

## MEDICAL RESEARCH COUNCIL

REPORT FOR 1933-4

(Concluded from page 433)

## STUDIES IN CLINICAL MEDICINE

Workers at University College Hospital have been testing the value of synthetic thyroid principle in the treatment of myxoedema; their results indicate that this compound is a true substitute for the natural thyroid, and active by mouth. Attempts to find a correlation between the blood esterase and the heart rate have not been successful. It has been shown that sodium chloride increases the susceptibility of pneumococci to dissolution by bile salts. Possibly, therefore, the bile salt treatment of pneumococcal empyema might be improved by increasing the sodium chloride concentration in the empyema cavity. The value of prostigmin in post-operative flatulence has been proved at St. Bartholomew's Hospital. At Guy's an attempt has been made to find out whether tonsillectomy reduces the liability to nephritis after scarlet fever; apparently it does not, nor does the administration of scarlet fever antiserum. At Manchester investigations into haemopoietin in the hog's stomach have confirmed its enzyme nature. There seems to be no relation between the iron and copper contents of liver and stomach preparations and their efficacy in the treatment of pernicious anaemia. Work on anaemia is also being carried on in Newcastle, with particular reference to the principle in yeast and wheat germ which is efficient. This factor appears to resemble Castle's extrinsic factor and to owe its therapeutic effect to the power of the stomach to secrete an intrinsic factor. Also at Newcastle it has been possible to produce temperatures of 104° to 105° F. by high-frequency within an hour, and to maintain them for six hours without serious discomfort to the patient.

At Liverpool it has been observed that the serum magnesium is increased in chronic nephritis with uraemia and in enlarged prostate causing retention of urine. It remains normal during epileptic fits, although generally it varies inversely with the blood calcium. From Edinburgh come reports on the nervous control of the human heart, and ephedrine by mouth has been found to be of value in preventing the attacks of unconsciousness of patients with heart-block.

The Council provides the expenses of a follow-up scheme at St. Mark's Hospital, London, where the grouping of cancer cases according to the proved depth of spread has been continued. The results indicate that the combined perineo-abdominal incision gives better results than the perineal operation. At Cardiff the surgery of the sympathetic nervous system is being studied, and the process of regeneration is being compared with that in somatic nerves.

## DISEASES OF WOMEN AND CHILDREN

Infections of the urinary tract in pregnant women are being studied in Glasgow, and an inquiry is being made into the late results of pregnancy pyelitis. It has been demonstrated that pyelitis after childbirth is the cause of 10 per cent. of puerperal morbidity. In the course of another research considerable variations have been found in the protein and mineral content of the amniotic fluid, but the significance of the variations is not yet clear. The incidence of contracted pelvis has been shown to be highest in Glasgow and Lanarkshire and low in the northern parts of Scotland. Research on the sources of infection in puerperal fever are still being carried out at Queen Charlotte's. Certain organisms, which resemble *Streptococcus pyogenes* but have biochemical properties different from those of the strains that cause most human infections, have been found incapable of causing puerperal fever, because of their susceptibility to destruction by the human blood. Attempts are being made to produce immunity to *S. pyogenes* by injections of a fibrolytic ferment. In Sheffield a mask has been devised to prevent droplet infection in obstetric cases. It has been confirmed that oestrin enhances the response to oxytocin.

The interrelations between pituitary function, the ovarian cycle, and calcium metabolism have been investigated at the London School of Economics, and the action of luteal hormone in pregnancy and parturition at Edinburgh.

Further work is being done on the effect of adding extra rations of vitamins A and D to the diet of children with measles. Investigation of a series of cases of "nutritional" anaemia which failed to respond to iron, copper, or vitamin B revealed that a chronic infection was responsible. It has been proved that boiling does not impair the nutritive efficiency of cow's milk or affect its digestion by the infant.

## WORK ON NUTRITION

From a number of studies of family diets and foodstuffs it appears that bone and vegetable broths have little nutritive value. A theory that pellagra is due to defective protein supply has received no support from further investigation. Attempts are being made to find a satisfactory method for measuring minute quantities of iodine in foodstuffs and soils, and it has been shown that very large goitres can be produced in puppies by restricting maternal iodine during successive pregnancies. Restriction in the young animal does not produce such large swellings. A great deal of work has been done on vitamin standardization and the relation of vitamin A to infection; it has been possible to express the relation between carotene preparations and vitamin A on a quantitative basis. The material on which the cod lives in spring and summer contains a measurable amount of vitamin D, and it seems probable that the store in the liver is derived from this source. The amount seems to depend solely on the age of the fish. The need for a full ration of unsaturated fatty acid has been shown by an inquiry into the influence of a fat-deficient diet on the skin. The stability of vitamin C in apples under conditions of storage and canning, and the active principle in apple juice which prevents scurvy, have received attention. The primary function of vitamin C in the dental tissues is in the activation of the formative cells, and it is necessary for the production of enamel and cement. Human beings have been found to have a limited power of storage of vitamin C, as well as of partial destruction of it within the body. This vitamin is present in relatively large amounts in a number of previously unsuspected sites in the animal body, including the suprarenal medulla and the lens of the eye. In vegetables various hexose sugars may serve as precursors. Vitamin B<sub>2</sub> has been found to be a complex of factors, of which flavine seems to be the growth-promoting component, but the flavine pigments recently isolated at Heidelberg can only partly replace B<sub>2</sub> in the diet. Some factor in this vitamin seems to have a beneficial effect on certain types of skin disease, and this is being investigated. It is now clear that vitamin E is an unsaturated alcohol, though it has not yet been prepared in a pure form.

According to work at Aberdeen, the so-called "diabetic centre" consists of two separate parts, pontine and medullary. An injury between the medulla and the pons leads to hyperglycaemia, whereas one below the medulla causes a rapid fall in the blood sugar. Further researches are being made on the relation of the two parts of the centre to the vagus nerves and pituitary and adrenal glands.

## PSYCHOLOGICAL AND PHYSIOLOGICAL RESEARCHES

The National Hospital, Queen Square, has worked on the central connexions of the autonomic nervous system and the nervous regulation of body temperature. A striking loss of myelin in the peripheral nerves has been demonstrated in subacute combined degeneration of the cord. The halogen content of the body fluids in epileptics has been studied with special reference to the effect of bromide treatment. At Oxford a study of the vagal control of the heart rate has been concluded, and the superior cervical ganglion has been shown to have a functional activity similar to that of a simple reflex centre in the cord.

The study of mental deficiency has been continued at Colchester, and a statistical analysis of over 200 cases has indicated that the mother's age is a more important factor than the order of birth.

Results of an investigation into the development of the bird's knee-joint in tissue culture indicate that bone, cartilage, and muscle have a strict regional determination before they can be recognized microscopically, and that the tissues destined to form bone, cartilage, and muscle do not originate in the situation which they finally occupy. Two oestrogenic compounds have been found to induce organization in embryonic tissues; and an impurity in crude glycogen acts in this way for amphibian tissues.

Investigations on the adrenal gland at Sheffield and St. Thomas's Hospital indicate that adrenaline releases a specific dilator at the sympathetic nerve endings. The inorganic constituents of the cerebro-spinal fluid in health and disease are being worked out at Cambridge, and a relation between chronic magnesium deficiency and scurvy has been established, though the two conditions are by no means identical.

These are but a few of the many and varied directions in which knowledge is being advanced with the assistance and under the supervision of the Medical Research Council.

## PHYSICAL SYMPTOMS OF ACUTE CONFUSIONAL INSANITY

### Dr. LEWIS BRUCE'S MAUDSLEY LECTURE

The sixteenth Maudsley Lecture under the auspices of the Royal Medico-Psychological Association was delivered by Dr. Lewis C. Bruce at the Royal Society of Medicine on February 28th. The subject was "Observations on the Physical Symptoms of Acute Confusional Insanity." Dr. Daniel Rambaut was in the chair, and introduced Dr. Bruce as one of the most brilliant and original minds in Scottish psychiatry.

Dr. Bruce began his lecture by remarking on the lack of knowledge as to the causes of insanity, and unless the cause were known the disease could not be efficiently treated. Could it be said that the incidence of insanity had been lowered or the probability of recovery enhanced? In only one disease, general paralysis of the insane, was the cause really known and effective treatment instituted. It was said that if only cases of insanity were obtained early enough the condition of affairs could be improved. But what was meant by an early case? The prominent symptoms of mania, delirium, confusion, which were seen in a mental hospital, were merely incidents in a long continued secret disease process, the underminings and premonitions of which were not readily assessable. There was a factor of hereditary transmission in certainly 40 per cent. of insanity cases, but there must have been a time in any family when there was no such predisposition, and therefore the knowledge of causation was no further advanced by bringing in heredity.

In the group of insanities of which he was speaking there was a prodromal period in some cases, but the alienist very seldom saw it. During this period there was confusion of thought, restlessness, sleeplessness, some disorder of the action of the heart and the stomach, and then the acute condition came on suddenly, with acute confusion, vivid hallucinations of sight and hearing, disorder of function, and great lessening of the common sensibility of the body. With care and nursing 90 per cent. of these cases recovered. From the primary attack, even if it lasted for as long as five years, the patient as a rule made a complete recovery; it was the secondary attacks which complicated the situation. In his own cases there were relapses in 40 per cent., and the curious thing was that the relapses always occurred in the cases which had recovered too readily. If the primary attack had lasted a considerable period, perhaps one year, perhaps even five years, the eventual restoration was

apparently permanent. Another curious fact was that while a second attack might be very similar to the first, if there were a succession of attacks the final condition so far as the mental symptoms were concerned was one often resembling the excited stage of manic-depressive insanity, and not to be diagnosed without the history.

### TEMPERATURE VARIATIONS

All who had seen cases of acute confusional insanity without any obvious cause must have been struck by the apparent illness of the patients. They were very often in what might be described as a "typhoid state," though the temperature actually was very little upset, rarely above 100°, and transient, afterwards tending to be sub-normal, though the patient still looked physically and mentally ill. Should the patient accidentally acquire an intercurrent infection such as erysipelas—which was common among these patients because they scratched themselves—and the temperature went up to 104° or 105°, the mental symptoms might absolutely disappear. These cases might be compared with other cases of confusion, such as apical pneumonia, where there was no doubt about the active cause. If one paid regard to the mental symptoms alone in such a condition it would be regarded as a case of acute confusional insanity; the same was true of puerperal states with confusion and a temperature running up to 104° or 105°. One might say that there were two distinct types of confusion, one in which no cause could be ascertained and there was no temperature, and the other in which there was a definite lesion and a high temperature. But there was a factor common to all these cases—namely, the mental symptoms. On the other hand, everyone had had experience of any number of cases of chronic toxæmia, pneumonia, and puerperal fever, not one of which had exhibited mental symptoms. Why was it that one individual out of a certain number developed mental symptoms when coming up against adverse circumstances? Was it due to hypersensitivity to a specific group of poisons, or to the fact that the individual was inadequately supplied with the defences which the majority of mankind possessed against the ordinary toxæmias met with in daily life?

Far back in the treatment of insanities alienists had tried to produce a febrile condition which would be safe and easily managed with the object of improving the patient's state. In recent years general paralysis had been treated by the induction of malaria. Very many years ago he had tried the plan of injecting a polyvalent streptococcus, but without producing any reaction. Then he tried the intravenous injection of staphylococcus vaccines, with scarcely better results. He also tried intravenous injections of typhoid and paratyphoid "A" and "B" and *B. coli communis* vaccines, and never had a single success, although high temperatures and strong reactions were produced. When malaria therapy came in, the first case in which he tried it proved a magnificent success, the patient making a complete recovery, but despite repeated trials he had never obtained another success in a confusional case. Yet other confusional cases cleared up after accidental contaminations with the streptococcus, and two of them after contracting scarlet fever.

He had tried to bring about recovery by inducing leucocytosis, but he had given up the use of vaccines for this purpose, because he feared that they unduly loaded the dice against the patients. Injections of sterile water were extraordinarily beneficial. He gave 1 to 5 c.cm., using it regularly in all the acute conditions, and it produced a rise in leucocytes. But whatever treatment was applied it had to be remembered that it was only the resisting power of the patient that was being raised, and that the patient was still suffering from a toxæmia; he was, so to speak, sitting on a volcano, and any adverse circumstance, mental or physical, which lowered his resisting power was likely to bring about another attack. The high neutrophil leucocyte count was a good sign as indicating that the patient had resisting power. The rise in leucocytes was protective in character.