10	+40	+10	5/5	7/0	TVI↓ Voltage improved.			7,460	55	

ABNORMAL ELECTROCARDIOGRAPHS .. Continued

R/N	Age	Day	Rhythm	ÂP deg	PR secs	ÂQRS deg	ÂT deg	R/S VI m.v.	R/S V5 m.v.	T, ST, etc.	X-Ray Score	Hb. Gm%	Blood pH	Gases $Pa0_2$	Interpretation
550	21/12	D1	ST	+45	0,12	+160	+30	9/9	4/6	TVI↓ ST elevation III, V6. ST depression V4R.	18	11	7,520	60	Acute R.V. pressure overload followed by localised L.V. damage probably due to Myocarditis.
		D2	ST	+50	0,12	+240	+40	7/10	2/4	TVI↓ Unifocal R.V. ectopics.			7,440	49	
		D6	SR	+45	0,13	Indet	+20	10/12	7/4	TVI↓ ST coning. Ectopics.			7,465	64	
		D13	SR	+20	0,12	+60	+10	15/17	2/2	TVI↓ ST elevation II, V6.	18		7,410	69	
570	7/12	D1	SR	+50	0,10	+15	+45	5/1	10/1	TVI↓	8	9,5	7,340	66	Leftward QRS axis.
		D3	SR	+60	0,12	0	+50	5/1	21/2	TVI↓			7,410	88	
581	22/12	D2	SR	+70	0,13	+110	+70	14/4	5/0	TVI biphasic.		11	7,360	74	Right ventricular pressure overload.
		D7	ST	+50	0,11	+60	+50	15/2	20/0	TVI biphasic.	4		7,420	72	
		D14	ST	+70	0,12	+70	+50	13/0	23/0	TVI↑					
603	7/12	D1	ST	+60	0,09	+110	+30	14/8	10/4	TVI↓ Q in II,III, aVF. V6	5	10	7,350	80	Biventricular overload.
		D8	SR	+60	0,09	+110	+50	19/13	14/14	TVI↓ Q in II,III, aVF.			7,390	64	
604	3 yr	D1	ST	+55	0,12	+70	+10	5/12	12/,5	TVI↓	12	10,5	7,400	68	Normal tracing D1.
		D14	SR	+10	0,12	+70	+50	6/9	5/0	TVI↑	18		7,450	53	Subsequently L.V.
		D28	ST	+45	0,12	+100	Indet	7/10	8/2	TVI↑ Flat T I, II, III, V5, V6.	18		7,440	61	damage, probably due to Myocarditis

ABNORMAL ELECTROCARDIOGRAPHS .. Continued

R/N	Age	Day	Rhythm	ÅP deg	PR secs	ÅQRS deg	ÅT deg	R/S VI m.v.	R/S V5 m.v.	T, ST, etc.	X-Ray Score	Hb. Gm%	Blood pH	Gases $Pa0_2$	Interpretation
632	2 yr	D1	SR	+70	0,11	+70	+40	11/0	32/0	TVI↓ QII, III, aVF, V4, V5, V6.	9	10	7,390	63	Left ventricular volume overload.
		D6	SR	+30	0,12	+40	+20	14/4	40/2	TVI↓ QII,III, aVF V5, V6.			7,500	61	
		D14	SR	+60	0,16	+50	+50	13/8	20/2	TVI↓ Q waves smaller.	2		7,450	62	
		D30	SR	+60	0,14	+60	+60	12/9	30/4	TVI↓					
705	8/12	D1	SR	+55	0,12	Indet	+70	11/7	24/8	TVI↓ QaVF, V5, V6.	1 Heart ↑	9	7,385	82	Biventricular overload.
		D9	ST	+50	0,08	Indet	+45	15/17	12/8	TVI↓ Q III, aVF.	3 Heart↑		7,460	59	
		D16	SR	+50	0,12	Indet	+70	17/9	28/22	TVI↓ QaVF.	2 Heart↑		7,385	62	
		D22	SR	+50	0,12	+60	+45	13/8	14/6	TVI↓ QII, aVF.					

ELECTROCARDIOGRAPHIC CRITERIA

Right Ventricular Overload

1. Taller than normal R waves in V3R, V1 with deeper than usual S waves in V6.
   Normal range of R wave expressed as percentage of RS deflection,
   in the 6 months to 3 years age group:
   V1 45-56% average (28 - 84% limits)
   V6 88-94% average (70-100% limits)
2. After 3 months of age, pure R in V1 indicates R.V.H.
3. R/S ratio in V1 greater than normal for age.
4. Positive T wave in V3R or V1 except when T waves are negative in V6 due to L.V. pressure overload.
5. Q in V1 always abnormal and represents either R.V.H. or altered conduction pattern.
6. r s R^{1} pattern in right chest leads with $R^{1} > 10$ m.m.
   This indicates either R.V.H. or right bundle branch block.
   (Krovetz, Gessner and Schiebler, 1969)

Left Ventricular Overload

A. 1. R in V6 >35 m.m.
   2. S in V1 >25 m.m.
   3. Depressed ST segments and/or flat or inverted T V5-6 with absent q in V5-6.
      The voltage of R may be normal or increased.
   4. Deep Q > 4 m.m. with tall, symmetrical T waves in V5-6.
      (Krovetz, Gessner and Schiebler, 1969)

B. 1. Left axis deviation i.e. after 3 months of age, axis negative.
      However, in the first few years of life, a QRS axis of 0 to 20-30° is so unusual that other findings compatible with LVH should be sought.
   2. R in a VL or a VF >25 m.m.

3. In Precordial leads

   R in V6 > 30 m.m.

   S in V1 > 20 m.m.

   S in V1 plus R in V6 > 45 m.m.

   Depressed ST segments and negative T waves in V5-6

   Q > 4 m.m. in V6 with tall symmetrical T waves.

4. Intrinsicoid deflections > 0,04 second in a VL, a VF, V5 or V6.

5. QRS-T angle > 50°.

   "The criteria are not rigid, and conventional voltage criteria may not be met." (Cassels, 1966).

Combined Ventricular Hypertrophy

Evidence of R.V.H. and any of the following suggests combined ventricular hypertrophy:-

1. Predominant R (voltage not necessarily abnormal) with tall positive T waves in V5-7.
2. Q in V5-7 > 3 m.m.
3. Left axis deviation.

Evidence of L.V.H. and any of the following:-

1. Predominant R or R' in right chest leads (voltage not necessarily abnormal).
2. R > Q in a VR.
3. S > R in V6.

(Krovetz, Gessner and Schiebler, 1969).

SECONDARY INFECTION AND MYOCARDITIS

Myocarditis		NO MYOCARDITIS					
		Other Cardiac Abnormality		No Cardiac Abnormality			
R/N	CXR Score	R/N	CXR Score	R/N	CXR Score	R/N	CXR Score
216	10	139	2	140	1	515	4
496	Lost	144	5	141	6	520	6
497	3	150	6	166	6	527	0
514	4	191	6	170	3	529	9
530	7	200	6	202	0	532	6
550	18	225	7	224	16	534	4
604	12	406	5	233	7	540	0
632	9	414	7	248	5	547	4
		417	10	411	0	552	4
		458	3	416	7	558	11
		519	6	438	11	571	2
		557	0	463	9	577	1
		570	8	466	8	590	7
		581	11	468	3	628	7
		592	2	469	3	629	4
		603	5	505	4	639	5
		705	1	513	2	655	4

n 7
Mean 9
SD 5,09

n 51
Mean 5,08
SD 3,36

The mean CXR Score of patients with myocarditis and those without myocarditis:
Student t critical ratio 1,83 : $0,1 > p > 0,05$.
The mean CXR Score of patients with cardiac abnormalities (other than myocarditis) and patients without cardiac abnormalities had identical mean values.

STATISTICAL METHODS

Four statistical methods were employed in the study :

1. The test of statistical significance applied to the means of paired observations was the Student's t test.

2. The correlation coefficient for base excess and arterial oxygen tension (Chapter VIII) was calculated using a programme for the IBM 1130 Computer.

3. Chi-Square was used in Chapter X, where it is specifically mentioned.

4. An outline of the method used for the calculation of weighting factors for variables in the linear-discriminant equation is given in Chapter X. The IBM 1130 Computer was programmed for this purpose.

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