

must be applied as a metallic soap. In such cases the physical texture and the mode of deposition of these films may be very important. The best frictional properties are obtained when the soap film has a close coherent texture, is evenly deposited over the surface and is well adsorbed. These films will lubricate until the softening point of the soap occurs. If, however, the adsorption of the soap to the surface is weak and there is a superincumbent layer of oil present, it may dissolve in the excess oil at a temperature lower than its softening point. If there are solvents present in appreciable quantities in the soap film, violent ebullition may cause them to disrupt the lubricant film. In both cases breakdown of the lubricant film will tend to occur at temperatures below the softening point of the metallic soap.

The softening point of a soap is not clearly defined and may cover a wide temperature range. The actual temperature at which the weakening of the soap film is sufficient to cause an appreciable increase in metallic seizure (and hence in the friction and wear) will clearly depend on the physical conditions of the experiment. With hard surfaces, where the pressures are high, or with extremely slow surface speeds, we should expect the breakdown to be discernible at lower temperatures. This is generally found to be the case—with any given metal and lubricant the transition temperature T is dependent in this way upon the load, speed and shape of the sliding surfaces. At higher sliding speeds the formation of a viscous soap film of appreciable thickness may lead to a hydrodynamic separation of the surfaces. The conditions are no longer those of true boundary lubrication and the friction may fall to a very low value (see the interesting paper by Beeck, Givens and Smith¹⁶ on quasi-hydrodynamic lubrication). The frictional behaviour of these soap films resembles in many respects the lubricating properties of thin films of soft metals deposited on hard substrates. This similarity has already been discussed in earlier papers. One of the most marked differences, however, is that even on rough surfaces a single molecular layer of soap may provide effective boundary lubrication, whereas metal films must be appreciably thicker (c. 10^{-6} cm.). The very high tenacity of the soap monolayer and its ability to prevent metallic seizure is, indeed, remarkable.

This view of the role of the lubricating film has been supported by recent work on the action of extreme-pressure lubricants and has led to the development of lubricants which maintain their boundary lubricating properties at very high temperatures.

BIOCHEMICAL ASPECTS OF MENTAL DISORDER

SOME aspects of the biochemistry of mental disorder were discussed at a meeting of the Psychiatry Section of the Royal Society of Medicine on May 24.

Recent biochemical investigations into mental disorder were surveyed by Dr. G. D. Greville, who opened the proceedings. He dealt in the first place with the excretion of hippuric acid by schizophrenic patients after sodium benzoate administration. Quastel and Wales found, in a routine examination of schizophrenic patients, that a group of eighteen catatonic patients showed without exception impaired rates of hippuric acid excretion. In a group of twenty-seven non-catatonic schizophrenics, all but four gave hippuric acid excretions of the normal value and normal range of variation. Since none of the cases chosen for examination showed signs of renal or hepatic impairment, Quastel and Wales suggested that a metabolic disturbance in the liver might be a characteristic feature of catatonic patients. Strom-Olsen, Greville and Lennon repeated this work with sixty-two schizophrenic patients of whom twenty-eight were considered to be catatonic. They found that only five of the catatonic patients gave abnormally low values of hippuric acid excretion, the proportion being about the same as among non-catatonic schizophrenic patients. Such a finding seemed not to indicate any noteworthy difference between catatonic and other schizophrenic patients so far as benzoate detoxication is concerned. There was agreement, however, that a small but not insignificant proportion (18 per cent) of non-catatonic schizophrenic patients without obvious renal or hepatic disturbance give abnormally low rates of excretion of hippuric acid under the standard test conditions.

Quastel and Wales then repeated their work using an intravenous method of benzoate administration to avoid a possible complication due to faulty absorption of benzoate from the gut and confirmed their original findings. Moreover, they obtained evidence that the clinical condition of the patient at the time of the test may have an important bearing on the rate of benzoic acid detoxication, for certain patients who had previously shown low rates of hippuric acid excretion exhibited normal rates after improvements in their mental condition due to treatment. Subsequent workers (Davies and Hughes; Finkelman *et al.*) have confirmed that abnormally low rates of hippuric acid excretion may occur in a large proportion of catatonic cases, but others (Gildea; Michael, Looney and Borkhovic) could obtain no evidence for such low excretions. Dr. Greville showed that the discrepancy between the results of the various workers could not be due to a failure to take into account the body-weight of the patients. Muscular rigidity may be a factor associated with the lowered rate of excretion according to Finkelman, but no satisfactory explanation is as yet forthcoming to account for the different sets of results.

Dr. Greville then turned to a consideration of the spontaneous hypoglycaemia which sometimes develops in the psychoneuroses and other abnormal mental conditions, and commented upon the development of emotional disturbances, often leading to behaviour of an anti-social character, during the periods of

¹ Bowden and Hughes, *Proc. Roy. Soc., A*, **160**, 575 (1937).

² Hardy, "Collected Works" (Camb. Univ. Press, 1936).

³ Sameshima *et al.*, *Bull. Chem. Soc. Japan*, **11**, 659 (1936).

⁴ Beare and Bowden, *Phil. Trans., A*, **234**, 329 (1935).

⁵ Bowden and Leben, *Proc. Roy. Soc., A*, **169**, 371 (1939).

⁶ Langmuir, *J. Franklin Inst.*, **218**, 143 (1934).

⁷ Bowden and Leben, *Phil. Trans., A*, **239**, 1 (1940).

⁸ Hughes and Whittingham, *Trans. Farad. Soc.*, **38**, 9 (1942).

⁹ Frewing, *Proc. Roy. Soc., A*, **181**, 23 (1942).

¹⁰ Isemura, *Bull. Chem. Soc. Japan*, **15**, 467 (1940).

¹¹ Bowden, Leben and Tabor, *Trans. Farad. Soc.*, **35**, 900 (1939).

¹² Tabor, *Nature*, **145**, 308 (1940); **147**, 609 (1941).

¹³ Dubrisay, *C.R. Acad. Sci.*, **210**, 533 (1940).

¹⁴ Lawrence, *Trans. Farad. Soc.*, **34**, 1 (1938).

¹⁵ Tanaka, *Mem. Coll. Science, Kyoto Univ.*, **21**, 85 (1938); **22**, 377 (1939).

¹⁶ Beeck, Givens and Smith, *Proc. Roy. Soc., A*, **177**, 90 (1940).

¹⁷ Bowden, Moore and Tabor, *J. Appl. Phys.*, **14**, 80 (1943).

¹⁸ Sakmann, Burwell and Irvine, *J. Appl. Phys.*, **15**, 459 (1944).

¹⁹ Bowden and Moore, *Nature*, **155**, 451 (1945).

hypoglycaemia. Hypoglycaemia frequently occurs in children whose ill-behaviour in this condition can often be improved by giving them sweets. He dealt with some of the work on carbohydrate metabolism which has been carried out on psychotic patients by means of glucose tolerance tests, measurements being made in these tests of the rates of appearance and subsequent disappearance of blood-sugar after oral ingestion of glucose. McCowan and Quastel showed that among manic-depressive patients, those exhibiting a high emotional tension gave a high hyperglycaemic index, a term coined by these workers to give a quantitative expression to the divergence between an abnormal and a normal oral-glucose tolerance curve. The patients on recovery showed a low or zero index, the value found in normal mental conditions where there is no complication due to physical factors affecting glucose metabolism in the body.

Gildea and his colleagues, as a result of their work on oral and intravenous-glucose tolerance curves in manic depressive patients, concluded that abnormal oral-glucose tolerance curves leading to a high hyperglycaemic index are largely due to delayed absorption of glucose from the gut. This conclusion is supported by the observation by Davis and Greville that in depressed patients there exists a correlation between the slope of the initial portion of the glucose tolerance curve and the hyperglycaemic index. The lower the initial rate of rise of blood-sugar, the more sustained is the hyperglycaemia. It seems probable that with a constant carbohydrate intake the factor which largely determines the initial stage of a sugar tolerance curve is the rate of absorption of the sugar from the alimentary tract. It thus appears evident that there is a correlation between this rate and the emotional state of the patient.

Dr. Greville finally mentioned recent work (for example, that of Gibbs) on the oxygen consumption of the brain as measured by differences between arterial and venous contents of oxygen, and by the rate of blood flow to the brain. It seems to be clear from the work of Wortis that there is no measurable difference between the rates of oxygen consumption of the brains of normal and schizophrenic individuals. Himwich and Fazekas conclude that cerebral oxygen uptake is normal in a group of undifferentiated mental defectives, but that it is probably reduced in mongolism, cretinism, phenylketonuria, and microcephaly. Little is known as yet of the changes occurring in the brain during the shock therapies commonly used in the treatment of schizophrenia, but there is evidence that marked changes of metabolism do take place. This is clear, for example, in insulin shock treatment, where a large reduction in the arterio-venous difference of oxygen content takes place, while the rate of blood flow is unaffected. It is unreasonable to expect that the cerebral metabolic changes will be identical in all forms of shock therapy, which differ so much in intensity and duration and which are by no means all equally effective.

The biochemical aspects of anxiety were discussed by Dr. D. Richter. He pointed out that the blood of patients with anxiety contains a substance which is absent from normal blood and which exerts a specific action on plain muscle. It has also been shown by Gellhorn and his colleagues that in emotional excitement there is a release of insulin into the blood. This is an effect which can be measured quantitatively, and should help in elucidat-

ing the details of the close association between anxiety states and the endocrine balance.

An emotional hyperglycaemia has been frequently reported, but many investigators have failed to confirm this. Dr. Richter has carried out blood-sugar estimations on patients with anxiety states and on normal subjects during air raids at the Neurosis Centre at Mill Hill. About one third of the subjects showed a slight rise in blood-sugar level when exposed to immediate danger, but the rise was never very great. He referred to further work at Mill Hill which showed that serum choline esterase activity is increased in anxiety states and in depression. A rise can also be produced in normal subjects by vigorous exercise or by exposure to low temperatures. The effect is attributed to an increased autonomic activity and is apparently specific for choline esterase.

Dr. Richter observed that during the last few years there has been a tendency to depart from the point of view concerning anxiety states held by Cannon and his associates. In acute emotional states there is a general lability of autonomic control in which many apparently unrelated biochemical factors may be involved. The pattern of responses, instead of being uniform, shows considerable variations in different individuals, and there is little evidence that they serve any useful biological purpose. A variety of biochemical factors may play a part in the onset of anxiety states, as for example, hypoglycaemia, aneurin deficiency or adrenaline release. Anxiety may be a symptom of almost any physical disability to which the individual is unable to adjust. Recent work on patients with 'effort syndrome' has shown how a biochemical lesion causing an impairment of physical efficiency can lead to the onset of an anxiety neurosis.

The discussion was opened by Dr. J. H. Quastel, who commented upon the diversity of results obtained by different workers on the rates of hippuric acid excretion in catatonic patients submitted to a standard test. He emphasized the dependence of these rates on the clinical conditions of the patients, and urged the great importance of close association and co-operation between the psychiatrist and the biochemist in correlating the results of a biochemical test with the patient's mental and physical condition at the time of the test. The lack of agreement between the results of metabolic investigations in the field of schizophrenia may be largely due to the fact that such a field is far from homogeneous and the individual schizophrenic patient shows much variation in mental state and physical condition over a period of time. For progress in such work it is essential to select a small field where there is some approach to homogeneity and to examine cases in such a field periodically. The interesting results of Gjessing on the metabolic changes associated with changes in the mental state are probably due largely to his selection and continuous examination of a small number of schizophrenics conforming to a special group of periodic catatonia which is characterized by repeated attacks of stupor and excitement. Gjessing concludes that the mental disturbance follows directly upon a disturbance of nitrogen metabolism, and suggests that at the time of change of phase a toxic substance is produced which is connected with the disturbance of protein metabolism and which acts in an inhibitive or irritant manner on the central nervous system.

Although there is no convincing evidence, in Dr.

OBITUARIES

Sir Peter Chalmers Mitchell, F.R.S.

Quastel's opinion, that impaired oxidations in the brain play an important part in schizophrenia, the sensitivity of the cortex to anoxia is such that localized changes may result in abnormal mental manifestations with but little overall change in the brain metabolism. It is important to take into consideration not only the availability of oxygen or of glucose (the main fuel of the brain) to the nerve cell but also that of a variety of other factors, all indispensable for the normal rate of oxidation of glucose in the cell. Among such factors are nicotinamide, aneurin, riboflavin and adenylypyrophosphate. If there is a local deficiency of these substances, or some interference with their activities, the results, so far as the nerve cell is concerned, may be as far-reaching in their consequences as the deprivation of the oxygen or of the glucose supply. The sensitivity of the cortical tissue to anoxia may be a factor concerned with the beneficial effects of shock therapy, but too little is known as yet of the effects of these treatments on the metabolism of the central nervous system to come to any definite conclusion.

Referring to the work on glucose tolerance tests and emotional states, it was pointed out that Lockwood has observed a dependence of the hyperglycaemic index on the affective state as indicated by the psychogalvanometer.

Interesting results are now being obtained with the use of the electro-encephalogram on the connexion between biochemical activities of the brain and its electro-physiological properties. Studies such as these should help to throw light on the manner in which biochemical and electrophysiological phenomena connected with the central nervous system are linked with the mental state.

Dr. R. Benesch referred to work carried out by him in collaboration with Dr. P. Ellinger on certain nicotinamide-deficiency syndromes, namely, pellagra and the acute psychoses of the Cleckley-Sydenstricker type. Ingestion of nicotinamide normally leads to the excretion of nicotinamide methochloride. Benesch and Ellinger have shown that large differences in the basal output of nicotinamide methochloride, and in the output after nicotinamide administration, exist between control subjects and pellagrins as well as acute psychoses with a suspected nicotinamide deficiency. The mental confusion present in such cases clears up after nicotinamide treatment. They further showed that human intestinal flora are capable of synthesizing nicotinamide, so that a diet may inhibit the development of pellagra quite independently of its content of nicotinic acid. Thus the nature of a diet and the type of bacterial flora it encourages in the human intestinal tract are important factors to consider in the development or treatment of nicotinamide-deficiency disorders.

In general discussion it was pointed out that choline esterase is exceptional in presenting an example of an enzyme passing into the blood concomitantly with the development of an anxiety state or of an increased autonomic activity. Its appearance in the blood, however, will not, according to Dr. Richter, invalidate its use as a test for liver function. Further discussion ranged around the association of incipient pellagra with porphyrinuria and the fact that sulphonal poisoning may produce pellagra-like symptoms.

It was suggested by Dr. Mackenzie that a patient might most profitably be presented for biochemical investigation at a time corresponding to a definite phase of his behaviour, rather than on the basis of his psychiatric classification.

PETER CHALMERS MITCHELL was born at Dunfermline on November 23, 1864, and died in London, as the result of an accident, on July 2, 1945. He was the eldest son of the Rev. Alexander Mitchell, and was educated at Aberdeen Grammar School, the University of Aberdeen, and at Christ Church, Oxford, where he was an exhibitioner. He also studied in Berlin and Leipzig. He became senior University demonstrator in comparative anatomy and assistant to the Linacre professor at Oxford in 1888, and during 1891-93 was organizing secretary for technical instruction to the Oxfordshire County Council. Afterwards he went to London as lecturer in biology at Charing Cross Hospital and at the London Hospital. During this period he carried out various comparative studies mainly on the anatomy of birds, and in the course of this work spent much time at the prosectorium of the Zoological Society. About this time he published his "Outlines of Biology" and "Thomas Henry Huxley: A Sketch of his Life and Work", an outstanding biography which perhaps more than any other of his writings reveals his literary gifts. He also translated Metchnikoff's "The Prolongation of Life, Optimistic Studies" and O. Hertwig's "The Biological Problem of To-day. Preformation or Epigenesis?".

Mitchell will be remembered mainly, however, for his very great services as secretary of the Zoological Society of London from 1903 until 1935. During this period, by a judicious blending of popular and scientific interests, it became the leading zoological society in the world, a great popular and scientific institution, and a model for the many similar societies which sprung up during the twentieth century. Some idea of its progress may be gathered by the fact that between 1903 and 1935 the number of fellows increased from approximately 3,500 to more than 8,000, and the annual number of visitors to the Gardens from approximately 690,000 to more than 2,000,000. During his term of office the Zoo was largely rebuilt, the most notable additions being the Mappin Terraces, Aquarium, Reptile House, Monkey House and Monkey Hill. In addition, he was entirely responsible for the creation of Whipsnade Zoological Park, a monument to his energy, imagination and organizing ability. He himself regarded Whipsnade as his crowning achievement on behalf of the Zoological Society, and there he made his country home after leaving Malaga. His "Centenary History of the Zoological Society of London", published in 1929, contains an excellent account of the growth of the Society and the development of its various activities, including both Regent's Park and Whipsnade.

Apart from his zoological interests, Mitchell devoted much of his time to journalism and for many years was scientific correspondent of *The Times*, a regular leader writer, and that journal's adviser upon scientific matters. He was also chairman of the council of management of the "World List of Scientific Periodicals" from its beginning until 1935, and remained an active member of that organization until his death. He was largely responsible for the preparation of the volume which, in its second edition (1934), gives the titles and standard abbreviations of more than 36,000 periodicals.

After his retirement, Mitchell went to live at Malaga, but in 1937 political events debarred him