ABSTRACTS OF THE CURRENT LITERATURE

INTERNAL MEDICINE

The battered child syndrome : C. H. KEMPE, F. N. SILVERMAN, B. F. STEELE, W. DROEGEMULLER and H. K. SILVER, *J. Amer. med Ass.*, **181 :** 17, 1962. From *Inter. med. Dig.*, **78 :** 555, 1962.

Serious and repeated physical trauma resulting in severe and permanent disability or even in death may be inflicted on infants and small children by parents and guardians. Either because of their unfamiliarity with and inability to identify the radiologic and clinical hallmarks of this condition or because of a natural dislike on the part of physicians to accept the fact that parents may harm their children, these cases often go undiagnosed and proper legal action to safeguard these infants and children is not taken. Referred to by the authors as the "battered child syndrome", this condition has also been called "unrecognized trauma".

A survey of 71 hospitals revealed 302 such cases in one year. Thirty-three children died and 85 suffered permanent brain damage. Legal action was taken in only one third of this series. In a survey of district attorneys' records for one year, 447 cases were discovered with 45 fatalities and 29 cases of permanent brain damage.

The clinical picture varies from mild trauma and failure to thrive to obvious evidence of injury to the skeletal system and soft tissues. The age range varies widely, but the majority of victims are younger than 3 years of age. Frequently the child appears neglected and malnourished.

The parents are often but not always of low intelligence and/or borderline socioeconomic status. Occasionally they are frankly psychopathic. Frequently there is a history of trauma inflicted by their own parents in their childhood. Alcoholism, sexual promiscuity, minor criminal activities and unstable marriages are common background factors. The parents are often immature, impulsive, self centered, and suffer from poorly controlled aggression. Not infrequently the beaten infant is the product of an unwanted pregnancy, a pregnancy that began before marriage, or an "inconvenient" pregnancy.

The diagnosis requires a high suspision index. Fairly characteristic aspects of the history are previous episodes suggestive of parental neglect or trauma and a marked discrepancy between the clinical findings and the history given by the parents. The fact that no further injury occurs while the patient is in the sheltered atmosphere of the hospital is also helpful. Careful, tactful, indirect questioning will often elicit pertinent information. Often the guilty parent is the one who gives the impression of being more normal.

The patients are usually younger than 3 years with a relatively large amount of radiolucent cartilage and loosely attached periosteum. The traction-twisting force which is usually brought into play during rough handlings results in epiphyseal separation and periosteal

shearing with subperiosteal hematomas. Direct trauma results in fractures. Reparative changes are usually apparent within 12 to 14 days after injury; for this reason a child may show no radiologic evidence of trauma when first seen. Since in children reparative processes are quite active, they often result in excessive new bone formation; the noninitiated may interpret these as neoplastic changes. The most important radiologic feature is the existence of various lesions of the bones in different stages of repair. Subdural haematomas with or without fracture are seen frequently, even in the absence of lesions of the long bones.

Features which differentiate the radiologic lesions of the "battered child" from other conditions include lack of relation to the rate of growth; often there are extensive bony lesions at the slow-growing end of a bone while there is no evidence of metabolic disorder at the rapidly growing end. Specifically, differential diagnosis is between "battered child" and scurvy, syphilis, osteogenesis imperfecta, familial cortical hyperostosis. The radiologic features are specific; the metaphyseal lesions encountered in this syndrome do not occur in other conditions.

Management may include separation of the child from the parents by court order. It is the duty of every physician to familiarize himself with the local social agencies that can assist in securing a safe environment for the child.

Bronchiectasis in childhood : NORMAN S. CLARK—*Brit. med. J.*, **5323** : 80, 1963.

Study has been made of 116 consecutive cases of irreversible bronchiectasis diagnosed in the Royal Aberdeen Hospital for Sick Children during the years 1946-55. The average annual incidence of discovered bronchiectasis in this region was 1.06 per 10,000 child population.

The history suggested that in almost 50 per cent. of the cases bronchiectasis had developed before the third birthday but that in only 25 per cent. of all cases was the child referred for investigation within one year of the onset of persistent symptoms. In nearly two-thirds of the cases the symptoms dated from an attack of pneumonia, pertussis, or measles.

A history of purulent expectoration was common but haemoptysis was rare. The presence of persistent localized rales was noted in almost every case. Other abnormal physical signs in the chest were present only in a minority of cases and finger-clubbing was seen only in one-third. Antral lavage was performed in 87 children and produced purulent secretion in 77. In 16 cases the original X-ray films were passed as normal or as showing only a doubtful increase of basal markings. Bronchography showed bilateral disease in 61 cases and involvement of more than two lobes in 57.

Bronchography was repeated in 79 children after an interval varying from six months to eight years and without operation intervening. In 15 cases bronchiectasis was demonstrated in 17 segments previously considered normal and in seven cases eight previously affected segments now appeared normal. The possibility of spread must be remembered when surgery is contemplated, and the interval between bronchography and operation should not be too long.

Three children have died as a result of their bronchiectasis and three are untraced. Surgical treatment has been completed in 75 cases, five have had unilateral resection and are awaiting operation on the other side, two are awaiting operation, and 28 have been treated medically.

A total of 104 resections have been carried out on 80 children, with two post-operative deaths. Post-operative atelectasis was common, particularly in younger children, and lobar or segmental

resection is now usually deferred to later childhood or adolescence. At final follow-up examination, between 6 months and 12 years after operation, 55 per cent. were considered to have recovered completely and a further 16 per cent. had minimal symptoms only.

The cases treated medically were not a homogeneous group and cannot be directly compared with the surgical group. In 18 of these cases complete resection of the affected lung would have been technically possible : at follow-up examination six of them were classed as "recovered" or "much improved".

These results are compared with previous reports of follow-up studies on childhood bronchiectasis, and it is suggested that lung resection offers the best chance of a satisfactory result in a large proportion of children with bronchiectasis.

AUTHORS' SUMMARY.

The achilles reflex : A diagnostic test of thyroid dysfunction : LAWRENCE SHERMAN, MARSHALL GOLDBERG and FRANK C. LARSON—*Lancet*, **1** : 243, 1963.

Alteration of the tendon-reflexes is generally accepted as a confirmatory sign of thyroid dysfunction. The ankle-reflex measurement can be used successfully as a diagnostic test of hyperthiroidism and hypothyroidism.

Examination of typical curves produced on the photomotogram by the ankle-reflex in hypothyroidism reveals prolongation of the contraction phase (mean duration 200 milli-seconds in euthyroids, 260 milliseconds in hypothyroids), as well as relaxation phase of the reflex, with relatively greater prolongation of relaxation. To the naked eye, delay in relaxation does appear to be the salient feature of the deep-tendon reflex change in myxoedema. Instruments, however, show that the entire reflex is slowed.

The R.A.I. test has become accepted in most medical centres as the "best" single test of thyroid function. For this reason, this test was chosen for correlation analysis with the reflex-time test. The result indicated a high degree of correlation. In addition, there was no significant difference between the R.A.I. test and the reflex-time in detecting either hypothyroidism or hyperthyroidism.

The averages of the reflex-time measurement as a test of thyroid function are : (1) the Achilles reflex is unaffected by the many drugs, patent medicines, and diet supplements that contain sufficient quantities of iodine occasionally to invalidate the P.B.I. test and R.A.I. uptake test ; (2) the test can be performed quickly and without elaborate equipment, with results available within minutes ; (3) patients who are being treated with thyroid hormones can be followed up with serial determinations of the Achilles reflex ; (4) in pregnant women ^{131}I need not be used to diagnose thyroid dysfunction.

Osteomyelitis in infancy and childhood : J. B. MAYER—*Monatssch. Kinderheilk.*, **110 :** 229, 1962. From *Inter. med. Dig.*, **78 :** 562, 1962.

The mortality rate from osteomyelitis in childhood was 18 per cent. before the sulfonamide and antibiotic era ; it was higher for infants up to 6 months of age (35 to 60 per cent.). Today the disease is no longer fatal. The author reports his experience with 45 patients with osteomyelitis, none of whom expired. These patients included 15 infants, 18 preschool children, and 12 school children. Some of these patients were followed for eight years.

The clinical picture included the classic signs of sepsis, but the local signs such as redness, swelling and localized tenderness were absent in about half of the cases. For this reason only eight of

the 45 children were sent to the hospital with the correct diagnosis.

The point of entry was not always obvious. In 13 instances the disease followed some cutaneous lesion, such as chickenpox, furunculosis, or eczema. In nine cases osteomyelitis occurred after a febrile illness, such as pharyngitis or sinusitis. Trauma could be incriminated in six instances and umbilical infection in three cases. Of special interest were six cases in which the pyogenic infection was probably iatrogenic in origin: exchange transfusion, prolonged transfusion, injection of analeptics or antibiotics. In the eight remaining instances, no entry site of infectious agents could be determined.

The causative agent could be identified in only 15 cases. This poor culture yield is probably explained by the fact that most of the children had already received antibiotics before they were admitted. The agent recovered was *Staphylococcus aureus* in 10 cases, *Staphylococcus albus* in one case, and in four instances a mixed flora.

Radiologically, the bone lesions became manifest sooner in infants and young children than in adults. Periosteal reactions and swelling are often visible within a week after the onset in infants, whereas in adults the diagnosis can never be made radiologically before the end of the second week. Furthermore, in adults and older children, the process has a definite tendency to expand along the diaphysis. In infants the abscess tends to extend toward the sides of the metaphysis or the epiphysis, leading to purulent arthritis. This complication has been found to occur in up to 65 per cent of cases by some authors.

The most feared complication is propagation of the infection toward an epiphyseal plate. Permanent damage to the bone and defective growth were invariably observed when epiphyseal infection occurred before the time of radiologic appearance of the epiphyseal ossification center. Epiphyses were involved in 14 cases. In six of them infection occurred at an age when the ossification center was not yet constituted. In these six cases it caused impairment of growth, sometimes with luxation of the joint (five shoulders). Correction of such a luxation is one of the most difficult tasks for the orthopaedic surgeon.

The preferred treatment consisted of two antibiotics together with a sulfonamide. Treatment as a rule was continued for two months after healing of the lesions was demonstrated on radiographs. The average duration of antibiotic therapy was, therefore, from four to six months. The affected limb was immobilized in a cast. Blood transfusions and gamma globulin administration were used as adjuvants.

Cori's disease (amylo-1.6-glucosidase deficiency). Report of a case in a Negro child: GEORGE HUG, CARL E. KRILL, EUGENE V. PERRIN and GEORGE M. GUEST—*New Eng. J. Med.*, **268:** 113, 1963.

A seven-month-old Negro girl with a clinical picture suggestive of glucose-6-phosphatase deficiency (Gierke's disease) responded to a "double glucagon test" with a blood sugar pattern typical for amylo-1.6-glucosidase deficiency (Cori's disease).

Histologic examination of liver tissue is of no help in determining the precise enzymatic defect. An excess of PAS-stainable material in muscle tissue excludes Gierke's disease and is compatible with Cori's disease.

On biochemical analysis, the amount of glycogen in the liver and muscle tissue was abnormally elevated. Activities of glucose-6-phosphatase, liver phosphorylase and muscle phosphorylase were within normal range. On structure analysis the glycogen isolated from liver and muscle

tissue had short outer chains and an increased percentage of end groups. The findings thus fit the description of a "limit dextrin" characteristic of Cori's disease.

The patient's liver and muscle homogenates failed to incorporate C-labelled glucose into the branch point of glycogen. This defect could be eradicated by addition of purified amylo-1.6-glucosidase. The homogenates thus fortified yielded a radioactive glycogen that was first exposed to crystalline phosphorylase and then to purified amylo-1.6-glucosidase. This step-by-step enzymatic degradation succeeded in demonstrating the incorporation of C-labelled glucose by the fortified liver and muscle homogenates into the branch points of the glycogen, whereas the straight chains of the molecule had not become radioactive.

Elevated tissue levels of glycogen, its structure of a limit dextrin, assay of enzymatic activities and restoration of tissue homogenates to normal metabolic activity of addition of purified amylo-1.6-glucosidase establish the diagnosis of Cori's disease.

AUTHORS' SUMMARY.

Milk allergy in infancy : EDITORIAL.—*Brit. med. J.*, **5330 :** 561, 1963.

It has for long been known that infantile eczema may be caused by sensitization to the proteins of cows' milk and that milk-free diets will relieve the symptoms in such cases. Confirmation of the aetiology is obtained when resumption of a milk diet causes a return of the eczema and the reinstitution of a milk-free diet again relieves the condition. One group of workers found that antibodies to milk developed in the majority of artificially fed infants after the age of 7 weeks. Others had previously shown that in certain types of nutritional disorders precipitins to milk protein were found in the affected infants' sera, and in 1958 one worker estimated that 6 per cent. of infants were allergic to cows' milk during the first few months of their lives. As the number of artificially fed infants increases with the decline in breast-feeding the incidence of milk allergy is inevitably rising. The clinical signs are now known to include such conditions as failure to thrive, gastro-enteritis, chronic or recurring pulmonary disease, and infection of the upper respiratory tract.

A group recently examined sera from 1618 infants and children and found precipitins in 87 (5.4 per cent.). Of these, 62 had recurrent respiratory disease, 34 were anaemic (haemoglobin 9.5 gm. per 100 ml. or less), 22 failed to thrive, and nine had persistent gastro-intestinal disturbance. Elimination of milk from the diet brought improvement in 22 of 24 children who were followed up for periods of four months to a year. Subsequent work showed that alpha-and beta-casein, alpha-lactalbumin and beta-lactoglobulin A and B were all allergenic and that heat treatment of milk did not cause it to lose all allergenicity. It was concluded that as these proteins were not completely inactivated by the processing of milk, the feeding of such milk to allergic infants could not be relied upon to relieve the symptoms. Goats' milk has been used as a substitute, often with very satisfactory results, but experiments suggest that this is not always a satisfactory alternative because the lactoglobulin and lactalbumin are immunologically related in the two species.

The present position with regard to milk allergy may be summed up as follows : Sensitization is common, but, as with rhesus incompatibility, causes symptoms in only a small proportion of infants. If the diagnosis is suspected a trial should be made with a milk-free diet such as a soya-bean preparation. Processed milk (for example, evaporated milk) and goats' milk may relieve the

symptoms in some infants but may not be of sufficiently low allergenicity for others. The condition is transitory; in mot cases cows' milk can gradually be reintroduced into the diet after periods varying from six months to two years.

INFECTIOUS DISEASES

Vaccination against measles in general practice : A. P. GOFFE, J. T. WOODALL, E. TUCKMAN, J. D. PAULETT, I. N. MANSER, L. M. FRANKLIN and P. A. L. CHAPPLE—*Brit. med. J.*, **5322:** 26, 1963.

The measles vaccine consisted of living attenuated measles virus, Edmonston strain. A total of 154 children were vaccinated either at the doctors' consulting-rooms or at homes. Each vaccinated child was seen on or about the twelfth day, or earlier if the parents had so requested, and reactions to the vaccination were recorded. During the six months after vaccination each doctor recorded every case of measles which was reported to him in any child in the families under study. At the end of this period every family under study in whom measles had not been recorded during this time was contacted to ensure that no case of measles had been missed. The information collected during the study was transferred to punch cards and analysed.

Of the 154 vaccinated children, 72 per cent. developed fever, mostly on the sixth to eighth day after vaccination. The mean duration of fever was 3.5 days. Rash was observed in 62 per cent. of the children, at a slightly longer interval after vaccination.

The primary object of the present study was to measure the protective effect of live attenuated measles vaccine used in the conditions of general practice during the winter months. No case of measles were recorded in a vaccinated child, whereas in the unvaccinated group all the pre-school children who came into contact with measles in the household developed the illness. During the epidemic, therefore, the vaccine conferred complete protection. It was not known for how long this immunity would persist, but there were good grounds for expecting it to be lifelong.

The frequency of fever and rash was of the order expected from previous studies, but the incidence of the other reactions observed seemed to be at variance with previous studies. A fifth of all vaccinated children were judged to have had severe reactions in the form of respiratory infection, marked debility, or convulsion. It was possible that latent agents, already present in the children, were activated in some way by the vaccination process, perhaps through some lowering of a general defence mechanism.

As it was virtually certain that a non-immune child who was exposed to measles within the family would develop the disease, which, with its complications, could be a serious illness, there were good reasons for wanting to prevent measles by active immunization. The requirements of such a vaccine were that it would give solid protection with a single injection, that immunity should persist, and that a minimum of reaction be caused. The vaccine studied here fulfilled the first criterion and may in time be found to satisfy the second. But, although one-quarter had no appreciable reaction at all, the severe reaction shown by one-fifth of all vaccinated children clearly ruled out the general use of the vaccine in its present form.

Vaccination against poliomyelitis : The present position in Australia— A. E. DUNBURY, GILLIAN GOULDING and J. J. GRAYDON—*Lancet*, **1 :** 377, 1963.

Since June, 1956, about 4,500,000 people in Australia had received three doses of C.S.L. Salk vaccine and only

two had been proved by virus isolation to have contracted type-1 paralytic poliomyelitis. The vaccinated group had certainly been challenged by type-1 virus, since, over the same period type-1 polioviruses had been isolated in 243 paralytic cases among the smaller unvaccinated population in the susceptible age-group.

There had been no proven cases of type-2 poliomyelitis in vaccinated persons; but, as there had been only three cases in unvaccinated persons, the vaccinated population might not have been significantly challenged by type-2 virus.

Protection against type-3 polioviruses had not been so good: 46 cases of paralytic disease in vaccinated persons had been proved by virus isolation, while, in the same period, there had been 181 confirmed cases in unvaccinated persons. Nevertheless, protection had still been substantial (83 per cent).

Poliomyelitis had declined in countries where Salk vaccine had been used extensively. In the United States and Sweden the decline seemed to have been greater than would be expected from the number of people vaccinated, suggesting that some herd immunity had been induced. This might have happened in Australia also; but, if so, the 1961-62 epidemic showed that, without more extensive vaccination, herd immunity could not be relied on for protection. The high attack-rate in children under school age, 35 per cent. of whom were unvaccinated, pinpointed the section of the community most at risk. Young children, with their unhygienic habits, promoted the spread of polioviruses, and probably provided the virus reservoir from which the older children and adults were infected. In many countries, preschool children had proved a difficult group to cover with Salk vaccine. More intensive programmes should be concentrated on this group, for the protection both of the children and of the rest of the community.

The antibody response to the type-3 component of C.S.L. Salk vaccine had been usually lower than the response to the type-1 and type-2 components, and the failure of the vaccine to protect a proportion of vaccinated people was probably due to inadequate potency of its type-3 component. Comparison of the attack-rates in those who had completed their course of injections one, two, three, and four years previously did not suggest that the risk of infection increased with the interval since vaccination. Susceptibility in vaccinated people was more probably due to a poor response at the time of vaccination.

Whatever the mechanism by which immunity was maintained after Salk vaccination, results in Australia showed that excellent immunity persisted to type-1 virus. If the amount of type-3 antigen in the vaccine were raised to the amount used for type-1, equally good potection against type-3 virus could be expected.

The Australian National Health and Medical Research Council had recommended that for routine immunisation against poliomyelitis in Australia, Salk vaccine should continue to give an antigenic mass comparable to that used for type-1. Furthermore, a fourth dose of vaccine was being offered to all who had received their third dose more than a year ago.

If everybody in the susceptible age-group followed this programme of vaccination there should be very little paralytic poliomyelitis in Australia. Special attention would have to be paid to all new arrivals to the community—by birth or migration—to prevent an increase of susceptibles that could become a focus for epidemics in the future.

Adenovirus infection in childhood. An epidemiological and clinical survey among Swedish children: GORAN STERNER—*Acta Paediat.*, Supp. 142, 1962.

Adenoviruses cause typical cytopathic changes in suitable tissue cultures. HeLa cells have been used extensively but other tissues, such as human embryonic lung, have also been employed. Multiplication apparently takes place in the nucleus of the infected cells, where crystalline arrays of virus particles may be seen by electron microscopy. The diameter of the virus particle, according to various authors, measures 65-90 mμ. Adenoviruses survive treatment with ether. All adenoviruses share a "soluble" antigen which gives a group reaction in a complement-fixation (CF) test. Neutralization of virus infectivity, however, is type-specific and the group has been separated by neutralization tests into at least 28 serotypes orignated from human beings. Haemagglutination-inhibition as well as CF techniques may, however, also be employed for typing. Cross-reactions have been observed in neutralization tests with hyperimmune animal sera, but are on the whole rare. Similar reactions are seen in human sera following an adenovirus infection, but are probably less frequent in children than in adults.

Adenovirus types 1, 2, and 5 are widely spread among infants and small children. Nevertheless it has been difficult to obtain sufficient data to associate these types of adenovirus with illness.

Adenovirus type 2 as a cause of epidemic outbreaks of fever pharyngitis and conjunctivitis sometimes combined with vomiting and diarrhoea among nursery children has been reported from Italy.

The conjunctivitis which is sometimes the only manifestation of the disease is often bilateral and is of follicular type. Epidemic keratoconjunctivitis is usually linked with type 8 although other types of adenovirus have been isolated from cases of similar diseases.

Skin rash was observed in the child from whom was recovered one of the first strains of adenovirus. Pharyngitis and tonsillitis are the most common findings in children with adenovirus infection. Outbreaks in military recruits of typical pneumonia without cold agglutinins have been reported due to adenovirus type 4 and 7. In view of the reports from various countries it seems probable that several types of adenovirus can produce a typical pneumonia in infants and small children.

Gastrointestinal symptoms such as abdominal pain, vomiting and diarrhoea were found in an early study in association with pharyngoconjunctival fever caused by adenovirus type 3. Gastroenteritis in combination with symptoms from the respiratory tract has also been reported in infections with types of adenovirus other than types 3 and 7.

Encephalitic symptoms and signs such as, convulsions, coma, paralysis and abnormal E.E.G. have sometimes been seen in critically ill children with adenovirus infection. Meningismus has often been mentioned in children with adenovirus infection.

In general the prognosis of adenovirus infection at all ages is good.

There is no specific treatment against adenovirus infection. Vaccines prepared against adenovirus types 4 and 7 or types 3, 4, and 7 have been used in military recruits and undoubtedly reduced the frequency of adenovirus infections.

TUBERCULOSIS

Outline of treatment of children with primary lung and hilar gland tuberculosis : W. VAN ZEBEN and L. VAN DER DRIFT—*Maandschr. Kindergeneesk.*, **31 :** 3, 1963.

During the period from April 15, 1957 to April 15, 1960, a total number of 130 children with active tuberculosis were treated in the sanatorium department of the Juliana Children's Hospital in The Hague.

The course run by the disease in seventy-five patients treated with com-

plete bed rest for primary tuberculosis of the lung (average period of hospitalization 13⅓ months) is studied in greater detail. In thirty-seven cases, segmental shadows were present at the time of hospitalization or appeared during the first six months of treatment despite tuberculostatic therapy. The following conclusions are drawn from the findings.

(1) During the first six months, an X-ray picture should be taken in two directions each month. Fluoroscopy should be avoided unless it will supply more information than do the exposures taken.

(2) When a segmental shadow is found to be present, bronchoscopy is indicated

(3) Treatment with tuberculostatic agents is indicated although endobronchial complications may occur despite the administration of tuberculostatics. Even though this form of medical treatment should not affect the primary complex, it will affect the haemotogenous disseminated lesions from which tertiary tuberculosis might subsequently develop. It therefore is advisable to give all three drugs, i.e., streptomycin, PAS and isoniazid, for the first six months and then to administer PAS and isoniazid for a period ranging from twelve to eighteen months.

(4) Clinical observation will be necessary in the great majority of cases, at any rate for the first six months. So long as a rise in temperature persists and the general condition is not satisfactory, the patient should be treated with bed rest.

When the general condition shows improvement, when there is a gain in weight and when the temperature is normal, partial mobilization may be permitted.

When the disease has markedly subsided within six months, the possibility of subsequent treatment at home may be considered, though condition in the home of the patient will have to be taken into account as well. In favourable cases, it will frequently soon be possible to permit the patient to attend school during the morning-hours.

During the period of hospitalization, careful attention should be paid to the psychological and pedagogical requirements of the child. Visiting by the parents should not be subject to restriction.

AUTHORS' SUMMARY.

NUTRITION

Diet and nutrition survey of Pondicherry establishment : Nutrition survey—Part II : S. P. DATTA, R. GOPALAKRISHNAN and V. NATARAJAN—*Indian J. med. Sci.*, **17 :** 201, 1963.

On the basis of diet and clinical nutrition survey the commonest deficiency diseases observed were iron deficiency anaemia, vitamin deficiencies of A, riboflavin and vitamin C and protein.

Anaemia. The mean intake of iron on the basis of diet survey reported in part I was 26.37 mg. with a standard error of ± 0.23. The recommended allowance is 30 mg. per head per day by the nutrition Advisory Committee of Indian Research Fund Association (I.R.F.A.) and I.C.M.R.).

If the figure of below 10 gm. of haemoglobin 100 ml. is taken for moderate and severe anaemia, it will be seen that the incidence among the population examined comes to adult males 10.4 per cent, adult females 24.6 per cent, male children (below 5 years) 45.2 per cent and female children 41.2 per cent. The incidence is higher among females.

Vitamin A. The average value of the daily intake of vitamin A in the local diet was 1749.21 I.U. with a range of 443.6-2610 I.U. It is nearly fifty per cent below the recommended allowance of 3,000-4,000 I.U.

It is apparent from the above that

there was higher deficient intake of vitamin-A in the diet which manifested itself in the form of pigmentation, bitot spots, night blindness and skin changes.

Riboflavin. The dietary intake of riboflavin was low in cent per cent of the families, the average being 0.77 mg. with a range of 0.26-1 mg. The clinical manifestations observed were mainly grayness at the angles of the mouth with or without fissuring and maceration of the epithelium, buccal stomatitis and glazed and fissured tongue. Facial seborrhoea and corneal vascularity were not observed in any case.

Thamine. The dietary intake was 1.6 mg. which was close to the normal requirement.

Vitamin C. The average intake of this vitamin on the basis of raw food was 48.63 mg. which was slightly below normal except in the group of Harijans.

Phrynoderma (follicular hyperkeratosis). This was supposed to be due to deficient intake of fat. The mean intake of fat was only 28.51 gm. which was 50 per cent below the recommended normal requirement. The incidence of phrynoderma was 2 per cent among the children below 5 years and 3.6 per cent among boys and girls of 5 to 15 years.

Protein. The average daily intake of protein was 68.34 gm. per adult unit per day with a range of 33.28-90.57 gm. and cereals of the diet contributing most of the proteins. As for other sources of protein, like pulses, the average intake was very low, 1.31 gm. per adult unit per day. Frank cases of protein malnutrition were not seen.

The following measures were suggested based on the Survey in this area :—

1. Socio-economic development of the area : Poverty and ignorance were the two main reasons for the prevailing deficiency diseases in the area. The average income among the families surveyed ranged from Rs. 23—Rs. 10/- per capita which is too low to buy the requisite quantity of food under the prevailing cost of living with the result that only one main meal was being taken by those labourers.

2. Nutrition education : This should be carried out at the women welfare centres, M.C.H. clinics, schools and village centres.

The stress should be on the three points : (a) Balanced diet for various age groups. (b) The nutritive value of various foods which are cheap and easily available depending upon the prevailing food habits. (c) The commonest deficiency diseases prevalent in that area and what food stuffs to be incorporated or increased in the diet to counteract those deficiencies.

3. Kitchen gardens and poultry : In the rural areas, the families who have small pieces of land should be encouraged to plant few trees and grow more vegetables which can provide the family with necessary vitamins and minerals. The trees recommended were papaya, lemon, drumstick, amla and curry leaves. Some of the vegetables which can be easily grown at home were corriander, agathi, amaranth, fenugreek and tomatoes.

4. Eradication of infecton : The incidence of hookworm and dysenteries was very high in the area and it put a great strain on and exhausted the reserves of the body specially for iron and proteins.

5. Feeding programme : All the measures mentioned above had to be taken up simultaneously to have an integrated development, but the vulnerable groups viz. pregnant, and lactating women infants, pre-school and school children had to be looked after during this transition period.

HUMAN GENETICS

A specific congenital brain defect (arhinencephaly) in 13-15 trisomy :

JAMES Q. MILLER, ERNEST H. PICARD, MUSTAFA K. ALKAN, SUSAN WARNER and PARK S. GERALD—*New Eng. J. Med.*, **268 :** 120, 1963. .

The article reports the occurrence of 13-15 trisomy characterized by the presence of an extra chromosome of the 13-15 or D group in a newborn male infant who was delivered prematurely and weighed 4 pounds 14 ounces.

The infant had multiple congenital anomalies including microcephaly, harelip, cleft palate, nasal deformity, microphthalmia, colobomas, abnormal external ears, polydactyly, rocker-bottom feet, abnormal palm creases, omphalocoele, abnormal scrotum, intra-abdominal deficiencies, hypoplastic optic nerve and absent olfactory bulbs and tracts. The child died on the seventh day of life despite therapy and postmortem examination revealed the latter three abnormalities.

Chromosome study of 34 leucocytes obtained from culturing peripheral blood revealed a modal number of 47 with trisomy in group 13-15. Nuclear sexing of buccal smears was negative.

The defects of the brain which were found in this patient, namely, absent olfactory bulbs and tracts and hypoplasia of an optic nerve and eye were manifestations of arhinencephaly, the neurologic component of a teratism that included nasal defects, harelip, cleft palate, microphthalmia, colobomas and polydactyly. These anomalies were usually found in patients with 13-15 trisomy.

So far anomalies of the brain relating to arhinencephaly have not been reported either in mongolism or in 17-18 trisomy, in both of which mental deficiency occurred. Since no anomaly of the brain was common to the three autosomal trisomies, the authors assumed that mental deficiency which was found in each, did not stem for a similar structural defect of the brain.

They concluded that 13-15 trisomy was an important etiologic factor in arhinencephaly.

A further survey of the chromosomes in the Japanese : S. MAKINO, Y. KIKUCHI, M. S. SASAKI, M. SASAKI and M. YOSHIDA—*Chromosoma,* **13 :** 148, 1962. From *Excerp. med. hum. Genet.,* **1 :** 336, 1963.

The chromosomes were investigated in a total of 6,596 cells derived from primary cultures, subcultures, and direct squashes of embryonic tissues of 135 foetuses and of testicular tissues of 2 adult males. In 96.18 per cent. of these cells the identical complement of 46 chromosomes has been found, varying only with respect to sex chromosome constitution (XX or XY). Two foetuses among a total of 127 (primary cultures only) were abnormal. Case I : The mother from whom this 3-month-old foetus was removed had no record of radiotherapy during the period of pregnancy. The primary culture of the muscular tissue showed remarkable chromosome aberrations which involved chromosome breaks, translocations and fragmentations at a frequency of 21 per cent. Chromosome diagnosis of sex proved this specimen to be a female. In samples from the second subculture, however, all the metaphasic cells studied possessed a normal chromosome complement of the female type, without any indication of abnormality either morphologically or numerically.

Case II : In the cells of the primary culture from the whole body of a 3-month-old foetus whose sex was not determined externally, 45 chromosomes were present. Of 50 reliable metaphasic cells studied, 49 cells gave consistent counts of 45, while the 50th cell contained the duplicated number of 90 chromosomes. The karyotype analysed in several cells with 45 chromosomes revealed that two acrocentric chromosomes

were completely lacking in group 13-15 in all cells, while one large metacentric chromosome similar in size and shape to chromosome No. 3 existed as an extra. The sex chromosome constitution was of a male type with an XY complex. In especially well-preserved cells the extra metacentric chromosome was distinguishable from chromosome No. 3 due to the absence of any secondary constiction in its longer arm. Another noticeable feature was the consistent occurrence of a large satellite on the short arm of one of the acrocentric chromosomes of group 13-15. An interpretation for these aberrations is given : a reciprocal triple translocation has occurred among three acrocentrics at the level of a nucleolus-organizing region and has led to the formation of one large metacentric chromosome and one acrocentric chromosome having a large satellite. A comparable chromosome aberration was reported by Lejeune *et al.* (1960) in a case of Klinefelter's type with 46 chromosomes. It is now generally accepted that 46 is the normal diploid number in man, and that no normal chromosomal variation has been found either within one racial group or between different groups. The controversial information supplied by Kodani, who reported that chromosome polymorphism occurred at a higher incidence in Japanese than in European and American whites, is mentioned.

Mongoloid twins with trisomy of chromosome No. 21 : M. MIKKELSEN and J. C. MELCHIOR—*Acta genet. (Basel).*, **12 :** 164, 1962. From *Excerp. Med. hum. Genet.*, **1 :** 338, 1963.

A study of the chromosomes in a 3-month-old pair of mongoloid and apparently monozygotic female twins has been carried out. Cells were obtained from skin culture. Both twins had a modal number of 47 chromosomes, among which 16 chromosomes in the group 6-12 including X, and five chromosomes in the group 21-22, Y. Considering that the children were chromatin-positive, it seems probable that there are three chromosomes No. 21. The finding of a No. 21 trisomy in both twins supports the assumption that the twins are monozygotic, as the possibility of non-disjunction in two ova at the same time is extremely small.

21-Trisomy in a fertile female mongol : M. W. THOMPSON—*Canad. J. Genet. Cytol.*, **4 :** 352. 1962. From *Excerp. med. hum. Genet.*, **1 :** 339, 1963.

In all five cases of fertile mongols examined cytogenetically to date, the mongolism has been of the standard trisomic type, and secondary non-disjunction at meiosis in the trisomic parent has been the obvious cause of the two cases of mongolism among the affected progeny. This is true even in case the mother of the proposita was so young that some possibility existed that the proposita's mongolism might be of the translocation type. In the present article, chromosome studies in a fertile mongol also showed her to have a standard 21-trisomic karyotype. The mother of the proposita, who was 22 at the birth of her mongol child, had a normal female karyotype.

THERAPEUTICS

The current status of the tetracyclines : E. JOAN STOKES—*Practitioner*, **190 :** 145, 1963.

The three well-established analogues, in order of discovery were chlortetracycline, oxytetracycline and tetracycline. The fourth was demethylchlortetracyline which was claimed to be more active against bacteria, longer lasting and less toxic in the required dose than

the earlier drugs. Experience had thrown some doubt on the clinical value of these claims. The deleterious effect of tetracycline on the development of teeth when given in the neonatal period had only recently come to light. This was a striking example of minor differences in chemical structure leading to different side-effects. Apparently oxytetracycline, which was very similar in structure and antimicrobial action, did not damage the teeth. Chlortetracycline was deposited in the bones of treated animals and could also probably cause damage. Little was known so far of the action of demethylchlortetracycline on teeth and bone although it seems likely that it, too, could lead to deposition and damage.

Low blood and urine levels for chlortetracycline were due in part to the greater instability of this drug at body temperature. As regards antibacterial activity all four drugs had a wide spectrum. They attacked gram-positive and gram-negative bacteria and the rickettsiae, but were useless for the treatment of true virus infections such as influenza, smallpox or poliomyelitis. There was complete cross-resistance between them although resistance of a particular pathogen to any of the four drugs might vary in degree. In levels attained in body fluids they inhibited bacterial growth but did not rapidly kill sensitive organisms. This meant that they could be expected to be effective in acute infections, in which the inflammatory reaction would quickly deal with bacteria which were prevented from multiplying, but were unlikely to succeed alone in chronic infection, and they were not suitable for treating symptomless carriers.

One of the advantages of the tetracyclines was that bacteria seldom developed resistance to them during treatment. Resistance was not easily produced by serial culture in drug-containing media and originally it was hoped that acquired resistance would not seriously limit their use. When chlortetracycline had been used for about a year resistant strains of *Staph. pyogenes* were encountered in hospital and it became clear that for this pathogen at least the hope was unfounded. Now resistant strains were common in most hospitals. Resistant *E. coli* and related coliforms were also common in urinary infection and were not always limited to those patients who received antibiotic treatment. *Streptococcus pyogenes* (group A and the genus, Haemophilus) were organisms which notoriously found it difficult to adapt themselves for survival in the presence of antibiotics, but resistant strains were now being recorded. In some outbreaks of streptococcal infection 50 per cent. of strains isolated had been found resistant to tetracycline. Resistance was of a high order and stable in subculture, the minimal inhibitory concentration being greater than 50 micrograms per ml. for most strains. Resistance was not confined to any particular type but the highest incidence was found in type 12 which was associated most commonly with nephritis. Fortunately, penicillin and erythromycin were still active against those strains and multiple resistance had not so far been encountered.

Resistant strains of Haemophilus were often isolated from the sputum of patients who had received prolonged prophylactic tetracyclines. The order of resistance was often not very high, but was enough to render the tetracyclines ineffective for systematic treatment against them. This would not greatly matter if these organisms were confined to treated patients but there was no reason to hope that in time they would not become widespread. since resistance was stable in subculture. It seemed therefore that, although the tetracyclines were at present successful as long-term prophylactics in chronic bronchitis this could not be expected to

last unless treatment could be alternated or combined with other drugs to prevent the development of resistance by organisms subjected to prolonged exposure.

Tetracyclines were very effective in acute mixed infections such as intestinal perforation and septic abortion. There was, however, a growing risk that at least one of the infecting organisms might be resistant to them and if the patient had recently received antibiotic treatment a more reliable choice would be a combination of newer drugs such as kanamycin and methicillin while awaiting laboratory guidance. Because of poor killing power no tetracycline was suitable for the treatment of subacute bacterial endocarditis. In exceptional circumstances one might be used in combination with another drug but, when given singly, although symptoms were quickly relieved, at the end of treatment prompt relapse was the rule.

In acute dysentery, salmonellosis and *E. coli* infantile enteritis the tetracyclines were usually effective but they were not suitable for the treatment of carriers because of their lack of killing power. Tetracyclines were not recommended as first choice for urinary infection. Proteus, a common urinary pathogen, was almost always more sensitive to sulphonamides than to tetracycline and in hospital tetracycline-resistant coliforms were almost as common as those resistant to the sulphonamides.

Since the tetracyclines had a wide spectrum they had not been much employed in combination. In general it was a mistake to combine them with penicillin, which acted best on rapidly dividing bacteria, because by inhibiting growth they would reduce the activity of penicillin. In brucellosis, however, a combination of a tetracycline with streptomycin (also most active against dividing bacteria) was the method of choice, tetracycline therapy alone being more likely to be followed by relapse. The probable explanation was that a tetracycline was the most effective single drug in brucellosis and the addition of streptomycin improved killing power whereas in acute infection with pyogenic cocci, penicillin alone was often the best drug, and the addition of tetracycline in these circumstances would reduce its high bactericidal activity.

In the past, tetracyclines had been some of the most useful drugs for the blind treatment of moderately severe acute bacterial infection; but, the position was changed. They have been superseded by other drugs for the treatment of staphylococcal infection, and were no longer reliable for suspected streptococcal infection. They should not be used for 'blind' therapy in urinary infection or for acute respiratory infection in patients who in the past had received long-term prophylactic tetracycline therapy. So far no analogue strikingly better than the three early drugs had been produced.

Consideracoes sobre a plasmoterapia. (Observations on plasma therapy) : RUY FARIA—*Pediat. Prat.*, **33 :** 295, 1962.

A group of 66 children, suffering from second and third degree acute dehydration was treated with liquid pasteurized plasma and the results were compared with a control series of 83 children suffering from similar disease and treated with whole blood transfusion. The mortality with plasma was 4.7 per cent. and that with blood 18.0 per cent. The average weight of the group receiving plasma was 5.700 ± 2.600 gm. while the other group receiving blood was 4.500 ± 1.800 gm. The mean age of the plasma group was 9.2 ± 7.2 months whereas the other group was 7.0 ± 5.8 months. Blood transfusion was more commonly resorted to in the lower age group and in infants suffering from severe degree of dystrophy and anaemia. Even then the value of plasma therapy in the treat-

ment of toxicosis and pre-toxicosis was stressed because of low mortality rate and ease of administration not requiring blood-grouping and not promoting iso-sensitization to any red cell agglutinogenic factor. Treatment with plasma also avoids any possibility of accidental transmission of any infectious disease, including homologous serum jaundice. The author also stressed the value of plasma enriched with gamma globulin in the treatment of severe infectious conditions, allergic states etc. Various types of plasma may be used such as, fresh plasma, liquid preserved plasma (pasturised or not) frozen plasma, and lyophilized plasma.

Current therapeutics—aldosterone : BELTON A. BURROWS—*Practitioner*, **190 :** 272, 1963.

It was recognized by 1943, with the separation from adrenal cortical extracts in crystalline form of six biologically active steroids (cortisone, cortisol, 17-*a*-hydroxydesoxycorticosterone, 11-dehydrocorticosterone, corticosterone, and deoxycortone) that the remaining amorphous fraction was more active in terms of survival of adrenalectomized animals and sodium-retaining activity than the isolated compounds. In the next decade the search for an additional 'mineralocorticoid' by many investigators culminated in the isolation of aldosterone. Crystalline aldosterone was shown to have one hundred times the salt-retaining activity of deoxycortone. Similarly, the ratio of cortisol to aldosterone in a normal adrenal vein blood was shown to be approximately one hundred.

Most of the clinical effects of aldosterone are mediated through the kidney, where the direct action of aldosterone, and its pharmacological predecessor, deoxycortone, has been demonstrated. Restoration of plasma and extra-cellular fluid volumes and normal blood pressure in adrenoprival dogs or men, which improves renal haemodynamics and measurable clearances, is probably secondary to the increased reabsorption of NaCl by the renal tubule. The correction of hyperkalaemia observed in adrenal insufficiency is probably related to the increased tubular secretion of potassium. Particularly is this likely to be the case in view of the absence of demonstrable intercompartmental shifts of potassium in the body with increased potassium excretion together with the excretion of hydrogen with a decrease in urinary pH. The increase in NaCl reabsorption produced by mineralocorticoids in adrenalectomized animals is most evident at low rates of NaCl excretion and may be minimized by NaCl loading or by the concomitant administration of glucocorticoids, which may increase glomerular filtration rate and hence the amount of NaCl filtered at the glomerulus.

The sodium-retaining effects of chronic aldosterone administration are apparently self-limiting. This 'escape' phenomenon may be related to an expanded extracellular fluid volume, without any direct evidence that it is due to increased glomerular filtration rate with an increase in filtered sodium.

Primary aldosteronism. With hypersecretion of steroid hormones by an adrenal tumour, one of three main categories of steroids hormones, represented by glucocorticoids, mineralocorticoids, or androgens, may predominate, leading respectively to Cushing's syndrome, Conn's syndrome, or virilism. The adrenal lesion in Conn's syndrome may be adenoma, hyperplasia, or carcinoma, although because the carinoma group produce excess urinary 17-hydroxicorticosteroids and 17-ketosteroids, as well as aldosterone, they do not fit Conn's definition. The classical syndrome consists of frequent episodes of severe muscular weakness and occasional paralysis, tetanic manifestations, usually

in the upper extremities, and with associated positive Chvostek and Trousseau signs, polydipsia and polyuria with predominant nocturia, severe headache and paraesthesia, hypertension, laboratory findings of hypokalaemia, alkalosis, hyposthenuria, proteinuria, and electorcardiographic changes.

Secondary aldosteronism. The excretion of a potent salt-retaining substance, later identified as aldosterone, in the urine of patients with hepatic cirrhosis was demonstrated in 1951. Increased amounts of aldosterone are excreted, and in some conditions studied have been shown to be secreted, by patients with the nephrotic syndrome or congestive heart failure and have been evoked by acute blood loss or sodium deprivation. The common denominator of these conditions may be reduced blood volume, either generally or at some specific receptor site such as the carotid body, denervation of which in experimental animals apparently blocks a reflex secretion of aldosterone resulting from decreased carotid arterial blood pressure.

Pregnancy is also associated with increased aldosterone production, apparently as a compensatory phenomenon following increased progesterone output. Progesterone administration has been shown to block aldosterone action at the renal tubule. This competitive effect apparently obeys the laws of mass action, as increased aldosterone administration can overcome the progesterone blockade.

Aldosterone antagonists. The synthetic compounds, such as the spirolactones, share with progesterone competitive inhibition of the aldosterone effect. Just as with progesterone, their blocking action may be short-lived if increased aldosterone production or other compensatory reaction by the adrenal gland occurs. Their action may be potentiated by the concomitant administration of chlorothiazides or glucocorticoids, which may promote the urinary excretion of water to accompany the increased excreton of sodium produced by aldosterone antagonists.

The spirolactones have an advantage in comparison with other diuretic measures in that the excretion of potassium is reduced, rather than increased. Their administration therefore does not have to be carefully controlled to avoid potassium depletion with, in cardiac patients, the associated complication of digitalis toxicity.

Another form of aldosterone blockade is produced by the administration of substances which inhibit aldosterone synthesis by the adrenal cortex, such as amphenone. The formation of cortisol and corticosterone is also blocked by these compounds, resulting in the stimulation of corticotrophin, which in turn leads to the increased prduction of deoxycortone and dehydrocortisone, both of which have sodium-retaining effects. The increased production of these latter compounds can be inhibited by the administration of glucocorticoids (cortisol or prednisone) so that a selective suppression of aldosterone production may be attained.

Ultimately, however, when divested of excess subcutaneous fiuid and ascites, the patient with so-called refractory oedema may be revealed as suffering from marked tissue loss, which may be referable to loss of intracellular constituents other than potassium. For example, low serum magnesium levels have been reported in patients with primary aldosteronism. The over-all effect on nitrogen balance and tissue wasting of other factors, such as anoxia of the tissues or inactivity, may outweigh in the long run the presently known action of aldosterone on salt and water metabolism in these patients.

SURGERY

Congenital diverticula of the anterior urethra in male infants : Report of

two cases : N. J. DEMOS, D. A. GILLIS and K. E. BARBER—*J. Urol.*, **88 :** 252, 1962. From *Inter. med. Dig.*, **78 :** 551, 1962.

Congenital diverticula of the anterior urethra is a rare anomaly, with only 99 cases reported through 1959. This article describes one case diagnosed immediately after birth and treated surgically at five days of age, and another patient treated surgically at 10 months of age.

The first patient was the product of an uncomplicated pregnancy, labour and delivery. The physical examination revealed a small hydrocoele on the right and a compressible ventral swelling of the penis. The child has had no complications since his surgical therapy.

The second child was seen at 10 months of age for evaluation of bilateral cryptorchism and a ventral penile swelling noted at the time of birth. He had been asymptomatic and the remainder of his physical examination was normal.

Five years following surgical therapy he was seen for intermittent dysuria and frequency. The appropriate urologic studies revealed delayed renal excretion on the right, mild bilateral ureteral reflux, a moderately enlarged and trabeculated bladder, and a narrowing of the urethra. The patient improved following urethral dilatations but has been lost to follow-up.

The clinical features of this anomaly may include the presence of a ventral penile mass without symptoms, dribbling or intermittent voiding, secondary infection, and the formation of strictures and pseudodiverticula following operative repair. One reported patient expired at 10 days of age from sepsis secondary to a urinary tract infection caused by urethal obstruction due to an untreated diverticulum.