attack. V. Mortensen[12] reported on 49 cases of post-scarlatinal nephritis and gave alternate cases diets low (40 g.) and high (125 g.) in protein; he found no difference between the groups, but the albuminuria ceased more rapidly in the cases on the diet high in protein.

As to experimental work, L. E. Farr[13] produced nephritic lesions in rats, and fed each group on a diet containing 5%, 18%, or 40% protein. The 40% group fared the worst. Although this experimental nephritis may not be comparable to the human disease, it is noteworthy that in the group on 18% protein, which is only slightly above the average human intake of protein, 8 out of 15 rats which survived the acute phase died at 5½ months of renal failure, while in the group on low protein 14 out of 16 completely recovered.

Thus, although in acute nephritis in man the evidence is scanty that a diet low in protein hastens recovery and a normal protein diet delays it, clinicians are naturally reluctant to depart from tradition or clinical impression until there is good evidence for doing so. This has now been supplied by R. S. Illingworth, M. G. Philpott, and J. Rendel-Short[14] in a carefully controlled study of acute nephritis in 42 children. Two comparable groups, allocated by random sampling, were treated identically except that one group was given a daily diet low in protein (average 0.3 g. per lb. body weight—0.7 g. per kg.) and the other a normal protein diet (average 1.23 g. per lb.—2.7 g. per kg.). Strict criteria for healing were adopted and included an Addis count of 500,000 or fewer red cells in the 12-hour specimen. Three months after admission the groups on low and normal protein contained five and four children in whom healing was judged to be complete. The failures numbered four in the low-protein and two in the normal-protein group, and there was one death in the low-protein group. This study therefore suggests that recovery will not be jeopardized by allowing patients a protein intake somewhere near their normal after the first few days of illness. On the contrary, the essential amino-acids thus supplied will help to preserve the nutritional state at its optimum.

HOME AND CLINIC TREATMENT OF TUBERCULOSIS

Sir Robert Philip established the first tuberculosis dispensary in Edinburgh in 1887. Its main functions were diagnosis, the making of arrangements for sanatorium treatment, and training the patient and his family in hygienic measures designed to limit the risks of infection.[1] Little out-patient treatment was given. From this beginning the dispensary idea spread, especially when in 1921 local health authorities took up the responsibility of looking after tuberculous patients. Even before the National Health Service Act transferred treatment to regional hospital boards many dispensaries had developed their functions, and in calling themselves chest clinics proclaimed a wider outlook. Refills of pneumothorax added another form of treatment to clinic work, and many clinics also were associated with the tuberculosis wards in the local hospital. To-day boards have provided chest clinics over the whole country, the chest physician (the former tuberculosis officer writ larger) thus being orientated more towards treatment, though he is also responsible to the local health authority for the preventive aspects of his work.

The war and its aftermath produced a great demand for beds; short spells of simple sanatorium treatment, available only to favourable cases, satisfied none when prolonged rest and collapse therapy offered better results. Despite provision of more beds the demand could not be fully met, and long waiting-lists for institutional treatment arose. There have always been more patients at home under the care of the family doctor than in hospital or sanatoria, but the situation called for a new attack. Several chest-clinic physicians—for example, C. H. C. Toussaint[2]—realized that the time had come to provide more active treatment, based on home and clinic. P. Stradling,[3] a firm advocate of such treatment even to-day when beds are easier to find, describes results in 64 patients whom he treated in this way in 1948 and has followed up for five years. Stressing the advantages of domiciliary and clinic management, he claims that patients fare as well under this system as when sent away to sanatoria. He used the relatively few beds then available to him for short periods of admission—largely for "medical collapse therapy," though 75% had to be sent elsewhere for "institutional convalescence." To-day a five-year assessment of the results of treatment in tuberculosis is inadequate, but few will dispute that many patients can be successfully treated under such a plan, and that it is no longer necessary to occupy sanatorium beds with those patients who can be happily managed in domestic circumstances. Chemotherapy is a valuable adjunct to domiciliary management, and, even if the patient needs admission to hospital later, is a sound preliminary to further treatment. Careful co-ordination of all the facilities available is an important function of the clinic; in addition to specialist medical advice and supervision, the patient may need the help of the almoner, district nurse, tuberculosis health visitor, home helps, ambulance, and other local health authority services.

The family doctor can thus again join in the active treatment of his tuberculous patient, for domiciliary and clinic management requires the close co-operation of chest physician and general practitioner. Under Stradling's plan patients may be admitted for short periods to the local hospital tuberculosis ward. P. Forgacs[4]

[1] Philip, R. W., *British Medical Journal*, 1904, **1**, 1357.
[2] Toussaint, C. H. C., *Domiciliary Management of Pulmonary Tuberculosis (Bishop Harman Prize Award, B.M.A.), Trans. med. Soc. Lond.*, 1950, **67**, 36.
[3] Stradling, P., *Tubercle (Lond.)*, 1955, **36**, 150.
[4] Forgacs, P., ibid., 1955, **36**, 109.
[5] Mitchell, R. S., *Amer. Rev. Tuberc.*, 1953, **67**, 401, 421.
[6] Report of B.T.A. meeting, *Tubercle (Lond.)*, 1954, **35**, 290.

describes a modification in which special short-term hospitals were used. The value of long periods of bed-rest alone have been questioned since R. S. Mitchell's[5] analysis of the records of patients with minimal disease in the Trudeau Sanatorium; chemotherapy has on the average reduced the length of bed-rest. Nevertheless, many patients with more extensive disease still need prolonged treatment in sanatoria. These are now in many cases chest hospitals which have become active centres of treatment—as different from the old sanatorium as is the chest clinic from the old dispensary. The resources of thoracic surgery are often necessary; many patients are best removed for a time from the stress of a domestic environment, which may well have influenced the illness for the worse; for many others poor lodging or family troubles prevent domiciliary treatment. In a discussion on this theme at the meeting of the British Tuberculosis Association[6] sanatorium treatment still found its advocates, though many tuberculosis workers recognize the merits of the domiciliary treatment of tuberculosis wisely applied and with adequate resources. Most beds for tuberculosis have been provided in special hospitals, which have a fine record in training medical and nursing staff, and these beds are still needed if we are to ensure prompt admission of every patient. So our present "sanatorium" beds must still be used (though if new buildings for tuberculosis patients are necessary they would be better provided near to centres of population), but they should offer facilities not available to the home or clinic, as well as the basic routines of rest, graduated exercise, and chemotherapy which are common to all methods of treatment.

ENDOGENOUS DEPRESSION IN CHILDREN

Much attention has lately been paid to depressive disorders, especially the endogenous type. W. Mayer-Gross[1] at the B.M.A. Annual Meeting in 1954 described it as the commonest type of complaint in psychiatric patients to-day. General practitioners agree with the high incidence of the condition, and it is thought that about one-third of psychiatric patients suffer from depressive disorders. The classical endogenous depression is well known to all physicians, but over the past few years many minor variants have been added to the list. In 1953 Raymond Greene and Katharina Dalton[2] described premenstrual tension, which often assumes the features of a short recurrent depressive illness. J. Malleson[3] bore out their contention and described patients who became psychotic to the point of suicide. Early this year A. B. Hegarty[4] described a variety of post-puerperal depression which he concluded "is a common and important condition and it is at present insufficiently recognized." Now J. D. Campbell[5] discusses manic-depressive disease in children. His paper is descriptive rather than statistical, but he claims to have seen a large number of such cases and so long ago as 1952 published the records of 18 patients. Mayer-Gross *et al.*[6] state that, although manic or depressive psychoses do not as a rule make their appearance before adolescence, occasional cases have been observed. The suicide rate under the age of 9 is negligible. From 9–12 years the figures over the past 50 years are only 2–4 per million, but thereafter the incidence rises steeply. The fact that children commit suicide suggests that endogenous depression may occur as a rare disease in late childhood or early adolescence.

According to Campbell this type of disease can be diagnosed only by observing the patient over a long period of time and by studying the family as a whole, since there is usually more than one case of the disease in the family. This suggests that the disease in childhood is premonitory rather than fully developed. The melancholy child is usually a likable person who gets on well with his teachers and fellows at school. He tends to be a leader and he prefers organization and social and literary activities to sport. He forms a good rapport with his physician. This point is important, for in so many psychiatric conditions affecting children the patient keeps his doctor at arm's length. A manic phase may be seen as well as a depressive, but it is the latter which attracts most attention. The child is tearful and depressed. Night fears are common and there are sleep difficulties. He does not want to go to school, because retardation makes work difficult for him, and remarks about his changed attitude and ability are too painful to be endured. He has feelings of unreality and often a morbid interest in death. In most cases the disease is mild and self-limiting but is liable to recur. Electroplexy is not advocated for the very young. These depressed children are sad and retarded, but they are rarely eccentric, delinquent, or negativistic. In fact they rarely present any of the usual behaviour problems for which children are commonly referred to a psychiatrist. The general practitioner may be called in because of the child's moods or for some collateral condition. The disease is thus more likely to be seen by the family doctor than by the consultant psychiatrist.

Endogenous depression is an insidious and polymorphous disease, often difficult to diagnose in adults. In children it is even more difficult to distinguish pathological from reactive depression. The exuberant spirits of the young can simulate the exaggerated activity of manic patients, and the child who is frustrated or deprived can plunge into the depths of despair. Only too often children cannot, dare not, or will not open up and give voice to their feelings in a process of psychocatharsis which is relatively simple in the adult. Campbell admits that circumstances of a sort are usually found to explain the low spirits, but he maintains that careful assessment will show such claims to be spurious, and that the depression is in fact endogenous. The fact that a manic-depressive psychosis is rarely diagnosed in Britain among children does not mean that it does not exist. Once attention has been drawn to any disease, it is always surprising how many cases come to notice. If endogenous depression of childhood is indeed as common as Campbell suggests, it is most likely to be found with increasing frequency by those general practitioners who are on the look-out for it, even though it has so far largely gone unrecognized.

[1] Mayer-Gross, W., *British Medical Journal*, 1954, **2**, 948.
[2] Greene, R., and Dalton, K., ibid., 1953, **1**, 1007.
[3] Malleson, J., *Lancet*, 1953, **2**, 158.
[4] Hegarty, A. B., *British Medical Journal*, 1955, **1**, 637.
[5] Campbell, J. D., *J. Amer. med. Ass.*, 1955, **158**, 154.
[6] Mayer-Gross, W., Slater, E., and Roth, M., *Clinical Psychiatry*, London, 1954.

RADIUM TREATMENT OF DEAFNESS IN CHILDREN

Few episodes of medical inquiry exemplify so cogently the importance of the statistical method in the evaluation of a remedy as that initiated in 1924 by the investigations of Crowe and his associates of the Johns Hopkins Hospital into the cure of deafness in children by irradiation of the nasopharynx. S. J. Crowe claimed that the treatment gave a high rate of improvement.[1] In addition, much was made of certain audiometric findings, which were said to show that high-tone deafness, usually attributed to a disorder of the perceptive elements, was frequently caused by Eustachian insufficiency and was indeed diagnostic of it. The results obtained by subsequent workers have varied. Some are encouraging; others, as for example those of N. Canfield and D. Sudarsky,[2] are equivocal, with an improvement rate of some 50%. Although the diversity of good and poor results might be attributed, in contradiction to Crowe's claims, to the operation of chance factors, the alternative cannot be excluded that they are due to the diversity of the clinical material. In other words, the results may be derived from suitable cases showing real improvement and unsuitable cases showing none. The statistical inadequacy of Crowe's original claims were early recognized, and two further reports from Crowe's department have gone far to remedy the defect.

For the first of these, published in 1950, we are indebted to S. R. Guild,[3] who took as his normal base line the audiometric changes in 259 white children, first examined at or about the age of 9 years. All were found to have normal hearing and were re-examined at the age of 16 years. None of the children were submitted to treatment by irradiation or otherwise, and at both examinations the audiometric findings were correlated with the nasopharyngoscopic appearances of the Eustachian orifices. One fact established by this investigation was the occurrence of a well-marked increase of acuity for the lower frequencies up to 1,024 cycles per second. This was clearly a physiological accompaniment of ageing, and could not, as previously, be attributed to radium therapy. Guild also made observations on a number of children with abnormal hearing treated with radium, and the results obtained in a small series of children with deafness for all frequencies seemed to suggest that radium therapy could benefit this class of case.

Guild's contribution has now been reinforced by a further comprehensive clinical and statistical study by J. E. Bordley and W. G. Hardy[4] from the same department. In the first stage of their work an otological and audiometric study was made of 5,000 Baltimore schoolchildren, white and coloured, with an average age of 8 years. Of these, 385, all with slight hearing defects, were selected for study and were re-examined regularly at six-month intervals for five years. 193 were treated with radium; 192, the control group, received no treatment. It was found, first, that radium reduced the amount of adenoids in the nasopharynx, though in this respect puberty itself also plays an important part. Secondly, an effect of radium (and not attributable to puberty) was to reduce lymphoid tissue round the Eustachian orifices. Thirdly, low-tone acuity notably improved both in the treated subjects and in the untreated control group. This confirmed the finding of Guild and his attribution of the improvement to a physiological process. Fourthly, acuity for high frequencies slightly improved in both groups of subjects. This confirmed Guild's view that high-tone deafness is unlikely to be caused by obstruction of the Eustachian tube by lymphoid tissue or to be improved by radium. Fifthly, these investigators noted real improvement from the radium—again in accordance with Guild's findings—in subjects with an all-frequency type of deafness probably caused by tympanic changes.

These two notable papers seem to justify the hope, so long deferred, that a method with such clearly defined advantages, both theoretical and practical, may now after all enter upon a period of intelligent and fruitful application. May it also be hoped that the sponsors of further investigations of this complex subject will accept as their base line the commendable standards, both clinical and statistical, which have been established by the contributions of Guild and his colleagues.

[1] Crowe, S. J., *Laryngoscope*, 1940, **50**, 658.
[2] Canfield, N., and Sudarsky, D., 1949, *Ann. Otol. (St. Louis)*, **58**, 957.
[3] Guild, S. R., *Trans. Amer. Acad. Ophthal. Otolaryng.*, 1950, **54**, 508.
[4] Bordley, J. E., and Hardy, W. G., *Acta otolaryng. (Stockh.)*, 1955, Suppl. 120.

CITRATE INTOXICATION

Symptoms ascribed to intoxication with citrate ion have been reported in adults who had received massive transfusions with stored citrated blood[1] and infants treated for erythroblastosis foetalis by replacement transfusion.[2-4] Citrate exerts its harmful effect partly by lowering the ionized calcium level of the body fluids, partly by acting as a cardiac poison.[5] As a result of its effect on ionized calcium it might be expected to cause tetany, and this has been reported in infants,[2 3] occasionally with dramatically fatal results.[6] Ringer showed that the frog's heart could not beat in the absence of ionized calcium.[7] The depressant action of citrate on the heart is further illustrated by experiments on dogs in which the conditions of cardiac operations were simulated.[8] J. P. Bunker *et al.*[1] reported episodes of hypotension in some of their patients, and in three of them the hypotension was accompanied by "spectacular elevations of citrate" in the serum. Although Stefanini[9] found that there was a well-marked prolongation of the blood-clotting time *in vitro* when the ionized calcium fell to 0.5 mMol* per litre, Bunker *et al.*[1] were

[1] Bunker, J. P., *et al.*, *J. Amer. med. Ass.*, 1955, **157**, 1361.
[2] Wexler, I. B., *et al.*, *J. clin. Invest.*, 1949, **28**, 474.
[3] Ames, R., *et al.*, *Paediatrics*, 1950, **6**, 361.
[4] Smith, H., *British Medical Journal*, 1955, **1**, 1089.
[5] Love, G. R., *J. Lab. clin. Med.*, 1923, **9**, 175.
[6] Mellone, O., and Yahn, O., *Arch. Cirurg. clin. exp.*, 1949, **12**, 369.
[7] Ringer, S., *J. Physiol.*, 1883-4, **4**, 29.
[8] Cookson, B. A. *et al.*, *Ann. Surg.*, 1954, **139**, 430.
[9] Stefanini, M., *Acta med. scand.*, 1950, **138**, 250.
[10] Lazard-Kolodny, S., and Mayer, A., *Physicochim. biol.*, 1938, **14**, 265.
[11] MacKay, E. M., *et al.*, *J. biol. Chem.*, 1940, **133**, 59.
[12] Sjöstrom, P., *Acta chir. scand.*, 1937, Suppl. 49.
[13] Stoppani, A. O. M., *Medicina, B. Aires*, 1946, **6**, 389.
[14] Natelson, S., *et al.*, *J. biol. Chem.*, 1947, **170**, 597.
[15] Perske, H., *et al.*, *J. Pharmacol.*, 1950, **100**, 273.
[16] Report of the Council on Pharmacy and Chemistry, *J. Amer. med. Ass.*, 1951, **147**, 658.
[17] Melrose, D. G., and Wilson, A. O., *Lancet*, 1953, **1**, 1266.

* 1 mMol = one-thousandth of the molecular weight in grammes.

unable to correlate the raised clotting-time with low level of ionized calcium in the serum in 3 of their 14 patients.

Treatment of established or incipient citrate intoxication is by injection of calcium chloride or calcium gluconate, but it is difficult to calculate the dose required, and too much is dangerous.[1] Nor does treatment seem to be invariably successful in altering the ionized calcium concentration of the serum[4]; indeed, the serum citrate concentration increases after injection of calcium gluconate.[2]

Citrate is metabolized in the liver[10-12] and the muscles,[13] and is excreted and concentrated in the urine by the kidneys.[14] Therefore citrated blood is contraindicated for patients with moderate or severe hepatic or renal impairment. Anaesthesia with barbiturates[15] and possibly hypothermia[1] depress the activity of the Krebs cycle, upon which the metabolism of citrate depends. Several substitutes for citrated blood are available. Heparinized blood has the disadvantage that it may cause post-operative oozing of blood from the operation site. B. A. Cookson *et al.*[8] recommended the use of oxygenated red cells suspended in Ringer–Locke–gelatin solution, but gelatin is quickly eliminated from the circulation, and should not be given if renal function is impaired.[16] D. G. Melrose and A. O. Wilson suggested transfusion red cells suspended in salt-free dextran.[17] Bunker *et al.*[1] concluded that blood from which calcium had been removed by passage over an ion-exchange resin was the ideal material for blood transfusion when citrated blood is contraindicated. The disadvantage of all these substitutes is the complicated method of their preparation, and further work is necessary not only to find some simply prepared medium in which red cells can be transfused, but also to define precisely the mechanism by which citrate exerts its effects and the best treatment for citrate intoxication once it has occurred.

HYPERGLYCAEMIA AND VISUAL DISTURBANCES

It has been known for very many years that transient disturbances of vision are by no means uncommon in diabetics. These disturbances are not related to, nor are they manifestations of, diabetic retinopathy, the haemorrhages, exudates, and retinitis proliferans of which have so far proved resistant to all forms of treatment. Diabetic retinopathy, in so far as it may be delayed (but almost certainly not prevented) only by the most rigorous clinical control of the diabetes, is not simply related to instability of the blood sugar concentration, but is a manifestation of some more fundamental metabolic disorder. These transient visual disturbances, however, do appear to show a simple correlation with the amount of sugar in the blood. It is well known that hyperglycaemia, particularly in young subjects, tends to be associated with myopia, while a fall in the blood sugar concentration, either during treatment or with an overdosage of insulin, is often accompanied by hypermetropia and difficulties with accommodation. The explanation of these changes was discussed some thirty years ago.[1] It is also well known that, again especially in the young, prolonged hyperglycaemia is apt to lead to cataract formation, and that the cataractous changes in the early stages are typical in appearance and are reversible, in that they may disappear completely when the diabetes is brought under strict control. True diabetic cataract, starting with opacification of the lens cortex, occurs only, or predominantly, in the young, but in this connexion some recent observations are not without interest. In 1952 D. W. Vere[2] noted variations in the brightness of the ophthalmoscopic red reflex in normal and diabetic subjects which could be related to alterations in the level of blood dextrose. In a more recent communication he and D. Verel[3] have confirmed these observations and shown that the changes occur equally in young and old. Myopia induced in the experimental subject by persuading him to accommodate is associated with brightening of the red reflex, while hyperglycaemia leads to its dimming. The observed alterations in the brightness of the red reflex therefore run counter to those which might have been expected purely from refractive changes, and the authors have shown that they are due to reversible opacification of the deeper layers of the cortex of the lens. The nature of the underlying biochemical disturbance in the lens is not known. Whether or not alterations in refraction are associated with these lens changes, whether or not they are the precursor of true diabetic cataracts, and, if they are, why, in the older subjects, the changes do not more frequently progress are further questions which remain to be resolved.

VISIT OF RUSSIAN DOCTORS

The news of the visit of the six Russian doctors to this country in October has aroused much interest and has stimulated Dr. L. Crome to write a letter (see p. 438) to which brief reference might be made. At the time of the visit in December last year of twelve Russian doctors under the auspices of the Society for Cultural Relations with the U.S.S.R., the British Medical Association was one of many organizations which helped to entertain them. "When to do this was less popular than now," the B.M.A. three years ago invited Russia to send a delegation of doctors to this country, and now that it has fortunately become easier for Russians to accept such invitations they are coming, coming as medical men interested in the work of their professional colleagues in the United Kingdom. We are happy to be able to state that the Soviet Relations Committee of the British Council is co-operating with the Association, financially and otherwise, in providing our Russian guests with every opportunity for getting to know something of medicine in Britain and something, too, of the British way of life.

[1] Duke-Elder, W. S., *Brit. J. Ophthal.*, 1925, **9**, 167.
[2] *Lancet*, 1952, **2**, 1017.
[3] *Clin. Sci.*, 1955, **14**, 183.