BRITISH PAEDIATRIC ASSOCIATION

Proceedings of the Twenty-eighth Annual General Meeting

The twenty-eighth meeting of the British Paediatric Association was held at the Old England Hotel, Windermere, from May 1 to 4, 1957.

BUSINESS PROCEEDINGS. Professor John Craig took the Chair as President, and the following members were present:


Professor Charles Dent (Still Lecturer) and the following Danish paediatricians attended as guests of the Association:

Dr. P. W. Braestrup (President, Danish Paediatric Society), Dr. K. Biering-Sorensen, Dr. E. Flamand Christensen, Dr. Paul Drucker, Dr. Carl Friderichen, Dr. B. Friis-Hansen, Professor Preben Plum, Dr. A. Rothe-Meyer, Dr. Annie Schondel, Dr. O. Steinecke, Dr. E. Terslev, Dr. F. Tudvad, Dr. Jorgen Vesterdal.

The following were present as guests of members of the Association:


The Annual General Meeting was held on May 2, 1957.

The Minutes of the last annual meeting were received and approved.

ELECTION OF OFFICERS. The following were elected:

- PRESIDENT: Dr. K. H. Tallerman
- PRESIDENT-ELECT: Dr. J. Forrest Smith
- TREASURER: Dr. R. Lightwood
- SECRETARY: Dr. P. R. Evans

EXECUTIVE COMMITTEE, 1957-60:

Dr. I. A. B. Cathie, Miss I. Forshall, Dr. F. F. Kane, Dr. M. MacGregor.

ELECTION OF MEMBERS. The following were elected:

- HONORARY MEMBERS
  - Mr. Denis Browne, Professor John Craig, Dr. W. E. Crosbie, Dr. H. L. Wallace

- CORRESPONDING MEMBERS
  - Dr. H. Bakwin (New York), Dr. S. Doxiadis (Athens), Professor R. Dubois (Brussels), Professor A. Ross (Montreal)

- ORDINARY MEMBERS
  - Dr. R. Astley, Dr. K. W. Cross, Dr. H. L. Ellis, Dr. J. W. Farquhar, Dr. J. Jacobs, Dr. J. H. Moseley, Dr. P. E. Polani, Dr. A. Russell, Dr. T. Stapleton, Dr. W. Walker

3. The Treasurer’s report was approved and the auditors were re-appointed for one year.

4. The Executive Committee’s report was received and approved, and is printed below.

5. Rules 4, 11 and 17 were altered to read:

- Rule 4. ‘... No candidate may be proposed for election to these offices unless his name, duly proposed and seconded, has been sent to the Secretary at least three months before the Annual Meeting.’

- Rule 11. ‘... Any member of the Association may, by letter to the Secretary, not less than three months before the General Meeting, propose the name of a candidate and shall at the same time state the grounds of recommendation of the candidate ...’

- Rule 14. ‘Notice of any proposal to amend or alter the existing rules, or to pass new rules, must be sent to the Secretary not later than three months before the next ensuing General Meeting, and must appear on the Agenda of the said Meeting in the form of a motion.’

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6. After full discussion it was agreed that, while working within the framework of the present constitution, membership should be increased to take in the majority of hospital paediatricians, as well as other medical men and women with paediatric interests, within three years.

7. Dr. Sheldon asked the Executive Committee to review the status of fever hospitals in relation to paediatric units throughout the country.

**Report of the Executive Committee, 1956-1957**

1. The Association will wish to congratulate Dr. John Hay on his appointment to the Chair of Child Health in the University of Liverpool, and Mr. Denis Browne on the award of the Ladd Medal. No doubt others have been honoured and the Executive must apologize for not noticing all the lights under the bushes.

2. Reports, etc. During the year two reports have been published: one the annual report of investigations into prematurity, which are being carried out in many parts of the country; the other, the report on hypercalcaemia which appeared in the *Lancet* and the *British Medical Journal*. Since publication of the latter report, the vitamin D content of some cereal foods has been reduced.

Two further reports have been completed and await publication. One on radio-iodine deals with the precautions which may be taken to evade the somewhat remote chance of producing carcinoma of the thyroid by investigations in which radioactive iodine is used. Another, on hospital accommodation for children, is separate from, but somewhat complementary to, the report produced by the Paediatric Committee of the Royal College of Physicians of London, and it is hoped that the two reports will be published at about the same time. As a consequence of discussion of this subject an attempt is being made to find out how many children are being nursed in adult wards, a topic of special interest in regions where the closure of children's units to provide adult beds has been proposed.

In addition to these reports, a sub-committee has prepared written evidence for submission to the Cranbrook Committee on Maternity Services, and another sub-committee has, at the request of the Division of Architectural Studies of the Nuffield Foundation, considered the Registrar General's diagnostic classification.

Other subjects under consideration are special clinics (such as chest clinics and epilepsy clinics) and a large survey of perinatal mortality to be carried out under the auspices of the National Birthday Trust Fund.

3. Guests. A dinner for about 200 people was held by the Association and the American Academy of Pediatrics at the Mansion House in London just before the opening in July of the very successful international congress in Copenhagen, which was attended by many of our members. We are extremely glad to welcome our Danish guests at our annual meeting this year.

4. James Spence Medal. The James Spence Memorial Committee has decided that a gold medal shall be presented from time to time in recognition of outstanding contributions to the advancement or clarification of paediatric knowledge. The Committee has asked the Association to make the award and has allocated £2,000 to the project. The Executive has thanked the Memorial Committee for its confidence and generosity, and is proceeding with the preliminary legal arrangements.

5. Windermere Lecture. The endowment of this lecture ended last year, but the board of directors of Messrs. Cow & Gate has renewed the endowment until further notice.

6. The History and the Album. One hundred and fifty-two copies of Dr. Cameron's history of the first 25 years of the Association have been sold, and 40 presentation or review copies given away.

Dr. George Davison has been raised to the dignity of Curator of the Album, and will be pleased to receive photographs of B.P.A. events or persons.

7. Standing Committees. Membership of the standing committees has been reviewed and re-cast more than usual. The Convalescent Homes Committee (joint with the I.C.A.A. and the Institute of Almoners) and the Tuberculosis Committee have been dissolved as they had not met for a long time. Professor Gaisford continues to represent us on the Joint Tuberculosis Council and Dr. Evans is our representative on the new National Committee on Poliomyelitis.

The Child Psychology Committee has been particularly active. The Underwood Report on Maladjusted Children suggested that to meet the needs the number of children's psychiatrists ought to be doubled (to 170), of children's psychologists doubled too, and of psychiatric social workers quadrupled. The committee wonders whether a paediatric training plus an analysis might not be a better equipment for a children's psychiatrist than the usual D.P.M. course, and it would like to discuss this with the Children's Psychiatry Section of the Royal Medical-Psychological Association. The Committee has asked all paediatricians for their views on the psychiatric services for children and adolescents. Too often there seems to be inadequate liaison with a paediatrician. The need for in-patient...
facilities is the subject of a recent memorandum of the Royal Medical-Psychological Association at present under review. The facilities for training students, registrars, paediatricians and other doctors need to be increased and the Postgraduate Federation has been approached, though each region will probably make arrangements. Preventive hygiene in maternal and child welfare clinics, the modifications in the law relating to children, and the procedures for dealing with educationally subnormal children have been under consideration. The Royal Medical-Psychological Association asked the B.P.A. to suggest speakers for a meeting on psychological factors in the causation of attacks of epilepsy. The committee hopes that the 1958 B.P.A. programme will include a discussion on a psychiatric or psychological aspect.

8. MEMBERSHIP. The Executive Committee has discussed policy regarding future membership of the Association at length, and recommend that there should be an increase, spread over five years, to include almost all established paediatricians as well as a leavening of paediatric surgeons, pathologists, physiologists, etc.

9. SPECIAL MILK FOODS. Some members have had difficulty in obtaining low-calcium or lactose-free milk foods by N.H.S. prescription. They should be obtainable on the ground that milk preparations used for specific treatment in certain diseases can be classed as drugs (see 1950 report of the Cohen Committee—The First Report of the Definition of Drugs Joint Sub-Committee of the Standing Medical, Pharmaceutical and General Practitioner Advisory Committees). The firms concerned have been informed by the Ministry of Health that everything possible has been done to arrange that prescriptions of these preparations will not be questioned.

George Frederic Still Memorial Lecture

Professor Charles Dent (London) delivered the Still Lecture, entitled 'Hartnup Disease: An Inborn Error of Metabolism', of which the following is a summary.

Our investigations on this disease (also called H. disease by Baron, Dent, Harris, Hart and Jepson, 1956) began in the year 1951, when a patient of a most interesting family (who have kindly agreed to give their name to the disease) was studied under Dr. E. W. Hart at the Middlesex Hospital. This patient was suffering from a rash apparently identical to that of pellagra and had in addition neurological signs of cerebellar ataxia. The rash had followed exposure to the sun, but true pellagra seemed an unlikely cause since there was an inadequate history of dietary deficiency. Furthermore Dr. Hart was suspicious of a more complicated metabolic upset since one of the patient's elder sisters had been previously admitted many years earlier with a seemingly identical disease, from which she had made a good recovery.

Of the many routine investigations done, nearly all gave normal results and the important negative ones were those which excluded any of the known porphyrias. Urine testing, however, showed the presence of a gross generalized amino-aciduria of quite unique pattern. Further investigation of metabolites of tryptophan was also undertaken in view of the pellagra-like disease and resulted in the discovery of a gross abnormality of indole excretion. The urine contained large quantities of indolyiacetic acid, of indolylacetylglutamine (Jepson, 1956), of indican and moderate quantities of tryptophan itself. There was clearly a very interesting metabolic disorder present.

There were eight sibs in the family and the parents were first cousins. Routine urine testing showed that four out of the eight sibs had an identical urine abnormality with regard to the amino-acid and indole excretion. Of these four, the eldest was the sister who had previously been admitted with the diagnosis of pellagra: two others appeared clinically well but one of them had a mild degree of skin photosensitivity: the fourth was our presenting case.

The amino-aciduria was thoroughly studied on all four sibs and shown to be entirely of renal origin. No other defects of renal tubule function could be discovered. We do not yet know the mechanism of indole excretion, but presume that it is associated with high plasma levels and results from this excessive accumulation in the body. The indican output (but not that of the other indoles) could be greatly increased by feeding extra tryptophan and entirely prevented by giving chlortetracycline, even with simultaneous extra tryptophan in the diet.

Between the various sibs we have now observed many attacks of the disease. It takes the form of a pellagroid rash following moderate exposure to direct sunlight. When severe there are also added signs of cerebellar ataxia, which is usually very mild and variable but has been completely crippling and associated with delirium on a few occasions. Both skin and neurological signs are completely reversible in a month or so of conservative treatment. Whether the improvement has been hastened by simultaneous nicotinamide therapy still remains doubtful. On a few occasions a co-existent infection has precipitated neurological signs without there being any rash. An ominous further feature is that the three older affected sibs show mental retardation which is more severe in order of increasing age.

We were puzzled as to the relationship of this disease to true pellagra (of which we have only negligible experience). Reading the British literature on alleged cases of true pellagra, it appeared that this could be identical with the disease occurring in our family. The American literature on pellagra described, however, a rather different clinical picture since the neurological complications were rare, but, when present, more often resembled a peripheral neuritis and rarely, if ever, a pure cerebellar ataxia. We therefore became suspicious that
perhaps many of the British cases might in fact have been cases of Hartnup disease. As the gross and highly specific biochemical abnormalities in the urine seemed to be quite constantly present, independently of the coexistence or otherwise of the pellagra-like disease, it seemed that it would be easily possible to re-diagnose any case of British pellagra previously described, providing that urine could be obtained from the patient. We have been fascinated therefore to discover retrospectively that the cases described as of pellagra by Hickish (1955) and by Hersov (1955) do in fact excrete urine with an amino-aciduria and with indole abnormalities identical with that of the four sibs in our particular family. Two further cases are also recently described from Holland (Jonxis, 1957) and one from Germany (Dr. H. Bickel, private communication), and Drs. Philip Evans and W. Henderson have kindly provided me with details of a further case (unpublished) in a girl of 5 years admitted in 1952 to the County Hospital, York, and later to The Hospital for Sick Children, Great Ormond Street. In this last case the child had developed a rash following an attack of infective diarrhoea, but neurological signs later developed, suggesting the possibility of a cerebellar tumour. The rash was finally noted to be indistinguishable from that of pellagra and both it and the neurological signs became normal after two months of hospital treatment which included additional nicotinamide. The diagnosis of this child from the case summary was: 'A case of pellagra with skin involvement and ataxia, the cause of whose origin cannot be traced in the dietary history'—an excellent, if cautious, summary of the clinical findings in the light of the knowledge then existing. We obtained urine from her five years later at a time when she was quite well: it showed the usual gross abnormalities of Hartnup disease.

From what we have said already it seems clear that the disease can be considered as a further example of an inborn error of metabolism in the sense that this term was used by Garrod, and that it is caused by an autosomal Mendelian recessive gene. We have not definitely determined the biochemical mechanism which must be the main cause of the disease. It is of note that the clinical signs only occasionally develop in patients constantly showing this gross biochemical abnormality. It is nice to think that it may be concerned with a disorder of tryptophan metabolism whereby a metabolic block exists somewhere in the course of its transformation to nicotinamide. In this way the subject can be considered to be always in a state of inadequate nicotinamide nutrition and therefore to be readily toppled over into gross deficiency by any factor further decreasing its supply or increasing its metabolic requirement. The block must be very early in the metabolic sequence since the metabolites which seem to be accumulating all contain intact indole rings, only the side chain being altered. There is a strong resemblance here to the abnormality in phenylketonuria where, however, it is the benzene ring, not the indole ring, which cannot be broken down. The relationship of the amino-aciduria to the indole abnormality seems, however, to be very obscure. From here we are led on to rather intriguing thoughts as to the possible metabolic causes of diseases alleged on usually inadequate grounds to be due to so-called 'resistance' to vitamins or hormones such as, for instance, 'vitamin-D resistant' rickets or 'parathormone-resistant' hypoparathyroidism. By the same way of thinking, Hartnup disease could be considered as exemplifying 'nicotinamide-resistant' pellagra. We are entitled also to ponder further as to the possible nature of the hereditary factors which so often predispose to the development of many other diseases in which the immediate cause is clearly environmental, although insufficient in itself to have any effect on the majority of apparently normal people. Even in known cases of Hartnup disease the clinical signs are exceedingly inconstant and may manifest themselves in bizarre ways which would not be expected to lead to a correct diagnosis if arising for the first time in another subject. It may well be, therefore, that the biochemical disorder is fairly common and should be more actively sought. We are suspicious, for instance, of any patient who might present only with a photosensitive rash or only with acute (and fully reversible) cerebellar ataxia following febrile disease. Fortunately the diagnosis of Hartnup disease can be readily made retrospectively by examination of urine sent by post.

REFERENCES


Scientific Sessions

Ruth F. Harris and J. P. M. Tizard (London). 'Electroencephalography in the Normal and Abnormal Newborn.' An investigation had been carried out to try to establish normal standards for the electroencephalogram in newborn babies and infants, and to determine whether the electroencephalogram will assist in predicting the outcome of cerebral disturbances in the newborn.

The technique used is bipolar recording from six silver cup electrodes, one frontal, one occipital and a pair on either side of the head to straddle the motor cortex. The pulse and respiratory rate are recorded simultaneously. Recording is done when the baby is quietly awake and during normal sleep.

There is little rhythmical electrical activity in the waking baby but when asleep there are bilaterally simultaneous bursts of activity from central and frontal areas lasting 2-4 seconds every 4-8 seconds with relative inactivity between episodes. These episodes are not accompanied by movement or change in respiration. It is thought that they indicate a lightening of sleep due to some internal stimulus because similar episodes can be evoked by the external stimulus of noise, which, without rousing the soundly sleeping baby will, after a primary auditory response, produce a burst of electrical activity.

A general simplification of pattern is seen in the electroencephalogram of older babies with increasing amplitude and short runs of rhythmic 10-14 cycles per...
second activity from the central areas. In the very immature infants electrical activity from the brain occurs intermittently.

From practical experience the following would be considered abnormal: Persistent focus or foci of sharp waves; spikes of high-amplitude rhythmic slow activity; marked asymmetry between the hemispheres or very low amplitude records. Most of these types of activity have been seen in clinically abnormal babies, e.g., in cases of cerebral haemorrhage, fits and anoxia.

Not all clinically abnormal babies have abnormal electroencephalograms.

It is possible that the electroencephalogram will be of some prognostic significance in later epilepsy.

O. Steinicke (Copenhagen). 'Persisting Abnormal Pyloric Motility following Hypertrophic Pyloric Stenosis.' The author reported work done in collaboration with N. Roelsgaard.

Radiological examination of 45 adult persons (aged 25-45 years), who had suffered from hypertrophic pyloric stenosis in infancy and had been treated by stomach emptying exclusively, showed persisting abnormalities of pyloric motility in 78% of the cases; 14 of the 45 had developed gastric ulcers.

Patients whose hypertrophic pyloric stenosis had been treated with modern antispasm or surgical therapy showed a much earlier radiological return to normality of pyloric motility.

In regard to antispamnodic treatment, residual changes were found in 37% of 49 cases aged 7-11 years and 21% of 47 cases aged 12-18 years.

In regard to surgical treatment, residual changes were found in 43% of 30 cases aged 2-6 years and in 17% of 29 cases aged 7-11 years.

These figures indicate that a return to normal occurs earlier after surgical treatment than after antispam therapy.

J. D. Allan (Stockport). 'A New Metabolic Disease.' This paper described the clinical features and preliminary investigations of a new disease.

The disease is essentially one of mental defect and constantly abnormal amino-aciduria in which epileptiform convulsions and temporary ataxia may occur. It is possible that a congenital heart lesion may be an additional anomaly and that clinical manifestations may not be apparent till some time after 1 year of age. This condition adds another to the list of metabolic disorders associated with mental defect.

The disease was described in two sibs. The urinary excretion of the abnormal amino-acid is constant. It is as yet unidentified. It has been demonstrated in urine, plasma and C.S.F. by chromatography. It is present in the cerebrospinal fluid in a much higher concentration than in the plasma from which it is cleared at the normal rate of glomerular filtration. Comment is made on certain physical characteristics, namely the facial appearance and the hair, and on the results of certain investigations, namely the E.E.G.s, the I.Q. rating, the blood groups, the pedigree and family and the alkaline phosphatase.

It is considered that the disease is probably of hereditary linkage and that its chief importance is in its relationship to the further elucidation of the causes of mental deficiency.

P. W. Brastrup (Copenhagen). 'Personal Experiences in Starch Intolerance in Childhood.' Twenty-five cases of starch intolerance in children from 1 to 8 years were observed in two years compared with four regular coeliac syndromes.

In 16 cases examined, radiographs demonstrated pathological segmentation and dilatation of the ileum as seen in the coeliac syndrome and sprue.

As all cases responded favourably to diet restricted alone in gluten, gluten intolerance would be a more adequate term.

Growth intensity was impaired before treatment in all cases where data were available, whereas most cases showed considerable increase above average in growth intensity on adequate dietary restrictions.

P. L. Mollison (London) and W. Walker (Newcastle-upon-Tyne). 'The Cause of Death in Haemolytic Disease.' The mortality in liveborn infants with haemolytic disease of the newborn can be reduced to less than 5% by the proper use of exchange transfusion; this implies that the total number of deaths in England and Wales should not exceed 150 a year. The fact that the number registered remains about 400 prompted the present enquiry.

Of the 400 cases certified as dying from haemolytic disease of the newborn each year, 100 died from some other cause, the commonest being kernicterus of prematurity. Amongst the 300 cases dying from haemolytic disease of the newborn, failure of antenatal prediction and failure to carry out an adequate exchange transfusion were very common.

Preben Plum (Copenhagen). 'Experiences with Drug Therapy in Cerebral Palsy.' In a clinical search for a useful skeletal muscular relaxant in cerebral palsy we have noticed a surprisingly good effect of myosine (5-ethyl-dihydro-5-phenyl-4-6-(1 H, 5 H)-pyrimidinedione) in athetosis. In 18 of 31 cases of athetosis the effect was good; in spastic patients there was some effect in some cases, but it was less convincing. Myosine was used in doses much smaller than usual in the treatment of epilepsy, most often 25 mg. three times a day.

P. J. N. Cox (London). 'Metabolic Studies in the Syndrome of Virilising Adrenal Hyperplasia with Salt Loss.' Sixteen cases of virilizing adrenal hyperplasia with an associated salt-losing syndrome have been seen at The Hospital for Sick Children, Great Ormond Street, in the past five years. Five of them have died, three are being treated elsewhere and eight are still attending the hospital.

With the increasing study of infants who fail to thrive in the first few months of life, some difficulties have been encountered in the early diagnosis of the disease in boys, who at this stage show no evidence of virilization.
The physiological basis of the electrolyte imbalance is poorly understood, and five cases have received special study from this point of view.

It has been found by others that A.C.T.H. aggravates the sodium loss, and it has, therefore, been suggested that the hyperplastic adrenal produces an abnormal hormone which prevents reabsorption of sodium in the renal tubule. It is now shown that the effect of A.C.T.H. is variable, and that inhibition of the secretion of A.C.T.H. by the administration of prednisolone may aggravate the disease instead of leading to improvement as might have been expected. The interpretation of these findings is discussed.

BENT FRIIS-HANSEN (Copenhagen). ‘Body Water Equilibrium during Weight Reduction and Changes in Body Composition.’ In a number of obese children the volume of total body water was measured by the heavy water method, extracellular fluid being estimated by the thiosulphate method. The intracellular fluid may then be calculated by subtraction.

In the fat children these body water compartments were lower than normal, when calculated as a percentage of body weight.

The volumes decreased only by 1-2% during an average weight reduction of 16%, indicating a loss of pure fat tissue (allowing for a slight growth during the observation period).

From these observations the amount of fat tissue in the body may be calculated before and after weight reduction. This is compared with the degree of overweight and the weight loss.

T. J. RENDLE-SHORT (Sheffield). ‘Infant Management in the Eighteenth Century.’ Before 1700 infant care was a mixture of folklore and ancient Greek empiricism. The eighteenth century marks the first movement towards infant management.

For this paper all the available English textbooks and pamphlets on the management of children published in the eighteenth and early nineteenth centuries have been consulted (they number about 30). The paper shows the development of ideas on such matters as the management of the newborn, clothing infants, sleep, teething and infant feeding.

F. TUDVAD (Copenhagen). ‘The Status of Prophylactic Vaccinations in Danish School Children.’ The extent to which the public will avail themselves of the free vaccinations against smallpox, diphtheria, tuberculosis, and poliomyelitis, which is open to all Danish children, was discussed. The figures, all of which refer to the school year 1955-56, include all Danish schoolchildren (634,300 from 4,037 schools), show the possibility of having at least 90% of all Danish schoolchildren vaccinated on a voluntary basis.

L. L. R. WHITE and M. BODIAN (London). ‘The Treatment of Neuroblastoma with Vitamin B_{12}.’ Conventional modes of therapy have only a restricted application in the treatment of neuroblastoma because of the high incidence of tumour spread at presentation.

It has been found empirically that prolonged treatment with vitamin B_{12} in massive dosage leads to regression of the tumour in a significant proportion of cases.

To date a total of 29 children have been so treated. Regression of the tumour was observed in 50% of these patients, and 25% are alive and well one and a half to six years from the onset. This favourable response was virtually limited to cases presenting in infancy.

K. S. HOLT (Sheffield). ‘The Siblings of Mentally Retarded Children.’ The adverse effects of mentally retarded children upon their siblings have been studied by visiting families with retarded children in Sheffield. In 169 families there were normal children in addition to those retarded. These siblings were considered in four groups: those younger than the defective child and either below, or of school age, and those older and either of or past school age.

The observations about those children older than the defective child and past school age were incomplete as many had left home, but between 20 and 24% of the siblings in the other groups were seriously disturbed by the retarded child.

There were 66 affected children from 57 families. Thus, in a third of the families visited there was at least one normal child affected adversely by the defective child.

Twenty-four children suffered physical attacks; 20 resented the attention given to the retarded child; 11 suffered through the help they had to give in the home; and 10 were ashamed and embarrassed by the defective child.

Inadequate parental care led to attacks, whilst excessive devotion to the handicapped child led to resentment and jealousy.

The effects upon the siblings caused 13 retarded children to be admitted to an institution, with benefit to the normal children.

Removal from home of the retarded children may not be the only solution of the difficulties and possibly fewer problems would arise if more help were given to the family as a whole.