A STUDY OF RICKETS; Incidence in London.

BY

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AND

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In order to ascertain the incidence of rickets in London a study was attempted during the months of February, March and April of 1925.

It was thought that these being the darkest months of the year, following on a long, sunless period, the incidence of rickets would be at its height.

Our first difficulty was to define the basis upon which rickets could be diagnosed. We had over and over again diagnosed rickets clinically . . . .

Commentary

J O FORFAR

The Archives of Disease in Childhood, although it became the official journal of the British Paediatric Association (BPA), was first published two years before the founding of the BPA. Appropriately, the senior author of this paper on rickets, Dr Donald Paterson, played a leading part in the founding of the BPA and was its first Secretary. He was a Canadian who came to Edinburgh University to study medicine. After qualifying there he moved to London where he worked for many years at Great Ormond Street and the Westminster Hospital, becoming a leading figure in British paediatrics. Dr Hector Cameron in his history of the British Paediatric Association 1928–1952 says of Donald Paterson, 'Under the smoke-screen of his magnificent hyperbole and invective, he judged shrewdly of every situation. He had determined to found a Paediatric Association for all Britain and nothing was in the least likely to stop him.'

The paper examined the incidence of rickets in children attending hospitals over the months of February, March, and April, in which the incidence of rickets was known to be highest. Children up to the age of 2 years attending the Infants' Hospital, Westminster, and St Thomas's Hospital were examined clinically and had an x ray of the wrist taken. Of the 339 children attending, four (1.2%) showed active rickets clinically and radiologically and 110 (32%) showed evidence of previous rickets clinically, although radiologically the rickets was shown to have healed. No evidence of rickets either clinically or radiologically was found in 225 (67%). Interestingly from a social point of view, another paper in the same issue of the Archives (by Drs W P T Atkinson, Helen Mackay, W L Kinnear, and H L Shaw) showed that children of the same age from a poorer part of London, attending hospital, showed an incidence of active rickets of 8%.

Although the title of Dr Paterson's paper emphasises a concern with incidence, an equally important element with which it deals is the preventive and curative effect of cod liver oil. Of the 339 cases studied, 313 (92%) had had some cod liver oil over a considerable period, indicating the extent to which at that time a prophylactic or therapeutic measure of this kind had been widely adopted by the public. Those of us whose early childhood spans that era remember with some revulsion the twin oils that were then so prominent in the family medicine chest—cod liver oil, so widely employed as a universal promoter of childhood health, and castor oil, so ritually administered as a cure for any childhood ill. None of the four active cases described in Dr Paterson's paper had had cod liver oil. Of the healed cases, 88% had had cod liver oil, leading to
the assumption that this oil had cured their rickets, but no evidence is provided that there was a temporal association between the administration of the cod liver oil and the cure of the rickets. The assumption might have been strengthened had the authors subjected their data to the discipline of the statistical analysis that would now have been imposed on them. This would have shown that there was a significant difference (p<0.05) between the 96% incidence of cod liver oil consumption in the cases without any evidence of past or present rickets and the 88% incidence in healed cases. There was clearly a difference between the two groups, but the reason for it cannot be determined with any certainty from the data given. It is doubtful if the conclusions drawn, correct although they may have been, would have satisfied the standards of logic demanded by present day editors of medical journals—even the gentle, friendly paediatricians who today control the editorial destiny of the Archives are seen by some to metamorphose at times into ruthless martinets as they set about culling sophistry from its pages.

Medicine contains many examples of the discovery of cures before any understanding of their scientific basis was possible. Cod liver oil for the treatment of rickets was a classic example, as were fox glove extract for the treatment of the ‘dropsy’ of cardiac failure, raw liver for the treatment of pernicious anaemia, and lime juice for the treatment of scurvy. Vitamin D is not mentioned in the article as that word was not yet in common currency and the chemical nature of vitamin D had yet to be discovered. This had to await the discovery of the specific sterol irradiated ergosterol or calciferol five years later and the demonstration that it could prevent and cure rickets. At that time and for many years thereafter that discovery seemed the final word on the subject of vitamin D. Much, however, remained to be discovered and has been discovered over the past few years. The individual response to vitamin D has been found to vary widely — the same intake of vitamin D may be adequate for one child and result in rickets in another; a vitamin D intake associated with health in one child can result in hypercalcaemia in another. Vitamin D dependent rickets and idiopathic hypercalcaemia of infancy represent extreme ends of this spectrum. The explosion of knowledge regarding the metabolism of vitamin D over the past few years has revealed that naturally occurring vitamin D—7 dehydrocholesterol converted in the skin by sunlight to cholecalciferol (vitamin D3)—is only active if hydrolysed in the liver to 25-hydroxycholecalciferol (25-hydroxyvitamin D) and then further hydroxylated in the kidney to 1α, 25-dihydroxycholecalciferol, the active form of the vitamin.

From a diagnostic and a therapeutic standpoint the discovery of these metabolites of vitamin D has been important. Before their recognition the estimation of vitamin D could only be made on the basis of a biological assay, inaccurate, difficult to standardise, and expensive. The ability to measure these metabolic products of vitamin D accurately, particularly 25-hydroxycholecalciferol, has been an important factor in recognising and categorising different types of rickets. From a therapeutic point of view the availability of analogues of 25-hydroxycholecalciferol where hepatic disease is a cause of rickets and of 1α, 25-dihydroxycholecalciferol where renal disease is the cause has added greatly to the armamentarium available for the management of different types of rickets.

Man is indebted to the cod for more than one of the cheapest types of protein. Cod liver oil enabled him to prevent and cure a disease that for centuries ravaged the health of children. Although rickets was first described nearly 250 years ago, the piscatorial saga that led to its prevention and cure has only been told over the past 60 years. To that saga the Archives of Disease in Childhood has contributed many important chapters.

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HEPATIC CIRRHOSIS IN CHILDREN, 
with special reference to the Biliary Forms.

BY
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The occurrence in hospital within a comparatively short space of time of four unusual examples of cirrhosis of the liver in young children has led us to make this communication.

Disorders of the liver in childhood have in recent years not attracted much attention in this country, and we feel that the mere ventilation of the subject, though we may have little new to add, may serve a useful purpose.

It is possible that others besides ourselves have been inclined to be guided in their views upon cirrhosis of the liver by a recollection of cases of alcoholic cirrhosis in the adult, and to recall such symptoms as . . . .

Commentary

A P MOWAT

The paper starts modestly with four case reports of children with chronic liver disorders recently intensively investigated by the authors but without reaching a diagnosis. Stimulated by this failure and by their concern that disorders of the liver in childhood had not attracted enough attention in this country, the authors have produced a very readable review of the subject as perceived in 1926.

Succinct case histories enhanced by superb photomicrographs illustrate descriptions of seven forms of cirrhosis. Much of the review remains as apposite as when written. Among the non-biliary forms they included multilobular cirrhosis, Banti's anaemia, Wilson's disease, and, somewhat surprisingly, icterus gravis neonatorum. They recognised that the latter was not associated with cirrhosis but thought it should be included since the areas of brain stained in this condition were similar to those affected in Wilson's disease! I imagine that both authors would have been pleased that this inclusion avoided the editorial censor since in 1926 Dr Wyllie was transferring from adult neurology via paediatric pathology to a distinguished career in child guidance, while Dr Poynton, whose career achievements included being a stylish middle order batsman for Somerset Cricket Club and BPA President, had just published a case report on Wilson’s disease.

Then, the brain damage in both was attributed to hepatic toxins. What has changed? In 1948 the association between excessive copper accumulation and tissue damage in Wilson’s disease was established. Three years later effective chelation treatment was introduced. The hepatic mode of presentation of the disease without neurological abnormality was emphasised in 1957. In 1986 delay in diagnosis in children is very frequent. Nearly 50% of those diagnosed at King’s College Hospital are referred late with liver disease so advanced that they die in spite of chelation treatment. Liver transplantation, which will correct the metabolic abnormality, can save these children, but donor livers are rarely available. The role of unconjugated hyperbilirubinaemia in the pathogenesis of kernicterus is well established. How to determine the precise risk of kernicterus in the individual infant still eludes us.

Banti’s anaemia, a concept of primary splenic disorder releasing toxins that cause cirrhosis, continued to have support until the 1950s when radiological, haemodynamic, and particularly histological studies confirmed that the primary disorder was portal vein obstruction or, more commonly, some
form of liver damage, particularly chronic hepatitis. In the '50s corticosteroid responsive autoimmune chronic active hepatitis was gradually defined. The concept of chronic hepatitis and multilobular cirrhosis remained confused until in 1965 Blumberg identified a serological marker for hepatitis B infection. Hepatitis B affects up to 90% in the first six years of life in some parts of Africa. At least 10% develop chronic hepatitis. More worryingly, viral deoxyribonucleic acid (DNA) becomes integrated with host DNA. Liver cancer may ensue. There is as yet no treatment for hepatitis B infection. Molecular biologists have used recombinant DNA technology to produce from yeasts a vaccine that is immunogenic.\(^2\) Given the correct priorities its use could lead to the elimination of this, the last important viral infection, which could be prevented by immunisation. Hepatitis A virus in contrast causes only acute hepatitis.

In considering biliary cirrhosis biliary atresia predictably had a prominent part. Death from a bleeding diathesis by 8 weeks of age was the norm. By 1940, it was clearly established that vitamin K was important in preventing haemorrhagic disease of the newborn and in that associated with cholestatic disorders. Sadly, the prothrombin time is still overlooked as an essential test in liver disease, and cholestatic babies still develop intracranial bleeding that could have been prevented by vitamin K.

Given the 10 year survival of 90% after surgical correction of biliary atresia in the first eight weeks of life, it is equally disappointing that in the United Kingdom referral is usually later.\(^3\) Paediatricians do not see all babies with jaundice at 4 weeks of age. Diagnosis is therefore delayed.

In considering intrahepatic disorders to be distinguished from biliary atresia familial cases were emphasised. In 1926 the only well characterised disorder was infantile polycystic disease. Today, there are over 20. The most frequent is \(\alpha_1\) antitrypsin deficiency, first associated with liver disease in 1968.

In 1986 not only is the complete chemical structure of this glycoprotein and the genetic composition of its variants fully established, but with the wonders of DNA technology mammalian cells may now be modified to synthesise the complete glycoprotein.\(^4\) This opens up the way to \(\alpha_1\) antitrypsin replacement therapy and antenatal diagnosis by analysis of DNA in chorionic villi.

The review completed, the authors returned to the undiagnosed cases. Two are siblings with photographs and features we would now recognise as being typical of glycogen storage disease, a condition defined clinically and pathologically in 1929. Now there are 12 different enzyme defects in glycogen storage disease, some of which are further subdivided into distinct pathophysiological variants with genetic, prognostic, and therapeutic implications.\(^5\) In the remaining two cases further laboratory investigations, including percutaneous liver biopsy, using the Menghini technique introduced in 1958, would also be required.

The last 60 years has seen considerable advances in the management of liver disease in children. There are still many poorly characterised disorders and much remains to be discovered about causes, pathogenesis, and treatment. With the exciting advances now occurring in cellular and molecular biology, we have an unrivalled opportunity to increase our understanding of these processes and to provide more effective help for our patients. We must strive to bridge the gap between the work of the basic scientist and clinical problems. Paediatric hepatology is still an emergent speciality. The opportunities for research orientated paediatric hepatologists have never been greater. The conclusion of Doctors Wyllie and Poynton that ‘It is often impossible to be certain either of the nature of the cirrhosis or of its origin’ still applies!

References


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FOUR CASES of IMMUNO-TRANSFUSION
with remarks on the Method

BY

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Immuno-transfusion is a comparatively recent extension of treatment by blood transfusion and the following case seems worth recording as an example of recovery from a desperate illness after other methods had apparently failed.

Summary and Conclusion.

1. Four cases of proved septicaemia treated by immuno-transfusion with one recovery and three deaths are described.
2. The success occurred in a pneumococcal septicaemia consequent upon empyema and seems attributable to the transfusion.
3. All four cases had previously undergone surgical operations.
4. Immuno-transfusion, though by no means a certain cure for septicaemia, offers a hopeful line of treatment in some cases.

Commentary

C A CLARKE

Clinical findings

The successful case was that of a boy aged 2 who had a left sided pneumococcal empyema with a positive blood culture. A pneumococcal vaccine was prepared from the patient's blood, and a dose of 1000 million organisms was injected into his father; five hours later 350 cc of the father's blood was removed, defibrinated, and injected into the child's median basilic vein. 'His temperature and pulse fell immediately and by the next morning he was much better . . . '. Six months later 'his general condition, except for a little bronchitis, remained excellent'.

Cases 2, 3, and 4 all died, one from Staphylococcus aureus infection after osteomyelitis of the femur and two from streptococcal blood stream infections.

I was not particularly impressed by the reason given for the recovery of case 1. Firstly, in the month after the immunotransfusion his temperature was never completely normal; secondly, he had another attack of orchitis similar to an earlier episode; and, thirdly, a small empyema developed on the right side. Again he had already survived two and a half months before the immunotransfusion, and pneumococcal infections tend to be less lethal than those caused by the Staphylococcus or Streptococcus. But still, he survived, and I wonder if he is still alive. Can he be traced, or does the Data Protection Act protect his data from follow up? It would be interesting to know his present antibody state.

The results in two of the many references that I looked up are contradictory. Kilgore is all gloom and doom. He reports three cases of Streptococcus viridans endocarditis: 'All three were 'improved' in their own and families' opinion, but in none could I see any beneficial effect other than temporary relief of anaemia and the psychic uplift to be expected from any strange and elaborate treatment'.

Greenslade on the other hand describes an orphan girl aged 6 who in one week had two extensive mastoid operations and one operation for lateral sinus thrombosis. Her chances looked hope-
less, but after immunotransfusion from a convent sister donor her condition improved immediately and she made a complete recovery. His other two cases were almost as dramatic, both recovering.

The scientific validity of immunotransfusion

Wright et al thought that the critical time for the patient to be transfused was about five hours after the donor had been injected; this was based on studying the number of colonies of bacteria surviving in vitro in the donor’s blood before and after his vaccination. They also found that the effect was non-specific and surmised that the vaccination had simply stimulated the donor’s phagocytes (opsonisation) and that these were much more effective in destroying the bacteria than were the patient’s own worn out cells.

I took advice on Wright’s hypothesis and the experts chorused: ‘In no way . . . ’—and who was I to judge? But I had a theory. Had the donors been ‘sensibilised’ by the patient—after all, they lived under the same roof? And I was reminded of the ‘little old man’ who was one of our Rh negative volunteers. He had no overt rhesus antibodies, but when we injected him with Rh positive cells the antibody appeared within 24 hours. On taking a proper history, we then found that he had had a blood transfusion in the first world war. ‘Sensibilisation’ surely?

The mystery to me is why Wright needed his particular opsonin theory; he was aware of the way antibodies were formed and knew that one could have donor panels for use in seriously ill patients and that therefore the time factor need not be critical. He seems to have thought, however, that these antibodies could not be specifically tested against the patient, whereas his stimulated phagocytes could.

Sensibilisation—or not—of the donor would account for the ‘hit or miss’ results, but why the 100% failure rate in subacute bacterial endocarditis? I suspect that the formation of immune complexes provides the answer; these are highly likely to occur in subacute bacterial endocarditis and were responsible for the fatal outcome.

Obviously, immunotransfusion took a back seat with the coming of antibiotics, but it is now coming into favour again in the form of gammaglobulin infusions, particularly for viral diseases (McCarthy K. Personal communication) against which antibodies are not yet well developed. Donor panels are available, and the technique seems particularly effective in viral diseases that are predisposed to by immunoincompetence.

But treating viral diseases is not new. In the 1930s a child in Great Ormond Street was extremely ill with generalised vaccinia. Alan Moncrieff contacted the army at Aldershot and obtained plasma from recently vaccinated army recruits. This was transfused into the child and resulted in rapid healing of its condition (Stroud CE. Personal communication).

Specific gammaglobulin infusions are also being advocated in severe bacterial infections where, increasingly, the organisms are resistant to antibiotics.

So did Almroth get it right? In some ways ‘No’ and in others ‘Yes’, but he was certainly a proper doctor for my heart warms to his views on statistics.

The statistician has done his very best to persuade the world that there is only one way, that being the statistical method, by which the efficacy of a therapeutic method can be scientifically put to the test . . . ‘, but this, because of heterogeneity, ‘is almost invariably fallacious’. Fortunately, there are ’non-statistical methods by which efficacy can be tested—words graphic enough to depict to the reader the desperate condition of the patient when treatment was initiated, and the resurrectional change that followed . . . .

Sixty years on we have a similar problem in reverse, relating to plasmapheresis in rhesus immunised women. Sometimes it works and sometimes it doesn’t, but no two cases are the same. For example, the antibody concentrations may be transiently reduced, but because of an antigenic stimulus acquired in the course of treatment there is a rebound effect. Again, more recently, there is evidence of a factor that normally inhibits antibody production and this may be removed by plasma exchange. The statisticians call for a properly controlled trial, but they are crying for the moon—read the case histories and see.

Envoi

G B Shaw and Almroth were friends and sparring partners, and phagocytes figure large in ‘The Doctor’s Dilemma’.

I wonder if there is anything in the five hour story? Almroth and his followers were remarkably sure about it. Why not try it in AIDS? — in vitro, of course, unless a non-specific stimulus would do the trick.

I recently met Leonard Colebrook’s great nephew at the ‘BODY’ tree planting ceremony at Cambridge. He is a general practitioner in Bedford and knows all about his ancestor.

I am most grateful to Professor Kevin McCarthy and Dr Nevin Hughes-Jones for their helpful advice and to Professor CE Stroud for his vaccinia anecdote.
Four cases of immuno-transfusion

References

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(Bernard Schlesinger was a founder member of the British Paediatric Association and became its President in 1953-54.)

(Sir Cyril Clarke, a former member of the Archives Editorial Committee, was awarded the James Spence Medal in 1973 in recognition of his contribution to the prevention of rhesus haemolytic disease of the newborn. He is a past president of the Royal College of Physicians of London.)
An Investigation of SCLEREMA NEONATORUM; with Special Reference to the Chemistry of the Subcutaneous Tissues. (Part I.)

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WITH

A HISTOLOGICAL REPORT

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Introduction.

Sclerema neonatorum is a rare but interesting condition peculiar to infants. The extraordinary confusion that has existed in the past in...

Commentary

M L CHISWICK

Chaussier coined the term 'sclérème' around 1815 to describe hardening of the skin in the newborn, and by the end of that century the expression 'sclerema neonatorum' was in general use. Much earlier descriptions of this disorder appear under a variety of names. One might think that sufficient time had elapsed for us to have learned everything there was to know about the pathogenesis of this disorder and that the subject was now closed. Not so—because we have been hampered by confused terminology. Only a few reports claiming to be about sclerema neonatorum refer to that disease as we know it today.

Harrison and McNee observed that in affected areas the fibrous trabeculae between fat lobules were thickened; acicular crystals of neutral fats were seen 'lying in bunches like sheaves of corn' around fat lobules; multinucleated giant cells were prominent; and calcium salts were seen to form a coating on some of the fat cells. Biochemical changes in the subcutaneous fat were not striking and consisted of a raised melting point and a questionable reduction in olein content. The authors correctly suggested that changes in fat metabolism were unlikely to be the primary event but instead were probably secondary to inflammation.

In a forthright presentation to a meeting of the Royal Society of Medicine at Brighton in 1959 Elliot emphasised the difference between subcutaneous fat necrosis and sclerema neonatorum and distinguished both of them from 'neonatal cold...
injury'—the condition that Trevor Mann and he had drawn attention to in the *Lancet* two years previously. Elliott emphasised that there was no need to postulate that the pathogenesis of subcutaneous fat necrosis depended on a chemical change in the fat itself. Yet, in a frequently cited paper based on one patient, Horsfield and Yardley, in 1965, propagated the notion that 'sclerema neonatorum' (in reality subcutaneous fat necrosis) might be a generalised disorder of fatty acid metabolism manifest by a raised ratio of saturated:unsaturated fatty acids locally in subcutaneous fat, epidermis, and dermis.

If we accept that subcutaneous fat necrosis is a localised chronic inflammatory response to trauma then what is the nature of the trauma? Today we speculate intrauterine compression injury. All sorts of things, which fortunately we cannot see, happen in the womb—so we are on strong ground here. Yet it is curious that whereas now most affected infants are healthy and have an excellent prognosis, 60 years ago it was not unusual for affected infants to be chronically ill with failure to thrive, fever, diarrhoea, and vomiting. Indeed, four of the five cases described by Harrison and McNee died. There are a number of plausible reasons for this difference. Firstly, overt birth trauma and presumably intrauterine compression injuries were more common then, and subcutaneous fat necrosis might merely have been incidental to the illness that led to admission to hospital. I note, for example, that the necropsy findings in one of Harrison and McNee's cases almost certainly describes the appearance of congenital hypertrophic pyloric stenosis. Secondly, infective diarrhoea and failure to thrive were so common one wonders whether affected infants were drawn from the poor community where lack of warmth in the home was compensated for by overtight swaddling. Thirdly, there is the possibility that a proportion of infants were the victims of physical abuse, with associated failure to thrive and chronic ill health. The purplish discolouration overlying lesions on the limbs would have been attributed to the fat necrosis rather than to bruising.

Sclerema neonatorum has a quite different appearance, and most paediatricians are familiar with the ominous sight of an ill preterm baby whose skin takes on a waxy pallor associated with a progressive induration and coldness. Sepsis or massive periventricular haemorrhage are common underlying conditions and most affected infants die.

In 1722 Usenbenz, a German physician, published 'Eighth month live birth, cold and rigid' —a paper that the present editors of the Archives would have warmed to because of its concise title. Usenbenz described a soldier's wife who gave birth at eight months to a baby girl at a hospital, in Ulm. The girl was extraordinarily cold and hard, and her cheeks could not be indented even with strong pressure. He likened her entire body to 'a piece of smoked meat'. In spite of wrapping her in warm linen and warming her in front of the fire, she remained 'stiff from head to heel . . . unresponsive and immobile, without the least cry having been heard'.

Underwood drew attention to this disorder in the first edition of his paediatric textbook in 1784 when he likened the condition to 'hydebound' in quadrupeds. The disorder was commonly observed in European hospitals at the end of the 18th and beginning of the 19th centuries. The French published works refer to 'enfans durs' or 'enfans gelés', thus providing the rationale for one form of treatment, which was to place the infant in a warm bath containing two or three litres of wine, followed by massaging the infant's body with brandy—which was no doubt pleasurable even if not effective.

Some of the infants referred to in the historical publications were probably not examples of sclerema neonatorum but were suffering instead from cold injury. Observing how sclerema neonatorum occurs today, I am impressed by how the rectal temperature often remains near normal while the skin temperature rapidly falls. The widening rectal–skin temperature gradient is associated with poor capillary return on blotting the skin and progressive pallor as the skin becomes indurated. All this in spite of the use of plasma expanders.

The pathogenesis of sclerema neonatorum is still unclear. The histology of the subcutaneous fat is quite unlike the chronic inflammatory picture described by Harrison and McNee. In fact, there is very little to see apart from thickened trabeculae between fat cells.

Sclerema neonatorum probably does reflect a change in the chemical composition and physical properties of subcutaneous fat, but accounts of the biochemistry of this condition are of limited value because they are generally based on isolated case reports and poorly matched controls. The ratio of saturated:unsaturated fatty acids is increased in the subcutaneous fat of preterm infants, and it would seem that this feature is even more pronounced in infants with sclerema neonatorum.

Earlier reports of sclerema neonatorum suggested that it was as common in term infants as in preterm ones—the latter usually presenting within a day or two of birth. Now the condition is virtually confined to our 'new population' of extremely preterm infants in whom I have the impression that it presents later—sometimes after the second week—just when hopes for survival are being raised. By this time, the
composition of subcutaneous fat has had time to be influenced by the nature of the infant’s diet, be that parenteral nutrition or milk. Bearing in mind that we have a new population of patients and also that changes have occurred in the nutritional care of preterm babies, re-evaluation of the biochemistry of subcutaneous fat in sclerematous infants and extremely preterm controls of the same postnatal age is long overdue.

We might also take the opportunity to rethink this interesting disorder in terms of the metabolic vulnerability of polyunsaturated fatty acids. Are these fatty acids sheltered and protected in the subcutaneous layer, or are they vulnerable to attack by free radicals? Peripheral circulatory failure and sepsis are circumstances that probably promote the production of free radicals. Might sclerema reflect structural changes in fat cell membranes brought about by free radical damage? Only a minority of critically ill preterm babies become sclerematous, and in them are the scales tipped by a relatively deficient ‘antioxidant system’? Someone had better do the work before sclerema neonatorum becomes extinct.

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THE SPECIAL SCHOOLS OF LONDON.

BY

F. C. SHRUBSALL, M.D.

Although, unquestionably to the ailing child, the restoration of health and relief from crippling conditions are of supreme importance, experience has shown that when the necessary measures are spread over a period of years under such conditions as to limit the possibilities of education, still more if they are such as altogether to prevent formal education, the child is unduly handicapped on reaching the employable age. This difficulty became obvious so soon as universal elementary education was made the law of the land.

From the first the by-laws of the various school boards laid it down that ill-health was a reasonable cause of absence from school; but . . .

Commentary

N GORDON

In the introduction Dr Shrubsall starts by saying that when the necessary measures to restore health and relieve crippling conditions are spread over a period of years, under such conditions as to limit the possibilities of education, the child will be unduly handicapped on reaching an employable age. In 1893 an Act was passed allowing provision for special education for blind and deaf children and in 1899 for those crippled, epileptic, or mentally defective. To start with this was on a voluntary basis, and it was not until after the first world war that it became a duty in all areas of England and Wales. A few years before 1926 hospital schools had been established for long stay patients.

At that time the London County Council provided special education for children who were blind, deaf, or physically or mentally defective and for stammerers and places in residential schools for those with epilepsy. The Council’s medical officers had to examine all such children and visit the schools from time to time; decisions could then be enforced by law. Dr Shrubsall describes the groups and school facilities as follows.

The blind, partially blind, and myopic

A blind child is one who is too blind to read the ordinary school books used by children. The instruction in the schools for the blind includes the teaching of braille and suitable forms of handwork occupations. At the age of 12 suitable children are transferred to residential schools for special trade training until the end of the school term in which they attain the age of 16. Children affected with myopia leave school at 14. They are naturally studious and more prone to read out of school, which should be discouraged unless from suitable type. (Considering that the association of myopia and the higher levels of intelligence has been recognised for so long, this might have received more study than it has.)

The deaf

A deaf child is one who is too deaf to be taught in a class of hearing children in an elementary school. Deaf children may be admitted to school at the age of 5 but this cannot be enforced by law until the age of 7. In such schools oral methods of instruction are used, special attention being paid to lip reading and pronunciation. At the age of 12 suitable children are transferred from schools for the deaf to residential schools for special trade training until the age of 16. Special classes are provided for those who are not severely deaf, and as soon as they have acquired powers of lip reading they are marked for transfer to an ordinary school. There is a special school in Penn for ‘the few oral failures’ and for children who are
deaf and also blind or mentally defective. A nurse attends all these schools to treat discharging ears. (No mention is made of any controversy between oral methods and signing.)

**Physically defective**

The usual ground for admission is some cause of crippling, or some organic disease, that renders attendance at an ordinary school disadvantageous but does not prevent a child being educated in a small class under constant medical and surgical supervision. An ambulance is provided for children who live at a distance and are unable to use public transport. Provision is made for a certain number of recumbent children, and a nurse is in constant attendance. The school is visited by the school doctor at least every four weeks and periodic visits are made by an orthopaedic surgeon. Attendance can be enforced to the age of 16, but when feasible the child is transferred back to an ordinary school.

The constant supervision in schools for the physically defective provides a valuable link with the hospital, as children can obtain further advice at the onset of any untoward occurrence. They are fully occupied under supervision so that the concern expressed by some that they will be turned into invalids is unjustifiable. Most children suffer from paralysis, quiescent tuberculosis of bones or joints, congenital deformities, and heart disease. Children with epilepsy are not admitted.

Older children are transferred to separate schools for trade instruction, adapted to their physical defects and to the possibilities of their obtaining local employment.

**Open air schools**

These are provided for children from the age of 8. One type is for debilitated and anaemic children and those liable to tuberculosis and another for those with definite pulmonary tuberculosis or tuberculous glands.

**Epileptic children**

There are arrangements for children who suffer from chronic epilepsy of such a degree as to make them unfit to attend an ordinary school but whose mental state allows them to derive benefit from education in residential epileptic colony schools, if they are between the age of 7 and 16. To derive this benefit children should be sent at a relatively early age. Physicians may postpone a recommendation for residential treatment and keep the children for considerable periods out of school, which is not always desirable.

**Stammering classes**

Arrangements exist for children of 8 years and upwards to attend for a course of three months at classes taken by specially trained teachers.

**Mentally defective children**

Before a child attending an ordinary school is proposed for admission to a special school he is seen by the school doctor and arrangements made to secure treatment for any defect such as poor vision, partial deafness, and mouth breathing. Then the child is examined by special medical officers. Generally, the children admitted are those whose mental age is estimated as less than three quarters of the normal. In these schools classes are small with specially trained teachers and a special curriculum, with separate schools for trade instruction for the older children. When possible the child is transferred back to normal school. At 15½ years all children are reconsidered, and those deemed to need institutional treatment due to lack of intelligence are referred for care under the Mental Deficiency Act. Those who can cope receive after care until the age of 18.

Such children, if kept in ordinary schools, may fall further and further behind due to a sense of inferiority. If they are transferred to a special class, however, they learn they may be of use in the world and receive praise instead of blame, to the benefit of their self-respect.

Dr Shrubsall sums up the aims of the special schools as to obtain the best possible combination of treatment and education and to secure the utmost cooperation between the school medical service, private practitioners (GPs), and hospital physicians and surgeons. The staff at special schools today surely have the same aims. It is perhaps surprising that there were so many provisions of this kind 60 years ago, although London may have been unique. No mention is made of numbers except that there were 4432 children on the rolls of schools for the physically defective out of a total school population of 697 882.

The problem of children attending special schools in 1986 will have changed in many ways, but there are several basic truths in this paper. Changes are on their way but will they be advantageous to all? Integration of handicapped children into normal schools seems to be a laudable objective and may benefit many of them but not all; and then only if schools are given the extra resources to cope with the extra problems that will undoubtedly arise. It will certainly not work if it is regarded as a money
saving exercise. Also there are dangers in generalisations. There are some children, not necessarily those with the severest handicap, who need the extra support, both in and out of the classroom, that only special schools can provide. I cannot express it more adequately than Dr Shrubsall.

In the same volume there is a short paper (pp 230–1) by Dr Dingwall Fordyce of the Royal Liverpool Children's Hospital. He makes the point 'that Intelligence Tests are valuable for the practitioner, particularly in assessing children with physical defects who suffer from long-continued or recurrent ailments, and for those with scholastic retardation and character anomalies.

'The intelligence quotient is, at best, one aid to a decision affecting the individual, but it is an important one; and combined with scholastic tests often gives valuable information as to aetiology, prognosis and desirable procedure.'

(Neil Gordon, one of the founders of paediatric neurology in Britain, was awarded the highest distinction of the British Paediatric Association, the James Spence Medal, in 1985. For most of his career he has worked in Manchester.)
LAMBLIASIS AS A CAUSE OF CHRONIC ENTERITIS IN CHILDREN.

BY

REGINALD MILLER, M.D., F.R.C.P.
(From Paddington Green Children's Hospital.)

Intestinal infections due to the flagellate, lamblia intestinalis, attracted attention in England in the early years of the war when the disease first reached this country from the Eastern fronts. Since 1916, with the exception of Clifford Dobell's report(1), hardly any further reference to the disease has been made in English medical literature. I can find no clinical study of the infection published in this country though many papers on the subject have appeared in America.

This paper is based upon the study of 23 children infected with lamblia and has been largely written without previous reference to the publications of other observers. The conclusions reached are (1) that the infection is now by no means a rarity in hospital practice amongst children; (2) that it produces a chronic enteritis; (3) that the resultant diarrhoea is often severe enough to cause the subjects of the disease to be considerably below their proper weight, and occasionally will produce retarded development and diminution of growth, suggesting that in lambliasis we have a further possible cause of infantilism of the enteritic type; (4) that even in children true "carriers" may be found, infected with lamblia, but without symptoms.

Commentary

A S McNEISH AND I W BOOTH

This paper, by the first joint editor of Archives, gives a brief account of 23 children with chronic diarrhoea and suboptimal growth in whom Giardia lamblia cysts were found in the stools. The text moves from factual description to generalised statements about 'lamblia' infection, emphasising that the clinical picture can vary from the asymptomatic carrier state to 'chronic enteritis with infantilism of the enteric type.'

From a modern standpoint this paper has three* defects. Firstly, Miller had no test to exclude coeliac disease, 'which lamblia may resemble more than any other.' Secondly, he could not test the clinical result of treatment, because no effective treatment against giardia was available. Third, giardia was common in the 1920s—the survey quoted in the paper suggested a carrier rate in England of 18–27%. The finding of the parasite in some of Miller’s patients may have been coincidental.

And yet Miller may have been right. G. lamblia is endemic throughout the world and is spread by faecal-oral contamination, with the added possibility of animal reservoirs of infection. Fifty per cent of all infection may be asymptomatic. The active clinical picture is of acute diarrhoea, leading to chronic diarrhoea in a variable proportion.

Attachment of the parasite to the mucosa of the small intestine is regarded as a crucial step in
pathogenesis. The exact mechanisms by which diarrhoea and malabsorption result are incompletely understood, but there is evidence for both mucosal and luminal factors. Enterocyte damage, mucosal inflammation, and on occasion direct invasion of the mucosa have been shown by light and electron microscopy, with the severest lesions being found in association with immunodeficiency.  

Intestinal bacterial overgrowth, inhibition of lipolysis, pancreatic insufficiency, and, rarely, inflammation of the bile ducts have all been found clinically or experimentally. The evidence that infection with the parasite can interfere with growth comes from experimental infection in young animals. Analysis of the limited retrospective and cross-sectional data in children suggests that G. lamblia can interfere with linear growth and often causes faltering in weight gain or even weight loss. The unique community based longitudinal studies by Mata of the children of Santa Maria Cauqué support this view. Why is there such a variation in the clinical picture? Differences in strain virulence and in host (immunological) susceptibility are proposed but are largely unexplored. Sixty years after Miller, there is much work to be done.

References

(Further information about Reginald Miller, who was the inaugural editor, is given on page 979).

(A S McNeish is Professor of Paediatrics and Child Health in the University of Birmingham and recently completed a five year term of office on our Editorial Committee. I W Booth is Senior Lecturer in Paediatrics and Child Health in the University of Birmingham.)
CURRENT PROBLEMS
IN THE
TUBERCULOSIS OF CHILDHOOD.
Infection, Diathesis, Artificial Pneumothorax,
Preventive Inoculation.

BY
ALAN MONCRIEFF, M.D., M.R.C.P. London,
(Medical Registrar, The Middlesex Hospital.)

It is a striking fact that tuberculous infection in infancy and childhood has not diminished in proportion to that of the adult. Aschoff, (6) quoting Gottstein, has particularly emphasised this, and he points out that there are still many problems with regard to the pathogenesis of phthisis yet to be solved. A review of certain views on these problems in the light of recent contributions to their study has been undertaken here almost entirely.

The paper is based on the author's MD thesis and is a review of certain aspects in childhood tuberculosis.

Commentary
B D BOWER

Summary

Childhood pulmonary infection is generally accepted as being caused by the human tubercle bacillus. The evidence from sputum and bronchial gland cultures is overwhelming; in Japan, where cow's milk is not used in infant feeding, pulmonary tuberculosis is as common as in the United Kingdom. The portal of entry is less certain. Suggestive evidence exists for the intestinal, the pharyngeal, and even the conjunctival routes, but that for the 'direct aerogenous' route is most convincing. Ghon, in particular, has shown the subpleural focus with infection of the draining lymph glands in 95% of 184 autopsies. (1)

The existence of an inherited tuberculous diathesis is still debated, but most of the evidence in its favour can be explained on another basis—that is, the amount of contact with infected individuals, which means the dose of bacilli inhaled. The striking results of separating newborn infants from their tuberculous mothers by comparison with those not so managed support this.

In the treatment of children with pulmonary tuberculosis artificial pneumothorax is used in France and Germany, but not in Britain. Results from several hundred children of all ages treated for up to four years are given and suggest that it can prolong survival, but the author evidently has no first hand experience of the method.

Prophylactic inoculation. Calmette and his school have produced an avirulent strain of the tubercle bacillus, 'Bilié—Calmette—Guérin', by 230 successive cultures. (2) This has been given orally to over 2000 newborns whose mothers have active tuberculosis and have refused to be separated from their infants. No tuberculosis has been detected in the infants when followed up, and no death was due to tuberculosis. In Britain various tuberculins and dead vaccines from attenuated bovine bacilli are being given by injection to child contacts, with some initial promise.

Discussion

It is difficult for most paediatricians working in Britain today to imagine the clinical scene in the
wards or outpatient clinics in 1926. Tuberculosis, still a contender for the title of 'captain of the men of death' with an annual death rate (at all ages) of 80 per 100,000 population, killed relatively slowly even in children. It therefore formed a large part of clinical medicine and surgery at all ages. Treatment was by indirect means—improved nutrition, general and local rest—and was slow in results when it worked at all. (Incidentally, why was artificial pneumothorax never a popular treatment for children in Britain in contrast to Europe?) Alan Moncrieff, then a medical registrar, knew the essential facts about the aetiology, pathology, and spread of childhood pulmonary tuberculosis; but he and his colleagues were impotent to influence its course. It was not until more than 20 years later that effective antibiotics became available and transformed the clinical and epidemiological scene.

Prevention, however, was receiving attention 60 years ago, particularly in France, and it is interesting to see that BCG was in existence and undergoing clinical trial at that time. It was first produced in a wooden shed in Lille in 1906, but it was not used to any extent in Britain until the 1950s. A freeze dried vaccine produced in this country was convenient to distribute and use and was soon accepted as effective. But it was the arrival of effective antibiotics and the organisation of case and contact detection nationally as well as locally that reduced the disease to its present relatively trivial proportions (annual notification rate of 12.2 per 100,000 for England in 1983 for all ages, and negligible mortality).

On a global scale it is far from trivial, and in Britain the results of the large scale immigration of Asians in the first two postwar decades still remind us of this. The incidence in Asians of all ages is still 25 times greater than in whites. For children the annual notification rates seven years ago were (per 100,000): for Indians 90; for Pakistanis and Bangladeshis 130; and for whites seven, and the proportions are likely to be similar today. The reservoir of carriers in older adults and the return visits of children to their country of origin will prevent a rapid fall in the rate of infection of Asian children in the near future. In spite of the much greater risk to this group, however, it is important to recognise that in Britain white children constitute the largest group of newly infected cases (50% of the total).

In a treatable disease diagnosis is particularly important. In childhood tuberculosis today early diagnosis may make the difference between complete normality and survival with severe handicap, for instance in meningitis. Yet because of its present rarity, diagnosis is more likely to be delayed in 1986 than it would have been in 1926. (Is it significant that only 15% of cases in 1977–78 were notified by paediatricians, while 73% were notified by chest physicians? The) Not only must the possibility of tuberculosis be considered when an Asian child presents with undramatic symptoms, but it must be realised that in Asian children the presentation is more likely to be with extrapulmonary symptoms, which may be misleading if the usual description of primary tuberculosis given in Western textbooks is considered typical. One must remember, however, that in Britain today the clinician is at least as likely to encounter tuberculosis in a white child.

Prevention must continue to concentrate on the Asian communities. After the diagnosis and treatment of open adult cases, contact tracing and chemoprophylaxis of children are the most important activities. BCG has been useful as a general preventative measure. But the point has now been reached where 2500 immunisations are required to prevent one infection. At present offered to 13 year olds of all racial origins, it may soon be sensible to offer it selectively, for instance to Asian newborns and children entering Britain.

References


(Information about the author, Sir Alan Moncrieff, who later became Editor of the Archives, is given on page 980.)

(Brian Bower, who is a Consultant Paediatrician at the John Radcliffe Hospital, Oxford, is a past member of our Editorial Committee.)
NEPHRITIS IN CHILDHOOD

BY

NORMAN B. CAPON, M.D., M.R.C.P.

(From The Royal Liverpool Children's Hospital, for the Medical Research Council.)

The investigations upon which this paper is based were undertaken primarily to examine the practical value of the so-called "renal efficiency tests" in children. Cases of kidney disease admitted to one of the medical wards of the Royal Liverpool Children's Hospital were systematically examined, and the results have been analysed. This has necessitated a general survey of kidney diseases, and of the special peculiarities of these diseases in children. So far as possible, the pathological and clinical aspects have been correlated in the classification adopted; and an attempt has been made to emphasise the necessity of taking a broad general view of each case studied.

The paper is sub-divided under the following headings:

1. Classification of nephropathies.
2. Methods of investigation.
3. Description of cases studied.
   (A) Acute glomerulo-nephritis.
   (B) Chronic glomerulo-nephritis.
   (C) Diffuse tubular nephritis.
4. Pathological findings in diffuse tubular nephritis.
5. Treatment.
6. Summary and conclusions.
7. Bibliographical references.

Commentary

G C ARNEIL

The personality of Norman Capon, a man of wit and wisdom complementing perspicacity and pioneering thought, shines through this very early attempt to rationalise the approach to nephritis in children. One must remember this was during a time when streptococcal acute glomerulonephritis was common as was chronic, acute, and lethal sepsis, antedating by 10 years the use of Prontosil rubrum and by 20 years the widespread use of penicillin. His paper is neatly compartmentalised and is perhaps best considered in this way.

Classification of nephropathies heads the list and like every subsequent attempt falls between the Scylla of clinical findings and the Charybdis of pathological dogma, until then unchallenged as it was, de facto, the last word. It may be summarised as nephrotic syndrome, nephritic syndrome, and chronic renal failure—not a bad start even today. We have now passed the zenith of pathological influence, but the pressures imposed by needle biopsy, light microscopy, electron microscopy, and immunohistochemistry backed up by some outstandingly dominant personalities has stressed the patience of many paediatric nephrologists. The acceptance that similar lesions may result from differing insults and that pathologists are not always
right, when biopsy examination is followed by clinical course, is restoring a more realistic balance. It is interesting to note that even then focal and interstitial nephritides were well recognised.

Methods of investigation are very revealing. Medical history, general examination, and urine examination were as good as or probably better than today. Serum biochemistry was crude and renal efficiency tests crude, lacking the sophistication and accuracy of modern clearance techniques and in particular isotope clearances.

The star item of the paper is, however, the inclusion of renal biopsy examinations, a very early example of this technique. That the concept of ‘minimal change’ stretches so far back is thanks to the vogue for bilateral renal decapsulation current at that time that led Campbell, a Glasgow surgeon reviewing his remarkably good results in the early 1920s, to suggest it was the anaesthetic and the operation (any operation!) that perhaps caused 50% to recover (stress of surgery equal to treatment with glucocorticosteroids?).

Description of cases studied is peppered with records of focal sepsis and systemic infection, which bring back memories to all paediatricians practising before the latter half of the 1940s.

Pathological findings are confused, with diffuse parenchymatous nephritis, diffuse interstitial nephritis, and other hoary old chestnuts confusing the issue. The morbid anatomy and histologies of a kidney decapsulated 86 days previously are of interest. The histology of glomeruli on biopsy examination reveals minimal changes, epithelial crescents, hyaline thrombus, and fibrous infiltration.

Treatment included dietic (high energy and protein), diuretics (alkalis and urea) sadly lacking chlorothiazides (1950s), frusemide, and antialdosterone agents. Elimination of septic foci contrast with prevention of viral infections and fear of fulminating gram negative septicaemia, which ‘bugs’ us today.

This is a refreshing leaf from history with an approach not dissimilar to that of today, albeit with less technology, pathological physiology, and no glucocorticosteroids, cyclophosphamide, or effective diuretics. If it is always true that we treat them, but God cures them, then at least we are able to help the Almighty a little more today as compared with 1926.

(Norman Capon was subsequently appointed to the Foundation Chair of Child Health in the University of Liverpool. He was a Founder member of the British Paediatric Association and was its President in 1951–52.)

(Gavin Arneil is Leonard Gow Lecturer and Professor of Child Health in Glasgow. He was the first Director General of the International Paediatric Nephrology Association. He is a past member of the Archives Editorial Committee and currently Editor of The Bulletin of the International Paediatric Association.)
CHRONIC ULCERATIVE COLITIS IN CHILDREN.

BY

GEOFFREY BOURNE, M.D., M.R.C.P.
(Physician to the East London Hospital for Children).

By ulcerative colitis is meant in this paper a chronic ulcerative condition of the colon, inflammatory in nature, and accompanied by frequent loose motions containing blood and mucus.

Other conditions associated with a minor degree of acute ulceration occasionally are found in infants and young children, but in them the acute enteritis, rather than the few ulcers associated with it, dominates the . . . .

Commentary

J A WALKER-SMITH

Dr Geoffrey Bourne, author of the article, was a physician on the staff of St Bartholomew's Hospital and King George's Hospital, Ilford. He was also physician to the East London Hospital for Children at Shadwell. He was regarded as a sound general physician with a special interest in children (Swain V. Personal communication). At St Bartholomew's Hospital he is best remembered for having established an electrocardiographic department. He was also an author, with several books to his credit, including one on politics. At St Bartholomew's Hospital until 1937 no full time paediatrician had been appointed, and so children were cared for by general physicians in adult wards. In 1942 the East London Hospital for Children at Shadwell amalgamated with the 'Queen's Hospital for Children', Ilford. For economic reasons Shadwell was eventually closed in 1962.

Dr Bourne began his paper with what is still today a good clinical definition for the colitis of chronic inflammatory bowel disease. Naturally, he was unaware of the current distinction between ulcerative colitis and Crohn's colitis, as Crohn and his colleagues only went on to describe that disease for the first time some six years later in 1932. What is remarkable, however, is that despite the fact that he was only reporting one child and reviewing the scanty world reports up to 1926 he firmly based his diagnosis upon two diagnostic criteria that have stood the test of time; firstly, clinical (diarrhoea with the presence of blood and mucus in the stools), and secondly, endoscopic—that is, sigmoidoscopic or proctoscopic (which he described as naked eye evidence of chronic disease).

He disregarded radiographic evidence alone, a view I would heartily endorse. Our current practice in the Paediatric Inflammatory Bowel Disease Clinic at St Bartholomew's Hospital is to use only endoscopy (colonoscopy and ileoscopy), with multiple biopsy for the diagnosis of colitis in childhood. Endoscopically, Dr Bourne insisted on the presence of ulcerated colonic mucosa for precise diagnosis. In his case report Bourne described the presence of a number of small ulcers on sigmoidoscopy. Were these in fact what now would be called aphthous ulcers? In fact, endoscopists now teach us, perhaps paradoxically, that such discrete ulceration is not a feature of ulcerative colitis but is characteristic of Crohn's disease. In ulcerative colitis there is typically a general granular appearance with increased friability and ulceration, which when present may be large and linear. Possibly, the case described was in fact one of Crohn's colitis or even, as the author mentions, a case of bilharziasis (schistosomiasis), acquired in Egypt because the patient responded to intravenous antimony tartrate.

Whatever the final diagnosis, in terms of current knowledge, the rarity of reported cases of ulcerative colitis—that is, chronic inflammatory bowel disease—in children up to 1926 is remarkable. At that time he could find only nine other what he described as well authenticated published cases in all
the published reports world wide. He mentions seven other reports that may also include some cases of ulcerative colitis.

Nevertheless, it is truly remarkable that ulcerative colitis should have been so rarely reported in the published reports up to that time. In a recent review from St Bartholomew’s Hospital 28 cases were described over 10 years, and the reports on ulcerative colitis in children are now extensive. Why has this remarkable increase in the number of published reports occurred? Does it reflect a true increase in incidence in developed communities in recent years? The disease is still uncommon in children in developing communities—for example, in India—but when Indian children are born in Britain they also develop the disease. Bourne, nor indeed his contemporaries, could have missed cases of chronic inflammatory bowel disease on any appreciable scale in the light of his clinical acumen and recognition of accurate diagnostic criteria and his knowledge of the disease in adults. Some environmental factors that have occurred in Western societies in the past 60 years must have been responsible for this change. It seems to be that an infectious agent, at least of the conventional type, is unlikely to account for this change, as in the last 60 years the environment has become progressively less hazardous microbiologically, with some notable exceptions of course, such as legionella and acquired immune deficiency syndrome (AIDS), that are related to special features of modern life. Could any such special features be involved here in childhood ulcerative colitis or must we look to some chemical or food related substance that triggers an inflammatory process in the colon that continues for immunopathological reasons? Bourne’s clinical acumen and accurate description thus leads to fascinating speculation about the nature of this disease.

Ulcerative colitis is as much an enigma to us today as it was to Bourne. Therapeutically, we have a better armamentarium, and the techniques of surgery have greatly improved, with subtotal colectomy and ileostomy being effective treatment. Yet only the discovery of the precise cause and the development of more effective therapeutic techniques, preferably for prevention but also of effective and curative treatment, will do away with what can only be described as mutilating surgery. Complete eradication of this unpleasant disease can be our only goal.

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(John Walker-Smith is Professor of Paediatric Gastroenterology in the joint academic Department of Child Health for St Bartholomew’s Hospital, The London Hospital, and Queen Elizabeth Hospital for Children. He served on the Archives Editorial Board 1976–80.)
CONGENITAL ABSENCE OF TIBIA.

BY

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I. Definition and Description
II. Clinical and Radiographic Features
III. Cases
IV. Diagnosis
V. Anatomical Descriptions
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Commentary

R W SMITHELLS

In this article an orthopaedic surgeon and his registrar report eight cases of a rare skeletal deformity, including five published previously. In an article running to 35 pages, including 12 photographs and eight detailed anatomical drawings, they describe the clinical, radiographic, and anatomical features and discuss aetiology and treatment. Their search of the published reports (which includes French, German, Italian, and American publications) revealed only 102 previously published cases, although the bibliography curiously omits a reference to Motta, who published a remarkable collection of 50 cases. The discussion of aetiology refers to many theories and concludes that 'the cause is defective development of the mesoblast under an influence at present unknown, but not traumatic, mechanical, vascular or atavistic'.

Although only eight cases are here described, the paper brings out two points that larger series confirm—namely, (a) the frequency of additional defects, by no means all skeletal, and (b) the familial tendency in some cases. It is interesting to compare this paper with that of Kalamchi and Dawe (1985), who describe 21 children with congenital tibial deficiency seen over 30 years. Despite reporting seven times as many new cases, the modern authors are constrained to four pages, including eight figures. They have no further light to shed on aetiology, they confirm the frequency of associated defects of many kinds (in 14 of 21 children), and share the views of Evans and Smith regarding treatment—namely, disarticulation at the knee and the fitting of a prosthesis for all but the mildest cases.

Interestingly, although several authors (including Evans and Smith) attribute the first reported case of congenital absence of the tibia to Otto (1841), no reference can be traced.*

*The reference to the article by Otto has now been traced but is reported to make no mention of congenital absence of the tibia.
Biographical notes

(With acknowledgements to Lives of the Fellows of the Royal College of Surgeons of England and to Dr P F Smith, Librarian, Institute of Orthopaedics.)

Evan Laming Evans (1871–1945) CBE, FRCS, MD. Educated at Eastbourne College, Trinity College, Cambridge, and St Bartholomew's, London. Before settling on a career in orthopaedics he worked as assistant bacteriologist in the joint laboratory of the Royal Colleges of Physicians and Surgeons; as a general practitioner; and in the South African war as surgeon and physician, winning the Queen's medal with three clasps; and he wrote his MD thesis on typhoid fever. His consulting work included the Industrial Home for Crippled Boys, and he had a special interest in congenital dislocation of the hip.

Norman Ross Smith (1897–1965) MB, CHB (Sydney), FRCS. After graduating in Australia he came to London and worked at St Mary's, Guy's, St George's, the West London, and the Royal National Orthopaedic Hospitals before settling in Bournemouth. He was orthopaedic surgeon to the Shaftesbury Society's Victoria Home for Crippled Children. He was a stalwart supporter of the British Medical Association and was elected an Honorary Fellow shortly before his death.

References


(R W Smithells is Professor of Paediatrics and Child Health in the University of Leeds. He is a regular contributor to the Archives, particularly on subjects relating to the prevention of congenital abnormalities.)
A CONTRIBUTION TO THE STUDY OF THE CAUSATION OF FOETAL DEATH

BY

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During the last few years, more attention has been paid to what has been, beforetime, a much neglected branch of pathology—the subject of foetal and neo-natal death. Its importance is obvious. The yearly wastage of foetal life assumes enormous proportions; nor is this all.

Commentary

J S WIGGLESWORTH

One hundred and sixty autopsies were performed at the Jessop Hospital for Women, Sheffield, as a consecutive series from March 1923 to March 1925, on infants who were stillborn or died in the first week of life. There were 117 stillbirths and 43 neonatal deaths.

Using a simple classification Dr Tingle considered that 17 (11%) of the cases were associated with maternal causes, mainly 'albuminuria' or eclampsia; 35 (22%) had placental causes, including placenta praevia, retroplacental haematoma, and infarction; and 129 (81%) had fetal causes, including trauma, infections, and anomalies. Twenty one cases were considered to have maternal or placental causes in addition to a fetal cause. Detailed analysis was restricted to the fetal causes. The major fetal cause of death was birth trauma, found in 105 (66%) of the infants. An unrecorded number of these cases were craniotomies; of the remainder, 58 (36% of all deaths) had tentorial tears. Intracranial haemorrhage was associated with the tears in 57 of the 58 cases. In 30 of the infants the bleeds were classified as 'much' in quantity, in 19 as 'moderate', and in eight as 'little'. Tentorial tears followed cephalic delivery in 30 infants, 17 of them with forceps, and followed breech delivery in 28, of whom 17 were delivered after version. Tentorial tears followed uncomplicated cephalic delivery at term in only two instances: other cases where forceps had not been applied were complicated by prematurity, contracted pelvis, or prolonged or precipitate labour.

Prematurity was considered to be a major factor predisposing to dural tears, being present in 17 (29%) of the affected infants. The intracranial bleeding was recognised as originating from the extension of a tentorial tear into a sinus in five cases and from a torn vein of Galen in one. The origin of bleeding was obscure in the rest, but dissection of fixed fetal heads indicated that the haemorrhage had arisen from tributaries of the vein of Galen.

Two liveborn premature infants were found to have intraventricular haemorrhage extending through the third ventricle, aqueduct, and fourth ventricle. Eight cases of haemorrhage into one or both adrenals were recorded; seven of them had been delivered by the breech, and five had associated intracranial haemorrhage. Other sites of bleeding included the pleural cavities, the lung substance, the perirenal tissue, and the kidney.

Although trauma was clearly the dominant factor leading to haemorrhage, the possibility of haemorrhagic diathesis was investigated by measuring clotting times of newborn infants and their mothers. Four infants had delayed clotting times and died at ages from 12 hours to 7 days. Two of these were the premature infants with intraventricular haemorrhage: the others had multiple bleeding sites.

Infection was recognised in 14 cases, of whom nine had pneumonia. Organisms cultured from the lung included Escherichia coli or coliforms in seven cases, mixed staphylococcus and streptococcus in one case, and a pure growth of pneumococcus in one.
case where the mother also died of pneumococcal sepsis.

Of the 10 infants classed as showing fetal anomalies, four had cardiac anomalies, of whom two showed features of mongolism and two had other anomalies. Pulmonary atresia was the most common cardiac lesion. Other forms of anomaly included a case of achondroplasia, without family history, and an infant with generalised oedema. Histological examination of the latter infant revealed massive haemopoiesis in liver, spleen, and kidney, with excessive iron deposition in the liver. This was considered to provide evidence for the destruction of fetal red cells by some unknown toxic factor.

The main conclusions of the study were that more fetuses died as the result of excessive trauma during delivery than from maternal or fetal disease, that the fatal results of trauma were due to haemorrhage, and that maternal disorders may predispose to fetal injury during delivery.

This paper reminds us of the dramatic improvement in perinatal survival that has occurred over the past 60 years. The appalling mortality due to perinatal asphyxia and birth trauma recorded by Dr Tingle is unsurprising given the poor nutritional background of the population at the time combined with lack of such vital adjuncts to modern obstetric and perinatal care as antibiotics, safe obstetric anaesthesia, routine availability of blood transfusion, and the skills of modern neonatology. The progressive and continuing fall in deaths from trauma and asphyxia has highlighted a series of less tractable problems that were obscured amidst the perinatal carnage of 60 years ago.

The problems of preterm birth were hardly recognised at the time when Dr Tingle wrote her paper and received little mention within it. The term ‘premature’ was applied indiscriminately to any infant of low birth weight, with resultant confusion between preterm and growth retarded infants. This may partly account for the association noted between prematurity and intracranial trauma.

Some currently important areas of perinatal disease do find mention in the text. Thus two ‘premature’ infants developed intraventricular haemorrhage. They differed from the majority of such infants recognised now in having severe clotting abnormality.

An infant with generalised oedema, from the description almost certainly a case of rhesus is immunisation (not elucidated until 1940), was correctly recognised as suffering from destruction of the fetal blood by some unknown ‘toxic factor’. Although rhesus isoimmunisation is now largely prevented, the problems of fetal oedema and non-immunological hydrops have become an important area for pathological investigation.

The problems of congenital anomaly, discussed by Tingle only in relation to the heart and skeleton, now assume major importance with development of methods of antenatal diagnosis, genetic counselling, and in a few cases intrauterine surgery. The infant described as having achondroplasia, most probably a case of thanatophoric dwarfism, represents a group of infants, the lethal short limbed chondrodystrophies, that require cooperation between pathologist and geneticist for diagnosis and will need continuing biochemical investigation to determine the underlying mechanisms. In the 1980s the patterns of perinatal death presenting to the pathologist change at an increasing rate. The cases now referred to a regional specialist include a high proportion of second trimester fetuses requiring delineation, confirmation, or exclusion of congenital anomalies or fetal disease to link with the range of investigative approaches available to the clinician. The area of genetic disease other than gross abnormalities found no place in Dr Tingle’s study but is now becoming a major concern to pathologists with availability of antenatal biochemical diagnosis for many enzyme defects and the development of DNA probes for disorders such as Duchenne dystrophy and cystic fibrosis. Investigation of the causes and mechanisms of perinatal death has become a far more exciting and hopeful field of study than it was 60 years ago.

(Clara Tingle (or Clara Cross as she became after marriage) graduated from, and proceeded to MD at, Sheffield University. Later she moved to south west England where she set up the Department of Pathology and worked as a Consultant Pathologist in Bath. She introduced exchange transfusion for rhesus incompatibility in that area. She died earlier this year in the Unit named after her at St Martin’s Hospital in Bath. She was, we believe, the only contributor to the inaugural issue of the Archives to have seen the beginning of its Diamond Jubilee year.)

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EFFECT OF ENCEPHALITIS LEThARGICA ON THE INTELLIGENCE OF CHILDREN.

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AND

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I.—INTRODUCTION.

Disturbances of mentality are probably the commonest and most striking of the after-effects of encephalitis lethargica. Duncan(5) found . . . .

Commentary

R J ROBINSON

This article is of historical interest for two different reasons. Firstly, it deals with a disease that swept round the world in the years immediately after the first world war, leaving devastating neurological disability in many of the survivors, but that then disappeared, its cause remaining an enigma. Secondly, it is fascinating to see that the approach used by these authors to the question ‘Does encephalitis affect intelligence’ was then clearly a novel one, though to us in 1986 it seems obvious and natural. It involved the use of psychometric testing on patients and controls followed by statistical comparison. Both methods were sufficiently unfamiliar to need full explanation, and the clear manner in which this is given makes the paper a pleasure to read.

The authors

Dr Shepherd Dawson, the senior author, was head of the Psychology Department at Jordanhill Training College, Glasgow. His interests included pathological factors affecting children’s intelligence and the application of statistical methods to such studies, on which he published a practical manual. This study, like much of his research, was carried out at the Royal Hospital for Sick Children, Yorkhill. He died in 1935, aged 54. He was a distinguished figure in academic psychology, and his obituaries confirm, as can be guessed from this paper, that he was ahead of his time in the scientific application both of psychological testing and of statistics. Dr Conn was presumably a member of Dr Dawson’s department.

The study

Forty six children (‘The number of cases is not so great . . . as could be wished’) had a definite diagnosis of encephalitis lethargica. They were given the Binet tests of intelligence as translated by Sir Cyril Burt. The controls were 974 children without encephalitis who had been tested in the same hospital. The mean intelligence quotient of the cases (84-63) was significantly lower than that of the controls (90-53). Subgroups from the cases were further analysed to see what factors were associated with the lowered intelligence. Intelligence was significantly lower in those whose disease had lasted more than 12 months, and the children who had been retested after an interval had mostly failed to show the appropriate increase in mental age. There was no difference in mean intelligence according to the presence or absence of a Parkinsonian syndrome or of behaviour disturbance.

No details are given of the ages or clinical features of the cases or controls, as would probably be expected now. Today’s Archives reader might be more struck by the apparently rather small effect of this severe illness on intelligence than by the fact that there was an effect.

Encephalitis lethargica

This disorder was first described by von Economo in
occurred in a pandemic lasting from about 1917 to 1928. More than a million cases may have occurred world wide, with perhaps half a million deaths. Though the diagnosis seems to have been regarded as straightforward, the clinical picture was evidently variable. The typical acute cases showed headache, disturbance of sleep rhythm (with an emphasis on somnolence by day), and ophthalmoplegias. A wide variety of other neurological disturbances, however, such as cranial nerve palsies, behaviour disturbance, or extrapyramidal disorders might occur in the acute stage. Sometimes the onset was more gradual. Epidemics occurred in waves, with greater numbers in the winter months.

This account is based on what I have read because there can be few living physicians with personal experience of the disease. The older of us, however, well remember seeing cases of post-encephalitic Parkinsonism, and this late complication probably occurred in most survivors, greatly adding to the burden of disability caused by the pandemic.

Encephalitis lethargica was generally assumed to be caused by a specific virus, but no definite infective agent was ever identified. Some link with the influenza pandemic of 1918–19 was often suggested but not generally accepted because there was no close time relation between influenza and encephalitis, and because the encephalitis pandemic seems to have started before that of influenza. A relation between the two disorders, however, has recently been argued again, and the newer understanding of slow virus infections, and of the long delay between acute measles infection and subacute sclerosing panencephalitis, makes a long latency between influenza and encephalitis more easily understandable. The exact cause remains a mystery.

**Childhood encephalitis today**

Though encephalitis lethargica no longer occurs, we still see children in whom a clinical diagnosis of encephalitis is made. They present with some combination of fever, fits, and depression of conscious level, their electroencephalogram is usually slow, and the cerebrospinal fluid may or may not show an excess of lymphocytes. In most cases the diagnosis remains a presumptive one, the main exceptions being herpes simplex encephalitis and encephalitis after an acute childhood infectious disease such as measles. In fact, a determined search for evidence of viral infection will reveal this in most cases. The viruses concerned, which include enteroviruses and adeno- and adenoviruses as well as those already mentioned, are common, whereas encephalitis is rare, suggesting an abnormality of host response. The mechanisms producing encephalitis are becoming clearer, some forms such as herpes being the result of direct viral invasion or replication in the brain, whereas others such as measles are due to an abnormal immune response. The major recent advances in treatment have been the use of antiviral agents, particularly acyclovir for herpetic encephalitis, and closer neurological monitoring, with control of intracranial pressure in severe cases.

Many children make a complete recovery after viral encephalitis, though the prognosis is less good when the agent is measles and much worse if it is herpes. Even after other encephalitides an appreciable morbidity occurs, and studies like that done by Dawson and Conn 60 years ago remain important and relevant. The editors would still be delighted to receive a paper as clearly written as this one.

I am grateful to Dr and Mrs R R Gordon of Sheffield for the biographical information about Dr Dawson, who was Mrs Gordon’s father. Dr Gordon is a member of the British Paediatric Association.

**References**


(Roger Robinson is Professor of Paediatrics at the United Medical and Dental Schools of Guy’s and St Thomas’s, London. He was Editor of the Archives from 1969 to 1982; further details are given on page 984.)