Papers and Originals

Intensive Therapy in Paediatrics

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An intensive therapy unit was opened at Alder Hey Children's Hospital in Liverpool on 1 September 1964 to deal with acute emergencies arising within the hospital or admitted from without, but excluding purely surgical conditions. It was established at a cost of £10,000, of which approximately half was expended on converting a cubicled ward of 120 by 24 ft. (36.5 by 7.3 m.). The remaining sum was spent on equipment. A pilot scheme had been in operation for several years, during which the techniques of resuscitation and controlled pulmonary ventilation in infants and children were explored. It became obvious that there was a real need for a unit in which these techniques could be applied together with newer methods of investigation, monitoring, and treatment of paediatric emergencies. This is a preliminary report on the work of this unit and a consideration of the place of an intensive therapy unit in a children's hospital.

The Unit

Site.—The unit is situated on the first floor of a three-storey building near the medical wards, the admissions department, and the hospital theatre.

Plan of Unit.—The layout adopted is not thought to be ideal, but has worked well in practice (Fig. 1). There are four main divisions: (1) the usual ward offices, consulting-room, and waiting-room near the entrance (rooms 1 to 6); (2) the resuscitation-room and four cubicles where intensive treatment is given (rooms 7 to 11); (3) the laboratory and sister's room (rooms 12 and 13), separating the resuscitation-room and cubicles from (4) an open area at the end for convalescent patients (14). Each of the cubicles for acute treatment accom-

modates two cots or incubators and the open area five beds or cots, making a total complement of 13. Since many patients are babies in incubators, this complement can be increased to 15 without difficulty when necessary. The accommodation provided would seem to be adequate for a hospital of 630 beds. There is a piped-oxygen and compressed-air and suction supply to all cubicles, the resuscitation theatre, and the open ward. The compressed-air and suction supply is provided by a compressor unit¹ situated outside the main ward.

Medical Staff.—An essential feature of the unit is the close co-operation between the medical and anaesthetic staff. There are three part-time consultant anaesthetists, and, on the medical side, one part-time consultant in charge of the unit. Experience has shown that there should be one medical and one anaesthetic registrar plus one part-time senior house-officer. When the registrar and the senior house-officer are off duty their duties should be covered by other colleagues in the hospital. There is a resident anaesthetist in the hospital at night, and, in addition, the ward is covered by the medical registrar on duty.

Nursing Staff.—Three sisters, three staff nurses, and six nurses in training form a satisfactory establishment.

Technician.—A laboratory technician works full time in the unit laboratory.

Equipment.—The resuscitation-room should be fully equipped as a minor operating-theatre in which such measures as laryngoscopy, bronchoscopy, and tracheostomy may be carried out. It is also a great advantage to have a laboratory sited within the unit capable of estimating pH, blood gases, and electrolytes, and of making ventilatory measurements at any time of the day or night.

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¹ Supplied by the British Oxygen Company.

FIG. 1—Plan of unit.

Monitoring of Patients.—Instruments should be available for detecting cardiac or respiratory arrest, but extensive continuous monitoring must not be regarded as a substitute for constant nursing observation.

Admission and Discharge.—Rather more than half the patients are admitted to the unit from their home or other hospitals; the remainder come from medical wards within the hospital. Fig. 2 summarizes the routes of admission and discharge.

FIG. 2.—Admission to and discharge from unit.

Management

The object of intensive management of all gravely ill patients is directed towards maintaining an internal environment which will permit the continuance of cell life until such time as the disease process responsible for the illness resolves. In disease the internal environment changes in such a way as to endanger cell life, largely as a result of failure of respiration, circulation, or renal function. The early detection and treatment of impairment of these functions is therefore the primary object of intensive therapy.

Respiratory Failure

Respiratory failure may be due to obstruction of the airway, disease of the lung parenchyma, or failure of the forces of respiration to maintain adequate ventilation.

Obstruction of Upper Airway

When obstruction of the upper airway produces a marked increase in respiratory effort, together with cyanosis when the patient is breathing air, an exact diagnosis is essential, and this necessitates laryngoscopy. Endotracheal intubation can then be considered. The degree of airway obstruction cannot be assessed by measuring the arterial PCO_2 , which may remain normal until immediately before acute cardiorespiratory failure, so that the decision to intervene must be based upon clinical evidence.

Lower Airway and Lung Disease

In the infant with a respiratory infection increased effort is not a reliable sign of respiratory failure, for brief periods of apnoea may occur and are of serious significance. There is central cyanosis when breathing air, and a capillary $PCO_2 > 45$ mm. Hg. The signs on auscultation are variable and do not accurately reflect the degree of respiratory inadequacy.

Rising respiratory and pulse rates, cyanosis when breathing oxygen, and a rising PCO_2 in the arterial blood, especially when in excess of 60 mm. Hg, are signs which call for intervention. Deterioration in the breathless infant with feeble cough is often due to accumulation of secretions in the airways. An endotracheal tube should be passed and the airways aspirated as often as is necessary. Continuous clinical observation, the regular monitoring of blood-gas tensions, and the use of instruments which give immediate warning of cardiac or respiratory arrest are all necessary at this stage. Failure to improve or a recurrence of the signs outlined above is an indication for controlled pulmonary ventilation.

Rarely has it been found necessary to resort to tracheostomy, and following the practice of Allen and Steven (1965) long-

term nasotracheal intubation has been used as a method of establishing an airway for the relief of obstruction, for carrying out repeated tracheobronchial suction, and for purposes of controlled pulmonary ventilation. Tracheostomy produces a train of complications in young children and is almost inevitably accompanied by sepsis. In infants it is often difficult to decannulate the tracheostomy when it has served its purpose, and the carrying out of tracheobronchial suction is difficult because the tube lies deep in the crease of the neck. The fact that non-irritant nasotracheal tubes are well tolerated for long periods by children has permitted an artificial airway to be established and intermittent positive-pressure ventilation to be instituted earlier in the course of the disease than would have been possible had a tracheostomy been the only alternative. Up to October 1965 this technique had been used in 100 cases. In two surviving patients, both intubated for periods in excess of eight weeks, grave strictures of the subglottic region developed. One was a newborn infant unable to control his airway because of cerebral birth injury, and he has a tracheostomy which may well be permanent. The other child, aged two years, with an acute myelitis subsequently showed some increase in the diameter of the trachea at the site of obstruction. No late complications were seen in infants intubated for periods of less than eight weeks. A maximum limit to the duration of intubation of three weeks is therefore recommended.

Thirty-two children were intubated to relieve an obstructed airway or to provide a means of carrying out repeated tracheobronchial toilet, and all survived. Sixteen other survivors were intubated for the purpose of carrying out intermittent-positive-pressure ventilation. A large number of intubated children died of their pre-existing disease, but in no case was intubation thought to have been responsible for the fatal outcome.

Management of Indwelling Nasotracheal Tubes

Adequate humidification of the inspired gases is thought to be of prime importance in the management of indwelling nasotracheal tubes. Inspired gas must be saturated with water vapour at body temperature, and this implies the use of a heated humidifier. Tracheobronchial suction is carried out as often as necessary to remove secretions, but routine suction is not performed unless there is evidence of accumulation of secretions (Bush, 1963).

The technique of tracheobronchial suction is important, since failure to remove secretions may cause considerable interference with pulmonary ventilation. An aseptic technique is essential to avoid contamination of the tracheobronchial tree, and suction must only be applied for the minimum time necessary to remove secretions. Before and after tracheobronchial suction the lungs are ventilated with 100% oxygen to avoid hypoxia during the suction. In endotracheal tubes with an internal diameter of 3 mm. or less an Argyle infant-feeding tube, size $3\frac{1}{2}$ Fr. gauge, easily passes and is satisfactory for aspiration of secretions provided adequate humidification is guaranteed. For larger endotracheal tubes an angulated rubber catheter is used, allowing both main bronchi to be aspirated. Any doubt about the patency of the tube or failure to remove secretions should be resolved by replacing the tube, and, if necessary, performing bronchial lavage through a bronchoscope. Encrustation and obstruction of the tube is regarded as evidence that humidification has been inadequate. It is essential that the size of the endotracheal tube should be correctly chosen, since a tube too large in diameter will cause subglottic trauma, while a smaller tube will offer too great a resistance to respiration. The correct size of tube is one that will easily pass into the trachea, and under no circumstance should the tube be forced through the larynx.

After extubation it may be necessary to remove any secretions that accumulate in the subglottic region, and on rare occasions a subglottic tracheal slough needs removal. This happens only

when a tube of too large a diameter is used, and should not occur if the tube chosen initially is of the right size. The persistence of stridor after extubation therefore demands a direct laryngoscopy to ascertain the cause of the respiratory obstruction and its removal.

The nasotracheal tube, when used for intermittent positive-pressure ventilation, has certain disadvantages in that the connexion to a ventilator is sometimes difficult to arrange in the smaller infant.

In order to overcome these difficulties a special tube has been devised consisting of a standard Portex endotracheal tube to which, at right angles at its distal end, is welded a second wider-bore tube. This is done in such a way that (1) the lumina of both tubes are in continuity and (2) the union of the smaller to the large tube is eccentric, so that there is no

FIG. 3.—Plastic naso-endotracheal tube.

protrusion of the latter towards the patient's nose when the tube is in situ (Fig. 3) (Rees and Owen-Thomas, 1966).

The advantages of this arrangement are that ventilator connexions may be made to the ends of the larger tube and not disconnected for the duration of the treatment. In order to gain access to the trachea for suction purposes it is necessary only to remove a plug from the distal end of the tube. In this way positive and rigid fixation of the endotracheal tube and the respiratory tubings can be made to a skull-cap arrangement and strapping attached to the child's head (Fig. 4).

Circulatory Failure

Minor degrees of circulatory failure are common in serious illnesses of childhood. They tend to be unrecognized, however, until the degree of hypoxia and acidaemia reaches a point at which a sharp fall in cardiac output occurs and the patient is in a state of acute cardiorespiratory failure ("collapse"), from which he may not recover.

FIG. 4.—Details of head harness. The lateral limbs are protected from the scalp by a thick layer of foam rubber. The tube is held rigidly by tapes fastening it to the head harness. The chin-strap ensures that the cross-piece does not exert pressure on the nasal septum.

There is a progressive diminution of pulse volume due to a small pulse pressure, with systolic pressure maintained at first but ultimately falling. The periphery becomes cold and cyanosed. There may be evidence of dehydration and blood or plasma loss. The central venous pressure may be high or low, depending on the degree of dehydration or cardiac failure. There are no signs of congestive failure unless the condition is of at least several days' duration or there is associated congenital or other disease of the heart. The pH is often low (in the region of 7 units), owing to base-depletion and also to a raised PCO_2 when there is associated respiratory failure.

When signs of circulatory failure appear it must not be assumed that it is due, for example, to "toxic" depression of myocardial function, and that therapeutic measures will be largely ineffective. Such assumptions tend to be made especially when a severe infection is the cause of the illness. A careful assessment of the cardiac state is required.

1. *Hypoxia* must be looked for, if necessary by measuring the arterial PO_2 , and, if present, appropriate treatment should be instituted.

2. *Acidaemia*.—A low pH (<7.2) depresses cardiac function (Darby *et al.*, 1960; Gerst *et al.*, 1964; Stewart *et al.*, 1962; Stewart, 1964). This may necessitate treatment for CO_2 retention or base depletion. Intravenous sodium bicarbonate will restore the latter and may rapidly improve cardiac output, but if O_2 deficiency is the cause steps must be taken to improve oxygenation, or acidaemia will rapidly recur. Sodium bicarbonate may be given according to the formula proposed by Astrup *et al.* (1960) either by mouth, if there is no urgency, or intravenously (1 mEq/ml. or 8.4%). When an episode of acute cardiorespiratory failure occurs 3 ml. of the 8.4% solution per kg. should be given intravenously immediately after controlled ventilation and cardiac massage have been started. Subsequent measurement of the acid-base state will determine further treatment.

3. *Fluid and Electrolyte Depletion*.—Dehydration and loss of Na, Cl, and K ions may cause acute cardiorespiratory failure. Four patients were admitted in a state of collapse due to gastroenteritis. One responded to correction of water, electrolyte, and acid-base abnormalities. Another required, in addition, intubation and assistance with ventilation for a short time during the acute episode of collapse, and subsequently made a complete recovery. The remaining two also required ventilation, but this had to be continued because hypoxic cerebral injury had occurred during the acute episode of failure before admission and was ultimately the direct cause of death.

4. *Calcium-potassium Imbalance*.—Both potassium depletion and excess potassium impair cardiac function. Potassium depletion may not be evident in the peripheral blood in the presence of acidaemia, but becomes evident as this is treated. If digitalis is being given, toxic symptoms may appear at this stage unless steps are taken to avoid hypokalaemia. Hyperkalaemia may require treatment with glucose and insulin, and if there is underlying renal disease the use of resins or peritoneal dialysis may be necessary.

5. *Intravascular Volume*.—This is one of the most important factors requiring evaluation. It is necessary to measure accurately the central venous pressure, and this is best done by introducing a polyethylene tube into the inferior vena cava via the saphenous vein. It is attached to a saline manometer, the bore of which should be about 2 mm. Before each reading the manometer should be filled to the top from the drip-bottle, to which it is attached by a three-way tap. It should be held in the hand when a reading is taken. The column of fluid should be seen to move freely both up and down, otherwise a valid reading may not be obtained. The correct pressure is the point towards which the fluid level falls and rises when the zero mark on the column is moved respectively above and below the zero level for pressure through the mid-atrium (mid-axillary line). Alternatively, an electrical manometer may be used, but this is usually less convenient for prolonged monitoring.

The information obtained is made use of as follows:

1. If the pressure proves to be in excess of 15 cm. above the mid-atrium in the presence of a low arterial pressure myocardial failure is present, and the institution of the measures already mentioned, together with the use of digitalis, is indicated. In order to obtain maximum output it may be necessary to add or remove a small quantity of blood in order to adjust venous

pressure to an optimum level (usually about 15 cm.). The persistence of a high venous pressure points to a myocardial fault, but the possibility of embarrassment of a failing heart by tamponade should be kept in mind and a paracentesis considered.

2. The venous pressure may turn out, however, to be <5 cm. in the presence, for example, of a severe septicaemia, where it may be thought on clinical grounds that a toxic effect had produced myocardial failure. In these circumstances the intravascular volume should be cautiously expanded with blood, plasma, or dextran, and the response of venous and arterial pressures noted. Not infrequently it is gratifying to find an entirely normal cardiovascular response to expansion of intravascular volume, the arterial pressure steadily rising to a normal level with a venous pressure not in excess of 10–12 cm.

3. The venous pressure may be normal (5–10 cm.) when first measured, with a low arterial pressure. The indication is to transfuse. The normal heart responds to transfusion by raising the arterial pressure, little or no change occurring in venous pressure. If there is impaired myocardial function it may be necessary to raise the venous pressure to 15 cm. before the arterial pressure approaches normal.

Clinical Experience

Patients are admitted to the unit for two main reasons: (1) the treatment of acute cardiorespiratory failure (collapse), its complications, and the disease causing it; and (2) observation when cardiorespiratory failure seems imminent.

These patients are admitted to one of the cubicles for acute cases for observation, biochemical assessment, and patient-monitoring for early detection of cardiac and/or respiratory failure. This forms an important part of the work of the unit, the object being to obtain early evidence of deterioration and thus to ensure appropriate and timely action to prevent an episode of acute cardiorespiratory failure with its attendant risks of cerebral and renal damage.

The second reason for admission explains why a relatively small proportion of patients in some groups—for example, bronchitis and bronchiolitis—required intubation or ventilation. It also explains why the mortality in other groups—for example, meningitis—is higher than it might have been. Admission in this latter group tended to be late, and frequently followed an episode of cardiorespiratory failure which had resulted in hypoxic brain injury from which recovery could not be expected. Table I summarizes the main groups of patients admitted.

TABLE I.—Main Groups of Patients

	No. of Patients	Age Range in Years	Died
Acute epiglottitis	10	1–7	1
Bronchitis and bronchiolitis	26	1/52–3	0
Bronchopneumonia	56	1/52–4½	19
Asthma	51	2½–11½	0
Respiratory distress syndrome	31	1/52	23
Meningitis	7	1/52–9	4
Acute myelitis (Guillain-Barré type)	3	3–11½	0
Poisoning	10	3–11½	1
Miscellaneous	15		11
Total	209		59

Acute Epiglottitis and Other Causes of Obstruction of Upper Airway

Ten patients were admitted with stridor due to acute epiglottitis, forming 10% of the total admissions to the hospital with stridor. Stridor was usually of short duration—three to six hours—and had increased rapidly. The degree of obstruction had become severe in all cases, and urgent endotracheal intubation was required to relieve it. This had to be carried out

as an emergency on admission in three cases because a state of collapse had occurred, with cardiac arrest. In the remainder it was done in order to prevent that happening. The duration of intubation was from 1 to 11 days, and only one patient required intermittent positive-pressure ventilation. This was due to the fact that during an episode of collapse before admission cerebral injury from hypoxia had occurred and proved to be irreversible, causing death several days later.

Fifteen patients were admitted for other causes of obstruction of the upper airway, including cystic hygroma of the neck, burns of larynx due to inhalation of smoke, glandular fever, measles, foreign body, and accidental hanging.

Bronchitis and Bronchiolitis

Of the 26 patients admitted only two required nasal endotracheal intubation. None required ventilation. They were admitted as a precautionary measure because it was felt that severe respiratory failure might occur.

Bronchopneumonia

Fifty-six children were admitted (Tables II and III), all with evidence of opacities on the chest x-ray film. They were a selected, severe group comprising approximately 12% of the total admissions with bronchopneumonia. The overall mortality was 19 (34%). Seven of the eight requiring endotracheal intubation and tracheobronchial suction survived. Out of the 13 ventilated patients who died seven belonged to a special group with renal failure, discussed below (azotaemic group).

Three patients had a giant-cell type of virus pneumonia, which in two was associated with frank measles, and all three died of respiratory failure due to progression of the lesion.

TABLE II.—Organisms Found in Cases of Bronchopneumonia

	No. of Patients	No. of Deaths
Virus	3	3
Staph. pyogenes	9	3
Other bacteria	44	13
Total	56	19 (34%)

TABLE III.—Bronchopneumonia in Children Aged 1 Week to 4½ Years

	Not Ventilated	Intubated	Ventilated	Total
Lived	23	7	7	37
Died	5	1	13	19
Total Mortality	28 18%	8 12%	20 65%	56 34%

Nine had staphylococcal pneumonia, and various bacteria were isolated from the remaining 44. Detailed virus studies were not carried out.

The pH, P_{CO_2} , and standard bicarbonate did not appreciably differ in the non-ventilated group and the ventilated group who survived, but values in the ventilated group who died were more abnormal (Table IV). The blood urea was appreciably higher in all ventilated patients, especially in those who died.

TABLE IV.—Effect of Ventilation in Children with Bronchopneumonia

Means and Ranges	Not Ventilated	Ventilated	
		Lived	Died
pH	7.26 (7.24–7.50)	7.36 (7.22–7.52)	7.06 (6.95–7.40)
P_{CO_2} (mm. Hg)	58 (36–150)	55 (21–100)	77 (24–150)
Standard bicarbonate (mEq/l.)	21 (18–26)	24 (21–28)	18 (7–27)
Urea (mg./100 ml.)	43 (20–85)	97 (28–240)	125 (17–336)

The PCO_2 was often high and did not diminish greatly after artificial ventilation had been established. As a result, when ventilated with oxygen these infants may appear pink, yet have capillary PCO_2 levels of 80 to 90 mm. Hg. The capillary PCO_2 is a good measure of the degree of respiratory failure in this group. It is usually not possible to discontinue ventilation until the infant is pink when breathing air and the capillary PCO_2 is <50 mm. Hg.

Bronchopneumonia in Infants (Azotaemic Group)

Seven infants between 10 days and 6½ months of age who were ventilated form a small group with special features which justify separate description. The onset was usually very acute, with a history of less than 12 hours, during which the infant refused feeds and became unresponsive. There was a slight increase of respiratory effort, or short periods of apnoea. There were either no abnormal signs or only a few crepitations audible on examination of the chest, and the x-ray picture on admission was normal. There was evidence of a low cardiac output with oliguria or anuria. The paucity of respiratory signs contrasted with striking evidence of cardiac and renal failure. The pH was usually in the region of 7 owing to a high PCO_2 and marked base-deficit (Table V). The blood urea was characteristically high, the mean value being 239 mg./100 ml. The response to resuscitative measures was usually only partial, and anuria or oliguria persisted after restoration of a good cardiac output. If renal failure persists repair of the base-deficit is followed by a rapid recurrence, and it may be possible to control the situation only with the aid of peritoneal dialysis. The sole survivor, who made a complete recovery, was treated by ventilation and early peritoneal dialysis. Death usually occurred within 48 hours. At necropsy two had cerebral venous thrombosis and two a lower nephron nephrosis.

TABLE V.—*Bronchopneumonia. Azotaemic Group of 7 Patients Aged 10 Days to 6½ Months*

pH	6.89 (6.5–7.19)
PCO_2	67 (24–150) mm. Hg
Standard bicarbonate	9 (7–12) mEq/l.
Urea	239 (115–348) mg./100 ml.
Sodium	142 (128–150) mEq/l.
Potassium	6.7 (5.7–8.6) mEq/l.
Chloride	115 (95–136) mEq/l.

Staphylococcal Pneumonia

Of the nine patients admitted with staphylococcal pneumonia three required pulmonary ventilation, and all three died. In two death was due to slow extension of the disease with the formation of multiple chronic abscesses during the period of ventilation; and in the third patient pulmonary ventilation became inadequate because of the presence of a large bronchopleural fistula. Therefore ventilation should be delayed as long as possible in this group. Intercoastal drainage of an empyema with an under-water seal is not a contraindication to ventilation. It may be difficult or impossible to achieve adequate pulmonary ventilation in the presence of a bronchopleural fistula, but this is not always so, and ventilation should be undertaken when the indications for it exist. When deterioration has occurred to the point at which controlled pulmonary ventilation is required the infection has usually been in existence for at least a week. Every effort must be made to gain control of it by the use of two suitable antibiotics in full dosage before it becomes chronic and resistant to all therapy. The necessity for controlled pulmonary ventilation should be regarded as evidence that treatment was not sufficiently early and vigorous.

Respiratory Distress Syndrome

Thirty-one neonates were transferred from neonatal units in the city because they had failed to respond to the standard

methods of treatment, and many required assistance with ventilation before admission. They were ventilated by the standard technique, acid-base abnormalities were corrected, and a glucose infusion was usually given. The fact that only eight survived would appear to emphasize the severity of the lesion in the group treated and the importance of abnormalities of the pulmonary circulation.

Asthma

Twenty-three patients were admitted in an acute attack of asthma. Five remained in status despite the usual measures, including steroids, and seemed to be in danger of cardio-respiratory failure. One patient required controlled pulmonary ventilation for 48 hours and subsequently recovered. In four bronchoscopy was performed and bronchial lavage was carried out with definite but limited improvement, which may well have tipped the balance in favour of survival.

Impaired or Incoordinate Forces of Respiration

Only diseases in this group actually observed are listed in Table I, and not all are discussed. Respiratory effort is diminished, producing hypoventilation, cyanosis, and raised PCO_2 levels.

Hypoxic Brain Injury.—Five in the series died from this cause. In three the initial lesion was meningitis, in one acute epiglottitis, and in one poisoning with Briggssoff. Cardio-respiratory failure resulted in severe hypoxic cerebral injury which was irreversible. One of the primary objects of intensive therapy is to avoid this situation.

Meningitis.—Six severe cases of meningitis were admitted because brief periods of apnoea had occurred or breathing had ceased altogether. Three were due to *Haemophilus influenzae* and one to *Proteus mirabilis*. In the remaining two no organism was isolated. All required ventilation. Two recovered completely and four died. They died of hypoxic brain injury and not of meningitis, for it had largely resolved by the time they came to necropsy.

Poisoning.—Ten patients were admitted with acute poisoning, but only one showed evidence of respiratory failure and required ventilation. This was due to poisoning with Briggssoff, a cleansing agent containing turpene, which caused cardio-respiratory failure. Resuscitation was successful, but death was due to hypoxic brain injury.

Acute Myelitis (Guillain-Barré Type).—Three patients were admitted with this condition and two developed a sufficient degree of respiratory failure to require controlled pulmonary ventilation: one for six days and the other for 11 weeks. All three recovered.

Status Epilepticus.—One patient was admitted with status epilepticus which had failed to respond to the usual measures. He was treated with relaxant drugs and intermittent positive-pressure ventilation. Anticonvulsant agents were continued. Ventilation was discontinued when there was electroencephalographic evidence that abnormal electrical activity in the brain had ceased.

Conclusion

Paediatric intensive therapy may be defined as the study, evaluation, and improvement of methods for maintaining vital functions, especially respiration and circulation, during serious intercurrent illness. At the present time this can be done best in a unit where the necessary personnel and equipment are concentrated. This makes it possible to examine the physiological problems, apply and modify techniques, and assess

results in order to ensure maximum effectiveness of the methods used.

Controlled pulmonary ventilation is technically simple and safe, but requires a high degree of attention and should not be undertaken without adequate facilities and experience. Clearly there is much to be learned about the support of vital organs during intercurrent illness and the use of instruments for temporarily taking over their function. Nevertheless, this unit has undoubtedly been responsible for the saving of lives that in the absence of readily available specialized therapy would have been lost.

Subclinical Small-intestinal Disease in East Pakistan

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Investigators in Thailand, South India, Puerto Rico, Haiti, and West Pakistan have noted a remarkably high incidence of malabsorption and histological evidence of chronic enteritis in surveys of asymptomatic apparently normal members of the native-born population (Sprinz *et al.*, 1962; Baker *et al.*, 1962; Angel *et al.*, 1963; Klipstein *et al.*, 1966; Russell *et al.*, 1966). These studies have usually been carried out as control observations in connexion with the investigation of patients with diarrhoeal illnesses. Reduced absorptive capacity for xylose has been shown, but the absorption of other substances has not been widely studied, and there has been little in the way of systematic inquiry into the problem. In this investigation it was decided (1) to determine the incidence of malabsorption in a group of asymptomatic East Pakistanis; (2) to test the absorption of substances other than xylose to gain a fuller picture of the extent of derangement of small-bowel function; (3) to correlate the presence of malabsorption with factors such as economic status, body weight, parasitism, and anaemia; and (4) to observe the natural history of subjects with evidence of subclinical bowel disease and the effects of treatment with tetracycline and folic acid on small-intestinal function.

Methods and Materials

Adult Pakistani employees of the Pakistan-SEATO Cholera Research Laboratory were asked to volunteer for the study. Of 113 employees approached 106 agreed to take part. They represent a cross-section of the total employee group, with a wide range in occupation (Table I) and economic status (Fig. 1). Absorption tests were performed at the laboratory under the supervision of a nurse trained in metabolic procedures. At the time of study all subjects were free of diarrhoea, though 6% of the group had experienced chronic diarrhoea during the year prior to the study.

The five-hour urinary excretion of D-xylose after a 25-g. dose by mouth was measured by the method of Roe and Rice (1948). Normal values for this laboratory in asymptomatic Europeans and Americans range from 5 to 10 g. Folic-acid absorption was studied by microbiological assay of serum with *Streptococcus faecalis* after a dose of 40 µg. of folic acid per kg. by mouth. Values of >40 mµg./ml. at one or two hours are

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regarded as normal (Chanarin *et al.*, 1958). The 24-hour urinary excretion of vitamin B₁₂ was measured after an oral dose of 1 µg. of cobalt-58-labelled cyanocobalamin (Amersham)

TABLE I

Occupation	No. Studied	No. with Xylose Less than 5 g.
Technician	29	11
Nurse	18	8
Administrative work ..	10	2
Sweeper	10	1
Bottle-washer	7	2
Physician	6	4
Guard	6	4
Field worker	6	3
Miscellaneous	14	7
Total	106	42

FIG. 1.—Xylose absorption and economic status.

given with intrinsic factor and a parenteral "flushing" dose of 1 mg. non-radioactive vitamin B₁₂ (Schilling, 1953). Normal values in this laboratory are 8 to 26%/24 hours. Faecal fat was measured according to a modification (Jover and Gordon, 1962) of the method of van de Kamer *et al.* (1949) on 72–96-hour collections. An average daily excretion of 5 g. or less was regarded as normal. Jejunal biopsies were obtained with the intestinal capsule of Crosby and Kugler (1957) and examined under the dissecting and light microscopes.

Results

Xylose Absorption

The mean xylose excretion of the 106 employees was 5.38 g. (S.D. 1.81). The values follow a normal distribution curve.

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