starch, is that sugar gives both glucose and fructose on hydrolysis, whereas starch gives only glucose. Alternatively, the bacterial flora might be modified in such a way that substances are produced that interfere in lipid or carbohydrate metabolism. Further complications in interpretation arise from subsequent studies by I. Macdonald and A. Nowakowska[4] on the effect of sex on the response to carbohydrate. Five healthy young women were found to react in much the same way as men to starch, but to differ in their response to sugar. Thus the inclusion of sugar in their diet resulted in decreases rather than increases in the total lipids, glycerides, and cholesterol in the blood.

A point to emerge clearly, in contrast to our perplexities over matters of detail, is that the various common forms of dietary carbohydrate cannot always be regarded as interchangeable. Their effects on the nutritional status and health of the consumer may be decidedly different. These differences lend colour to suggestions that sugar, rather than saturated fats, may be the most important dietary factor in the aetiology of atherosclerosis.[5-7] For the present it would be rash to select sugar unreservedly as our "scapegoat" to the exclusion of other nutritional factors. But mere possibility that excessive sugar consumption may be atherogenic will undoubtedly enhance the interest and importance of further research by Dr. Macdonald and his colleagues.

Chemistry in the Brain

Progress in medicine, and particularly in therapeutics, has usually been empirical. Theoretical explanations have followed, not preceded, the discoveries. Every scientist hopes that this order will be reversed, for too rarely have therapeutic advances come from increased knowledge of physiology. The latest number of the *British Medical Bulletin*,[1] which is on the pharmacology of the nervous system, brings the reader up to date with recent studies on the action of drugs, including naturally occurring constituents of the brain such as acetylcholine, brain monoamines, and γ-aminobutyric acid, on electrical activity or metabolic processes in nervous tissue. The localization in the brain of behavioural and other effects of drugs is also considered. Electrical recordings from single neurones subjected to microinjections of drugs play a large part in the work reviewed here. A chapter by Sir John Eccles on inhibition in the central nervous system is a welcome summary of this fascinating problem and includes much work completed only last year. New methods, however, are not confined to the study of recordings from single neurones. W. Feldberg and his colleagues have localized the actions of drugs in the brain by applying them to restricted parts of the cerebral ventricles, and their work has given rise to new theories of temperature regulation by hypothalamic activity. Most of the remaining articles deal with advances in chemical methods and the insight gained recently into the interrelationships between drugs and some aspect of brain metabolism. W. D. M. Paton and W. G. Spector strike a more general note by reviewing the present state of the theory of anaesthetics, and show that more is now known about where anaesthetics interfere with consciousness than on the precise way in which they do so. The last chapter illustrates an important topic which has only recently received much attention—the direct effect of hormones, more particularly oestrogens, on brain activity. Only restricted areas of the brain are affected by the action of oestrogens, and this determines certain aspects of sexual behaviour.

Therapeutic progress in the treatment of mental disease by drugs has acted as a stimulus to research in the pharmacology of the brain. And it seems reasonable to expect that the progress reflected in the present volume will lead to further advances in the use of drugs to combat mental illness.

[1] *Brit. med. Bull.*, 1965, **21**, 1–96.

Calcitonin

The level of calcium in the plasma is normally constant within remarkably close limits. It has usually been taught that this constancy is achieved by the parathyroid glands acting through a single hormone, conveniently called parathormone, which raises the concentration of calcium in the plasma. The possibility that a second hormone might be at work arose when P. H. Sanderson and his colleagues[1 2] found that if dogs were given an infusion of calcium salts the plasma calcium returned to normal more rapidly if the parathyroids were present than if they were absent. H. Rasmussen[3] pointed out that parathormone is too slow in its action to account for the remarkable constancy of the plasma-calcium level, and so the stage was set for a search for a second hormone with a more rapid effect on plasma calcium than parathormone.

A brilliant series of researches on dogs by D. H. Copp and his collaborators[4-6] has established that there is indeed a second hormone, and they have named it calcitonin. The new hormone was found actively to lower plasma calcium and there seemed little doubt at first that it came from the parathyroids. Copp and E. C. Cameron[5] were able to show that when certain preparations of commercially prepared parathormone were injected into dogs a transient fall in plasma calcium occurred before the expected rise. They attributed this fall to the presence of calcitonin as a contaminant. I. MacIntyre and his collaborators were able to confirm that calcitonin exists,[7] but their work on goats[8] pointed strongly to the thyroid as the origin of the hormone rather

[1] Sanderson, P. H., Marshall, F., and Wilson, R. E., *J. clin. Invest.*, 1960, **39**, 662.
[2] See *Brit. med. J.*, 1963, **2**, 1009.
[3] Rasmussen, H., *Amer. J. Med.*, 1961, **30**, 112.
[4] Copp, D. H., Davidson, A. G. F., and Cheney, B., *Proc. Can. fed. biol. Soc.*, 1961, **4**, 17.
[5] —— and Cameron, E. C., *Science*, 1961, **134**, 2038.
[6] —— —— Cheney, B., Davidson, A. G. F., and Henze, K. G., *Endocrinology*, 1962, **70**, 638.
[7] Kumar, M. A., Foster, G. V., and MacIntyre, I., *Lancet*, 1963, **2**, 480.
[8] Foster, G. V., Baghdiantz, A., Kumar, M. A., Slack, E., Soliman, H. A., and MacIntyre, I., *Nature (Lond.)*, 1964, **202**, 1303.
[9] Munson, P. L., in *The Parathyroids*, edited by R. O. Greep and R. V. Talmage, 1951. Thomas, Springfield, Illinois.
[10] Hirsch, P. F., Gauthier, G. F., and Munson, P. L., *Endocrinology*, 1963, **73**, 244.
[11] Baghdiantz, A., Foster, G. V., Edwards, A., Kumar, M. A., Slack, E., Soliman, H. A., and MacIntyre, I., *Nature (Lond.)*, 1964, **203**, 1027.
[12] Seecof, D. P., *Amer. J. Path.*, 1927, **3**, 365.
[13] Foster, G. V., MacIntyre, I., and Pearse, A. G. E., *Nature (Lond.)*, 1964, **203**, 1029.
[14] Frame, B., Frughtman, M., and Smith, R. W., *New Engl. J. Med.*, 1962, **267**, 1112.

than the parathyroids. This may seem surprising, but P. L. Munson[9] had already found that in rats parathyroidectomy alone resulted in a more rapid fall in plasma calcium than did combined excision of the thyroid and parathyroid glands. Moreover, when P. F. Hirsch and his colleagues[10] investigated the possible cause of this they found that the rat thyroids contained a substance which could lower plasma calcium. Hirsch and his co-workers named this hypocalcaemic factor thyrocalcitonin. It is tempting to think that calcitonin and thyrocalcitonin are the same substance, but further work on purified extracts will be required to find out if they are. A step in this direction has recently been taken by MacIntyre and his group,[11] who have been able to obtain from the thyroids of pigs a highly potent extract which lowers the level of calcium in the blood. Their preparation is a polypeptide or a protein of low molecular weight, but since hot concentrated hydrochloric acid is used in the extraction process the molecular weight of the natural hormone could be considerably higher.

Though MacIntyre and his colleagues have termed the hormone calcitonin, it might have been more prudent at this stage to have called it thyrocalcitonin, since there may yet prove to be two hypocalcaemic factors, one arising from the thyroid and the other from the parathyroids. There seems little doubt, however, that the thyroid gland is the source of a hormone with properties different from those of the thyroid hormone. The question arises whether the two hormones are secreted by a single or two different types of cell. The thyroid gland contains a small proportion of cells which are especially rich in mitochondria and are apparently metabolically distinct from the majority of the thyroid cells.[12] G. V. Foster and his colleagues[13] have now shown that the concentration of enzymes in these mitochondrion cells changes in response to changing level of plasma calcium. They suggest that these cells could be the source of calcitonin.

The discovery of a new hypocalcaemic factor is bound to affect our approach to calcium metabolism both theoretically and practically. Many questions present themselves. How does it act and on what organs ? Will a knowledge of its actions help us to understand some of the more intractable clinical problems, such as idiopathic hypercalciuria ? The answers to such questions must await preparations suitable for general use. We may not have to wait long for them, and when available they may prove helpful in treating hypercalcaemia of infancy and of other causes. Finally, ought we now to be on the look-out for calcitonin-secreting tumours in cases of persistent hypocalcaemia ? B. Frame and his colleagues[14] have already described a patient with hypocalcaemia and clear-cell hyperplasia of the parathyroids in whom they considered that an excess secretion of calcitonin could have been the explanation of the hypocalcaemia.

Toxic Effects of Drugs

The Committee on Safety of Drugs presided over by Sir Derrick Dunlop is receiving every week up to 100 reports of adverse reactions, according to a letter it has sent to doctors and dentists. The columns of this and other journals have carried reports of fairly frequent reactions to some of the tranquillizers, so it comes as no surprise to read in the letter that " the Committee has been particularly impressed by the frequency of suspected reactions to some of the newer drugs acting on the nervous system." Despite the large number of reports the Committee is receiving it is holding out its plate for more. Only from early and full reporting of suspected reactions to new drugs in particular can the Committee gain enough data quickly to assess their value and to take action, if necessary, to prevent therapeutic mishaps. In addition to seeking the help of all doctors in providing information the Committee has obtained the part-time service of some in various parts of the country to follow up reports of adverse reactions.

In going about its task in a thoroughly practical and helpful way the Committee has gained the confidence of both the medical profession and the pharmaceutical industry. It deserves every support if sick people are to get the fullest benefit which pharmaceutical manufacturers are making possible.

Wellcome Trust

The fifth report of the Wellcome Trust, now published, is another reminder of how much medicine, both at home and abroad, owes to the Wellcome Foundation. Over £7m. has been distributed by the Trust since its creation under the will of Sir Henry Wellcome in 1936, and £2m. of this was allocated during 1962–4, the period covered by the report. Grants towards the costs of building included those to the Royal Society for meeting-rooms in its new premises at Carlton Gardens, the library of medical history in the new Royal College of Physicians, and research laboratories for the clinical pharmacology department at the University of Yale. At $230,000, the grant to Yale is the largest sum ever allocated to the United States of America.

There are now five Wellcome Research Professorships and the report gives details of a new research chair in zoology, which is to be held by Professor L. C. Beadle at Makerere University College in Uganda. Professor Beadle has made an intensive study of the ecology of African fresh-water swamps and he is to write a book about his findings, which have an important bearing on the prevention and control of tropical diseases. Dr. R. Lainson is shortly to set up a new unit at Belem at the mouth of the Amazon in Brazil, where he will study the life-history of *Leishmania braziliensis*. Infection with this parasite results in the condition known as espundia—characterized by the destruction of the skin and mucous membrane of the mouth and nose and of the cartilages of the nose and throat. Five new Wellcome Senior Research Fellows and 100 other new Fellows were appointed during 1962–4, while travels grants totalling £75,000 were made to help scientists to study in other centres and to attend conferences. Centres receiving research grants range from Cagliari in Sardinia to Mysore, and from Addis Ababa to Oslo. The findings in the co-operative research scheme on megaloblastic anaemia, which has been carried out at the Hammersmith Hospital in London, Nairobi, Vellore, and Singapore, are still being studied, but already it is realized that the aetiology and correct treatment of the anaemia among the different countries vary considerably. The Wellcome Trustees are to be congratulated on this record of their far-sighted policy.