

behavioural consequences. There are people of subnormal intelligence easily led astray or bewildered in city life; demobilized old soldiers on their own after 30 years of service life; solitary men who with even a little friendly supervision will cease going out drinking: all can receive support from a long-stay hostel. Long-stay hostels for people in these two categories are preventive medicine of a most important kind.

Thirdly there are groups of people for whom their home (or present social setting) is an obvious precipitant of behavioural disorder. They include some disturbed children, disturbed adolescents, drug addicts, alcoholics, and recurrent delinquents, and they need a therapeutic home from home. Both local authorities and the health service have much to learn here from the work of private organizations such as the Simon Community and the Richmond Fellowship.⁸ A range of therapeutic hostels is needed to serve the different groups, and the problem arises of how far the treatment will be by social workers and how far by psychiatrists. Because psychiatric illnesses often tend to be prolonged (even if there are intermissions) but are eventually mastered, there is a continuing need for the convalescent services of transitional hostels to help people back to normal work and to renew their social relationships, broken by the illness.

Studies are needed of the variety of functions that hostels must serve as well as of the role of the doctor, social worker, nurse, teacher, and lay helper in each. The Second Green Paper² proposes that hostels will be operated by both health boards and local authorities according to the degree of medical care required. Will this create unhealthy rivalry between doctors and social workers?

A recent publication from the Buckinghamshire County Council⁹ deserves to be widely read as a start to the debate. Written by a social worker, it sets one local authority's modest provision of hostels against the general background and points above all to the need for the special training of hostel staff and a supportive rather than hierarchical administration. Where it could say more is in closer analysis of the population's present needs and how medical and social services can collaborate to serve them. There may be a need for more censuses of private hostel and lodging-house residents, and other factual surveys may be required as a basis for good planning. Perhaps this latest paper will stimulate others to discuss these questions.

Phenylketonuria

Now that the semiquantitative estimation of phenylalanine in capillary blood has virtually superseded the Phenistix testing of urine as a screening procedure it is appropriate to consider what has already been achieved by the treatment of phenylketonuria, and also to review the organization which has to be set up to deal with cases detected by screening programmes. It is generally agreed that the dietetic treatment of phenylketonuria will, if started early enough, prevent severe mental retardation, but rigid proof of the beneficial effects of treatment has been hard to obtain. Recently F. P. Hudson and his colleagues¹ have analysed 184 cases in which treatment was

started before the age of 4 months. In 97 cases whose treatment had continued for at least 2½ years the mean intelligence quotient was 90.4, while that of their parents was 105.5, of their unaffected sibs 105.2, and of affected sibs (including both treated and untreated individuals) 53.3. A previous combined study² showed an inverse ratio between the intelligence quotient and the age at which treatment was started.

Some of the stimulus for the setting up of regional screening programmes was provided by a circular from the Department of Health and Social Security³ which recommended that the testing should be done between the 6th and 14th days of life by means of the Guthrie bacterial inhibition test. The exact timing and methods used are not yet uniform, so that some comparisons between them will be possible. Some centres, for example, are using one-dimensional chromatography, which will also detect other disorders of amino-acid metabolism such as tyrosinaemia, homocystinuria, maple syrup disease, histidinaemia, and hyperprolinaemia.

Obtaining a blood sample is a more serious matter than the testing of urine, and parents should be informed of the purpose of the test well in advance of the taking of the specimen. The result of the test, even if negative, should be given to the parents. All staff concerned in taking blood specimens should be formally instructed in the correct technique and sufficiently informed on the subject to deal confidently with parents' questions. The medical officer of health is notified of all births and can keep a register of all infants tested, so he can arrange for the testing of any infant whose test was omitted. A positive screening test requires confirmation by a second similar test. When two tests are positive the laboratory should inform the midwife or health visitor who took the blood, the medical officer of health, the family doctor, and the paediatrician in whose area the infant lives. The baby should then go into hospital for further investigation. In some regions centralization of the biochemical investigation of positive cases may be necessary, but subsequent treatment and supervision should be possible locally if adequate facilities are available.

Haemostasis and the Uterus

The haemostatic mechanism appears to be designed to work locally in immediate relationship to damaged tissue, with drastic limitation of its more remote effects. The stimuli for contraction of blood vessels, adhesion and aggregation of platelets, blood coagulation, and the activation of the fibrinolytic system arise in the damaged area where the blood is in contact with unusual surfaces and where tissue materials gain entry to the circulation.

This powerful but local effect overwhelms the circulating inhibitors, normally in considerable excess. Where blood flow is halted, active products accumulate, and they favour haemostasis by promoting contraction of blood vessels, plugging by platelets, and formation of fibrin. In moving blood the active factors diminish in concentration as they are carried away from the site of injury and become diluted in the mass of the circulation. Moreover, intermediate substances in the process of coagulation are rapidly cleared into cells of the reticuloendothelial system in the liver and elsewhere.^{1 2}

The capacity of the reticuloendothelial system to clear the active intermediates of coagulation may have great significance

¹ Hudson, F. P., Mordaunt, V. L., and Leahy, I., *Archives of Disease in Childhood*, 1970, **45**, 5.

² Dobson, J., et al., *New England Journal of Medicine*, 1968, **278**, 1142.

³ Department of Health and Social Security, *Screening for Early Detection of Phenylketonuria*. London, H.M.S.O., 1969.

in the aetiology of thrombosis. Experimental evidence casts doubt on the possibility that stasis alone produces massive venous thrombosis, for blood usually remains fluid in vessels with a normal endothelial lining when they are isolated from the general circulation. Conversely, the formation of a thrombus in static blood is observed in the presence of active intermediates of coagulation,³ whether they are produced locally in response to an alteration of the endothelium or at a remote site before they are cleared from the blood.

Laboratory tests for the coagulation intermediates in the blood, and hence of a potentially "hypercoagulable" state,⁴ are imperfect. It has long been suspected that activation may occur in a small part of the circulation and yet produce little evidence of its existence in conventional tests applied to blood collected from an antecubital vein. The studies reported by Dr. John Bonnar and his colleagues in the *B.M.J.* this week at page 564 are important in offering a direct comparison of platelet, coagulation, and fibrinolytic measurements in blood collected simultaneously from the uterine vein and from a peripheral vein during caesarean section. Qualitatively similar but quantitatively much greater changes were found in the blood from the uterine vein. This confirms the interpretation of the remote changes as evidence for the stimulation of coagulation and fibrinolysis locally in the uterus and throws light on the clearance mechanism at work.

The early shortening of the clotting time, kaolincephalin time, and partial thromboplastin time is related to the appearance of increased factor VIII levels in the plasma, perhaps due to the activation of this factor by traces of thrombin.⁵ This is followed by a fall in the concentration of platelets, coagulation, and fibrinolytic factors, as they are consumed more rapidly than they can be replaced. In each case pronounced changes in uterine blood are almost obscured in peripheral blood. Later, a rise is observed in the concentration of those factors which had fallen; the increased utilization could perhaps have stimulated an increased production of the factors.

The study underlines the significance to be attached to raised levels of factor VIII in one-stage assays on peripheral blood as evidence for the existence of the local stimulation of coagulation somewhere in the body.⁶ Evidence is presented to show there is simultaneous activation of coagulation and fibrinolysis within the uterus. Greater concentrations of the fibrin-degradation products of fibrinolysis in the uterine vein than in the arterial circulation have been observed previously at caesarean section.⁷ The two enzyme systems responsible for the presence of fibrin in the body are closely related and appear to be activated by similar stimuli.⁸ The steady accumulation of fibrin degradation products up to 10 to 14 days suggests that the stimulus to coagulation continues for relatively long periods. If active intermediates continue to circulate, they could contribute to the incidence of thrombosis in the puerperium.

These observations do not diminish the importance of

myometrial contraction in the arrest of bleeding after child-birth, but they show there is an additional need for normal platelet function and fibrin formation. Complications of pregnancy which intensify the stimulus to coagulation and fibrinolysis may lead to very low blood levels of platelets and coagulation factors, with an excessive accumulation of the products of fibrinolysis, all tending to cause a failure of haemostasis.⁹ Nevertheless, bleeding is not inevitable unless both uterine contraction and blood coagulation fail together.

Safety of Food Additives

The health hazards that may be associated with the use of substances added to food are constantly reiterated. The latest report of the Food Additives and Contaminants Committee¹ contains decisions and recommendations on the safety of 98 substances which have been used, or proposed for use, as emulsifiers and stabilizers in our food. These substances are intended to maintain a uniform dispersion of two immiscible substances, and some are used in basic articles of diet such as bread, margarine, and chocolate. Others are needed in the preparation of "convenience" foods. These are complex, pre-mixed foods designed to save time for working wives.

The large number of compounds included in the present list is accounted for by the committee's honesty in discarding the seven groups of substances which together with three individual compounds were considered in earlier reports. Instead they rightly identify the individual compounds. They next recommend that specifications for chemical identity and purity be demanded for all substances proposed for addition to our food. To simplify the problems the report proposes that a number of substances be "defined out" because of their close resemblance to food constituents. Proteins and malt extracts are thus excluded, but various starch derivatives get less generous treatment.

Another principle which emerges is that certain staple articles of diet such as bread and potatoes are protected in that some emulsifiers must not be added to them, while milk and flour itself must be kept free of all added emulsifiers. In the ever more affluent society bread and potatoes may soon cease to be staple articles. On the other hand, if the young are to be considered as particularly sensitive targets for potentially injurious substances, then additives to chocolate and sweets should surely require special scrutiny. However, though chocolate may be considered a natural food, it is doubtful whether any proposed additive with the characteristics of theobromine, present in cocoa beans, would ever be accepted as an additive to boiled sweets. The pharmacological characteristics of the natural ingredients of our food are not presumably the concern of a committee on additives and contaminants.

It is easy enough for the reader to be critical of some of the apparently fine distinctions drawn between the biological effects of some of the materials considered in this report. Why should the sucrose esters of fatty acids be rejected while dioctyl sodium sulphosuccinate is accepted? What is perhaps more surprising is the acceptance without comment of carrageen on the basis that it has been used in food and pharmaceutical preparations for many years. Recent experi-

¹ Spaet, T. H., *Thrombosis et Diathesis Haemorrhagica*, 1962, 8, 276.

² Wessler, S., Yin, E. T., Gaston, L. W., and Nicol, I., *Thrombosis et Diathesis Haemorrhagica*, 1967, 18, 12.

³ Wessler, S., Reiner, L., Freiman, D. G., Reimer, S. M., and Lertzman, M., *Circulation*, 1959, 20, 864.

⁴ Duckert, F., and Streuli, F., 1966, *Thrombosis et Diathesis Haemorrhagica*, 1966, Suppl. 21, 185.

⁵ Rapaport, S. I., Schiffman, S., Patch, M. J., and Ames, S. B., *Blood*, 1963, 21, 221.

⁶ Penick, G. D., Roberts, H. R., and Dejanov, I. I., *Federation Proceedings*, 1965, 24, 835.

⁷ Basu, H. K., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1969, 76, 481.

⁸ Ogston, D., Ogston, C. M., Ratnoff, O. D., and Forbes, C. D., *Journal of Clinical Investigation*, 1969, 48, 1786.

⁹ Scott, J. S., *British Medical Bulletin*, 1968, 24, 32.

¹ Ministry of Agriculture, Fisheries and Food, Food Additives and Contaminants Committee, *Report on the Review of the Emulsifiers and Stabilizers in Food Regulations*, 1962. London, H.M.S.O. Office, 1970.

² Marcus, R., and Watt, J., *Lancet*, 1969, 2, 489.