

a term used in the game of poker. It is well to remember that cards in the discard are re-shuffled and find their way back into subsequent games.

CEREBRAL REACTIONS TO ANTISYPHILITIC THERAPY

Severe cerebral reactions during antisymphilitic therapy are fortunately rare but have a high fatality rate. Of these reactions the most important is so-called "haemorrhagic encephalitis." The name is not a good one, as the condition is mainly not inflammatory but rather one of increased permeability of the capillaries; in this it has features in common with purpura. Causation is unknown, but most observers agree that it is the toxic action of arsphenamine derivatives on the smaller blood vessels of the brain and possibly allergic in nature. Others consider that syphilis itself is the cause, but this is to some extent negated by the observation that the condition has been recorded in other diseases treated with these drugs. Symptoms usually come on rapidly after the second or third injection, and are characterized by nervous irritability, headache, epileptiform convulsions, and unconsciousness. Treatment is likely to be successful only if energetic and undertaken without delay: venesection, repeated spinal fluid drainage, and injections of adrenaline are indicated—the last-named is probably the most important, and injection should be repeated as often as once every hour. The pathological features are congestion of the brain, with multiple haemorrhages and in some cases areas of necrosis. An increased protein content of the cerebrospinal fluid has been described, but otherwise the fluid is usually normal.

Two articles elsewhere in this issue record more or less typical cases. Halcrow describes a case which might be a textbook picture. He considers the cause to be a toxic action of the benzol radical on the capillaries and advocates the use of the term "haemorrhagic encephalopathy." Nelson and his colleagues describe 4 cases, 3 of them pregnant women, only one of whom recovered. They also regard the condition as due to a toxic action on the capillaries, but consider that syphilis itself cannot be excluded and that in pregnant cases toxæmia of pregnancy may be an additional factor. Thomas *et al.*¹ have reported 8 cases, 2 fatal, out of a series of 764 treated with massive dosage of mapharsen. It is generally agreed that haemorrhagic encephalitis occurs more frequently with intensive therapy than with the more time-honoured methods, but the fact that in the latter the condition usually comes on very early in treatment suggests that it is due to idiosyncrasy rather than to heavy dosage. Courville and Marsh² record 12 cases, in 7 of which multiple symmetrical foci of haemorrhagic necrosis were found and in one a gross haemorrhage into the brain; they regard the condition as due to a peculiar susceptibility to arsphenamine of certain blood vessels of the brain. In a case described by Lichtenstein³ the parenchyma of the spinal cord was mainly affected—in fact a demyelination. He regards the condition as due to sensitivity of the nerve tissues or the vascular bed to the arsenic. The demyelination may be the result of vascular changes, but the author regards it as a direct poisoning of the nerves by the drug. This case appears to be in a different category from those already quoted.

Haemorrhagic encephalitis is fortunately very rare, occurring only once in some thousands of cases; all are agreed that it cannot be foreseen or provided against and that it may follow relatively small doses of arsenicals. Certain blood vessels of the brain appear to be susceptible to the toxic action of the drug, some individuals showing

a particular idiosyncrasy. The walls of the capillaries give way, leading to haemorrhage and perhaps necrosis. The symmetrical distribution of the lesions bears out this theory. It is of interest to note that mapharsen, which is claimed to be generally so much less toxic than most of the arsphenamines, appears to be unduly so as regards this condition.

DIET AND TRINITROTOLUENE POISONING

The relation of diet to the manifestations of T.N.T. poisoning in human beings has not hitherto received close attention. If the results of animal experiments can be translated in terms of human reaction, some investigations recently carried out by Himsworth and Glynn¹ may make a most important contribution to the prophylaxis of T.N.T. poisoning in munition workers. In any case, they shed much light on the mode and site of action of T.N.T. in producing its well-known toxic effects. The development of toxic symptoms in rats after the administration of T.N.T. appears to depend to a remarkable degree on the nature of their diet: a high-fat diet is accompanied by severe symptoms and pathological lesions, while with a high-carbohydrate or high-protein diet these ill effects are slight or absent. The two most striking manifestations of T.N.T. poisoning in human beings—cyanosis and toxic jaundice—are not of course reproducible in rats, while the aplastic anaemia which has accounted for a certain number of deaths in T.N.T. workers is modified in rats into a severe erythroblastic hyperplasia of the bone-marrow. But lesions of the liver, comparable to those found in human cases of toxic jaundice, and the excretion of T.N.T. derivatives in the urine, point to a fairly close parallelism in the toxic process in both species. The "fat" diet on which the complete picture of chronic T.N.T. poisoning alone developed contained 50% of fat in the basic mixture, while the "protein" contained 60% of casein and the "carbohydrate" 90% of wheatmeal bread. The first and most striking manifestation of the toxic process was the appearance of a bright red pigment in the urine within half an hour of administration of T.N.T. mixed with the food. The composition of this pigment and its relation to the colourless pigment giving the Webster test in the urine of T.N.T. workers are uncertain, but the fact that it was absent from the urine of one animal with severe liver damage, just as the Webster test becomes negative when T.N.T. jaundice develops, suggests that the red pigment and the Webster chromogen may have a similar significance. The dependence of the appearance of the red pigment on the nature of the diet was shown by its specially prolonged excretion by rats on the fat diet. With very small doses of T.N.T. (0.01 g. per kilo body weight) none was excreted by rats on the fat or carbohydrate diet but a trace by those on the protein diet—a fact explained possibly by the diuresis always present on this diet and the consequent washing out of the pigment before it can be changed into a colourless compound. It is suggested that the pigment is formed at an early stage in the disposal by the body of T.N.T., and represents a dosage larger than the body can deal with.

The remaining features of chronic T.N.T. poisoning in rats are loss of weight, increased appetite, changes in the blood picture, hepatic lesions, and loss of hair. Loss of weight, in spite of a higher total food intake, was characteristic only of the rats on the fat diet, and, from experimental exclusion of other possible explanations, it is concluded that the fat diet in some way influences the animal's metabolism so that its ability to dispose of the T.N.T. within

¹ *Amer. J. Syph. Gon. V.D.*, 1942, 26, 529.

² *Arch. Derm. Syph.*, 1942, 46, 512.

³ *Arch. Neurol. Psychiat.*, Chicago, 1942, 48, 740.

¹ *Clin. Sci.*, 1942, 4, 421.

its tissues is impeded. The changes in the blood picture—a fall in the haemoglobin content, the appearance of normoblasts, reticulocytes, and polychromatic cells, and an increase in polymorphonuclear cells—were also more conspicuous in rats on the fat diet, while liver lesions were found only in these rats. The liver changes ranged from fatty infiltration to acute necrosis of the parenchymal cells. The severity of the lesion bore no relation to the amount of T.N.T. given, but a preliminary period of feeding on the fat diet appeared to predispose to the development of the more severe disturbances. Certain peculiar features of the incidence of hepatic damage similar to those in the incidence of toxic jaundice in T.N.T. workers were observed. Thus, there was a latent period between the administration of T.N.T. and the appearance of liver changes, and only very slight lesions occurred in rats surviving 30 days.

It has already been suggested by Voegtlin, Hooper, and Johnson that the absence of cases of severe T.N.T. poisoning among workers in a factory studied by them might be due to the good quality of the diet provided. The results of this investigation appear to point to the same conclusion, with the corollary that a diet in which fat preponderates to a great extent is not to be regarded as one of "good quality."

HEALTH EDUCATION FOR GIRLS

One of the first results of the publication of *Our Towns*, on which we commented in a leading article on May 8, has been to direct closer attention of those responsible for or interested in youth organizations to the training they give in hygiene and healthy living. The National Association of Girls' Training Corps in its leaflet No. 6 already provides for a course of lectures in hygiene, the first three of which, to be given by a doctor, are concerned with (a) the body and its functions: minor ailments; (b) the skin and its functions: common skin troubles; and (c) general questions about the maintenance of good health. Dr. Sarah Roberts of Bedford has sent us a copy of her own scheme of lectures in social hygiene for girls from 16 to 18. The lectures fall easily into three groups. First comes personal hygiene, which covers roughly the same ground as the first three lectures of the Girls' Training Corps. Then there come two excellent groups of lectures on public hygiene and social hygiene. Dr. Roberts says that there is more chance of women using the public health services if they learn the "whys and wherefores" when they are young. She therefore explains the functions of maternity and child welfare clinics, nurseries, and school clinics, and discusses the work of district nurses, health visitors, and welfare workers. Immunization and vaccination, milk- and water-borne diseases, fumigation and sanitation, and institutional provision are other subjects in this section, the object of which is to bring home to the girls the value of and the reason for all these social services. In the lectures on social hygiene Dr. Roberts deals first with family life, particularly with the position of the mother as the hub of that circle. The mother should, she holds, have at least an elementary knowledge of the child's mind and body from childhood to maturity if she is to understand children at all. Next comes development, which includes anatomy, and discussions on puberty, adolescence, maturity, etc., followed by talks on pregnancy and childbirth. The final subject is hygiene of the community, including healthy living to produce healthy children, venereal diseases, tuberculosis, etc. Dr. Roberts says it is her aim to impart some worldly knowledge to these girls which will be of use to them through life and help

to reawaken a more urgent sense of social responsibility. She advises simple language, using as few medical terms as possible, and has found the girls interested and orderly. She concludes with the suggestion that a course of this kind might be included in the syllabus for day continuation schools.

HYPOGLYCAEMIA AND THE BRAIN

Histological study of the brain in six fatal cases of hypoglycaemic coma by R. D. Lawrence, A. Meyer, and S. Nevin¹ has led them to conclude that a process akin to anoxia is concerned in this condition. Three of their cases were in diabetics and two in schizophrenics—all receiving insulin treatment—while in the sixth there was an adenoma of the pancreatic islets. Though there was some difficulty in estimating the duration and intensity of coma in these cases, the condition seems to have lasted for periods varying from three-quarters of an hour to 17 days. The histological changes differed somewhat in accordance with this variation. In cases in which coma had persisted for 36 hours or longer the cerebral cortex had undergone necrosis in many areas, with disappearance of numerous nerve cells. Selective involvement of the outer or inner laminae composed of these cells was particularly noted, also involvement of parts of Ammon's horn, an area known from Spielmeyer's work to be particularly liable to ischaemia. The corpus striatum and, to a less extent, the cerebellum were also affected, but the brain stem tended to be spared. There was widespread degeneration of neurones that had escaped complete destruction. Where coma had been of shorter duration earlier stages of the degeneration were present. These observations agree with certain others previously described both in hypoglycaemic coma and in conditions known to be of an anoxic character. An outstanding difficulty in the past has been to decide whether the basis of the disturbance may be primarily vascular, or whether there is a more direct action upon the neurones. Lawrence and his co-workers point out that in depriving the neurones of the glucose which forms the sole substrate for their oxidative processes a suspension of activity leading to degeneration and necrosis is entailed. Anoxia is not, strictly speaking, a correct term for this, and they therefore suggest a new word—oxyachrestia.

RESEARCH IN INDUSTRIAL MEDICINE

The Medical Research Council has arranged with the London Hospital for the establishment there of a department for research in industrial medicine. Dr. Donald Hunter, physician to the hospital, has accepted a part-time appointment to the Council's staff as physician-in-charge of the department, and the Council will appoint research assistants to work under his direction. The hospital is providing accommodation and facilities, and will be responsible for the treatment of cases under investigation. The primary purpose of the department is to undertake clinical researches into disorders affecting industrial workers, including both occupational diseases and others of a more general kind. This work will be done mainly in the department itself, but the staff will make visits from time to time to other parts of the country where special problems for investigation may be brought to the notice of the Council. The department will also be responsible for teaching and instruction in the subject. This arrangement supersedes that made last year for the appointment of a whole-time director of research in industrial medicine attached to the Council's headquarters. This post had become vacant through the appointment of Prof. A. W. M. Ellis to the Regius Chair of Medicine at Oxford.

¹ *Quart. J. Med.*, 1942, 11, 181.