pilot studies in breast screening is acknowledged, but the group suggests that there is need for a limited extension of this service. This should be within a co-ordinated programme of research designed to answer certain fundamental questions about cost effectiveness, risks, and the identification of women most likely to benefit. Screening clinics will need to be backed up by expert diagnostic and biopsy services, so that methods can be standardized and information of importance not lost.

Screening clinics apart, the group emphasizes the reduction in mortality which could come from the development of efficient services for the diagnosis and treatment of breast cancer, particularly if associated with an attempt to encourage women to seek treatment early. In times of fixed resources the cost and effect of all medical services must be considered, and large programmes of screening should not have priority over the establishment of an efficient service for the management of patients with established disease. The recent statement by the Minister of State that joint committees will be set up with the Medical Research Council to plan how these problems might be investigated indicates that the Health Departments are fully aware of the needs.[3]

[1] Fisher, B., *et al.*, *New England Journal of Medicine*, 1975, **292**, 117.
[2] Shapiro, S., Strax, P., and Venet, L., in *Seventh National Cancer Conference Proceedings*, 1973, 663.
[3] Hansard, House of Commons, 28 April, 1975, col. 9.

Neuropharmacological Aspects of Migraine

Our understanding of migraine is hampered by lack of knowledge of its cause and by lack of precision in defining the condition. The pathophysiology of the attack is, perhaps, a simpler problem than that of aetiology and is increasingly agreed to be based on vasoconstriction followed by vasodilatation in cranial blood vessels, but even so the question of definition remains a stumbling block. Where does the simple vascular headache end and the entity migraine begin; and in particular are our pharmacological models of migraine simply those of any vascular headache?

In the past few years there has been no lack of biochemical and pharmacological candidates for a causative role. Any assessment of their claims to explain the condition should be made within the defined context of classical migraine—an aura of focal cerebral signs, commonly visual, leading to hemicrania often with nausea and vomiting—since it is from this that the accepted pathophysiology has been derived. Of the substances proposed as an initiator of the migraine attack serotonin has proved the most enduring. It is a vasoactive amine causing an increase in pulse rate and variable blood pressure changes, and it has vasoconstrictor, antidiuretic, and emetic effects. A number of observations link it with migraine. Increased urinary excretion of its main catabolites is found early in many migraine attacks.[1] A slight rise in plasma serotonin levels has been found at the start of the migraine attack, but more convincingly a marked fall has been noted at the onset of the headache phase.[2] These changes seem specific for migraine and are not found in other equally severe headaches.

Serotonin appears to be released from platelets, its main carrier cells in the blood, and a serotonin-releasing factor has been found in the plasma during a migraine attack.[3] Reserpine, which is known to lower the plasma serotonin concentration, commonly causes an attack in those liable to migraine; while phenelzine, a monoamine oxidase inhibitor, increases endogenous serotonin production and is claimed to reduce the frequency and severity of attacks. Serotonin itself, given intravenously, may also relieve an attack.[4] Methysergide, which remains one of the most effective prophylactics in migraine, may act by competing for certain serotonin receptor sites, thus allowing more to be available at others—and accounting for both the serotonin antagonist and simulating effects noted.

The picture is, however, less simple than at first appears. The potentiation of some adrenaline effects by serotonin, and the possible role of prostaglandins as a release factor, add complexity and widen the range of interpretation. While these observations, and the emetic and antidiuretic properties of serotonin, may seem to make a strong case and perhaps justify the phrase "low serotonin syndrome" for migraine, there are difficulties, cogently argued recently by Sjaastad.[5] Migraine attacks begin with vasoconstriction; serotonin is only a mild vasoconstrictor and the rise in its level at the start of an attack is only slight. Reserpine, besides reducing blood serotonin, also affects noradrenaline and dopamine activity. Methysergide, with large antiserotonin properties nevertheless appears to prevent and in some cases abort migraine attacks. Monoamine oxidase inhibitors are also effective, though there is some evidence that monoamine oxidase activity is already reduced in migraine sufferers. Moreover the serotonin levels are variable within a group of migraine patients in attacks, and in individual cases these may not be correlated with headache. These difficulties can be overcome by calling on the complexities of pharmacokinetics, but the place of serotonin as a main mediator of the migraine attack must still be regarded as sub judice.

[1] Sicuteri, F., Testi, A., and Anselmi, B., *International Archives of Allergy and Applied Immunology*, 1961, **19**, 55.
[2] Curran, D. A., Hinterberger, H., and Lance, J. W., *Brain*, 1965, **88**, 997.
[3] Anthony, M., Hinterberger, H., and Lance, J. W., *Research and Clinical Studies in Headache*, 1968, **2**, 29.
[4] Kimball, R. W., Friedman, A. P., and Vallejo, E., *Neurology*, 1960, **10**, 107.
[5] Sjaastad, O., *Acta Neurologica Scandinavica*, 1975, **51**, 200.

Braille Anniversary

Louis Braille, born in 1809 the son of a village cobbler near Paris, was blinded at the age of 3 years. He received some education in the village school, and at the age of 10 he was admitted to the National Institute for the Young Blind in Paris. Letters used for reading by the blind at this time were those of the ordinary Roman alphabet and made of lead or wood, so that they protruded above the surface.

During the year that Louis Braille enrolled at the institute a French artillery officer, Charles Barbien de la Serre, began to interest the Paris Academy of Sciences in a system of raised dots and dashes which he had invented to enable soldiers to communicate with each other while on night operations. Louis Braille worked on this system and at the age of 16, 150 years ago, produced his system of reading based on six raised dots used in mathematical variation to express letters, punctuation signs, and mathematical signs. The system has been revised to some extent but basically remains the same as when it was introduced. He enlarged the system later to cover musical notation. Braille writers enable blind people to communicate by writing letters. Braille died in 1851 aged 42, and nine years passed before his raised type came into general use.