

can manipulate molecular structures to make new materials with virtually any property or characteristic which we desire. Above all, we can now do this on a scale which only a few years ago would have been regarded as wholly unbelievable." It is in this context that the struggle to minimize the risk of accidental injury must be carried on, and it is notable that the best firms set a standard unsurpassed in any other country.

One of the objectives of the inspectorate has long been to get the bad firms up to the standards of the good ones, for in the long run it is not so much legislation and Government inspectors that make a safe working environment; it is the people who run the factory, manage the mine, or control the chemical reactions. At the same time the workers themselves are on occasions surprisingly careless or nonchalant despite a knowledge of the risks and the means of avoiding them. Safety and production must be a unity. This principle is still too widely neglected, and in introducing his report at a press conference last week the Chief Inspector went so far as to declare that industry must fundamentally change its attitude to industrial hygiene and safety. This is an old theme,² and it is regrettable that its truth has not yet been as generally accepted as it should be.

¹ *Annual Report of H.M. Chief Inspector of Factories 1970*, Cmnd. 4758. London, H.M.S.O., 1971.

² *British Medical Journal*, 1967, 3, 507.

New Studies of Strokes

In 1761 Morgagni¹ described "blood-filled cavities" in the brain and claimed "we must take this as strong evidence that here is the seat and cause of contralateral hemiplegia." Morgagni's collection of clinicopathological correlations made an immense impact on medical thought, and cerebral haemorrhage became synonymous with strokes. When, therefore, Robert Graves described in 1843 a patient who suffered five short attacks of hemiplegia in every respect complete but leaving no trace of paralysis behind, he contended that "the circumstances in this case prevent us from assigning each attack to a separate effusion of blood. My object in making these observations is not to retard but to advance the progress of morbid anatomy by pointing out errors of some generally received opinions."² Four years later Virchow put forward in a paper published in the first volume of his newly founded *Archiv* a new concept of strokes—"ischaemic apoplexy"—of which embolism was the most common cause.³

The next important milestone in our better understanding of strokes was the publication of the now almost forgotten paper by S. P. Hicks and S. Warren 20 years ago.⁴ They had studied 100 brains with apoplectic infarctions in which the lesions were sufficiently large to permit careful study. In 60 brains no "mechanical occlusion" of the cerebral vessels could be detected—that is, all the cerebral vessels were patent. In a somewhat similar but smaller series P. O. Yates and E. C. Hutchinson⁵ found "no significant stenosis or occlusion of intracranial arteries" in 46% of their cases with cerebral infarction. In a recent morbid anatomical study the corresponding figure was 35%.⁶ The explanation of why in a large proportion of fatal cases of cerebral infarction no block can be found in the intracranial arteries was soon provided by the results of carotid angiography, which after the introduction of the percutaneous

technique was performed with increasing frequency. Many unsuspected cases of carotid occlusion were thus disclosed, and the extracranial arteries contributing to the formation of the circle of Willis were subjected to greater scrutiny.

The outcome of this work is that atheromatous stenosis of the extracranial arteries is found to be relatively common in persons over the age of 50. Statistics show that the incidence of atheroma of major cervical vessels increases with age⁷ and that in 11% of bodies over the age of 50 examined at necropsy at least one artery supplying the brain is occluded.⁸ Stenosis of a neck artery is, however, usually symptomless,⁹ and the lumen of the carotid artery has to be reduced by some 80-90% before the rate of flow through the stenosed artery is seriously affected.¹⁰ Atherosclerosis may lead to thrombosis and thus to total occlusion of one or more neck arteries. But so great is the functional efficiency of the circle of Willis that people with even bilateral carotid occlusion as well as remaining free of symptoms may show the normal augmentation of cerebral blood flow by inhalation of carbon dioxide.¹¹ In addition to the integrity of the circle of Willis¹² many factors are concerned in maintaining the constancy of cerebral blood flow despite changes in the perfusion pressure.¹³⁻¹⁵ When one of the arteries contributing to the formation of the circle of Willis is seriously abnormal, transient cerebral ischaemia may result.^{16 17} If an ischaemic attack of that sort exceeds a critical period, cerebral infarction will inevitably result. During cerebral ischaemia the physiological autoregulation mechanisms may become impaired.¹⁸⁻²⁰ In these precarious circumstances a defect of the controlling system may lead to cerebral infarction despite the absence of a block in the intracranial arteries. To account for the patency of these arteries—a fairly common finding—the hypothesis of a disappearing embolus has been invoked.^{6 21}

These considerations indicate that the difference between a transient and a completed stroke may under certain conditions be only marginal, a conclusion which is supported by the study of a large series of transient strokes. Of these cases 62% developed completed strokes at a later date, an event which could not have been predicted on the basis of any one "factor either in the original clinical findings or the subsequent clinical behaviour."²¹ In contrast, thrombosis of extracranial arteries in conjunction with factors favouring either the spread of thrombus or embolism will give rise to cerebral infarction associated with obstruction of intracranial arteries.

In two recent reports including post-mortem data embolism from the heart was found to be a surprisingly frequent cause of internal carotid artery occlusion in association with cerebral infarction. The incidence was 45%⁶ and 22%²² in the two reports respectively. Attention has recently been drawn to the difficulty in differentiating clinically between strokes due to cerebral infarction and those due to localized cerebral haemorrhage.²¹ Seven patients who originally presented themselves with strokes associated with raised blood pressure died later of massive cerebral haemorrhage. Necropsy showed that in each of these cases haemorrhage was the cause of the original stroke. It was concluded that the bleeding probably originated from "miliary aneurysm," first described by J. M. Charcot and C. Boucharde,²³ who considered it to be the principal cause of cerebral haemorrhage. They found these microaneurysms in relation to "petites artères de l'encéphale." Rediscovered on a number of occasions,^{24 25} they are now considered to be a feature of longstanding hypertension. The adverse effect of co-existing hypertension on the prognosis for cerebral vascu-

lar disease has been emphasized,²¹ as also the value of hypotensive therapy in such cases.²⁶

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Drugs for Ceylon

Nearly all the technically advanced countries and many of the undeveloped ones too help their poorer citizens to receive medical aid that would otherwise be beyond their reach. Whether from skill, luck, or indolence, we do not all have the same purchasing power, and different communities have evolved an enormous variety of social devices to mitigate the harshness of poverty and sickness. But where countries instead of individuals are concerned many remain severely handicapped in the world's markets.

An adverse balance of trade has for some years bedevilled Ceylon's capacity to buy abroad some of the goods she needs, and by 1970 a crisis had overcome her foreign exchange. It was in these circumstances that her Government invited Dr. S. A. Wickremasinghe, a general practitioner as well as a member of Ceylon's parliament, and Professor S. Bibile, professor of pharmacology in the medical faculty of Ceylon University, to inquire into the import, manufacture, and distribution of drugs. They were also asked to recommend steps to ensure that drugs are available to people who need them in adequate quantities and at reasonable prices. At page 757 of the *B.M.J.* this week they give a short account of the task and their conclusions. As they rightly point out, the cost of drugs has provoked the authorities even in such a relatively well-off country as Great Britain to look for cheap sources of supply, and here too doctors are accustomed to advice, propaganda, threats, and even retribution with the aim of persuading them to prescribe economically. But Wickremasinghe and Bibile's report takes the matter a stage further. Doctors in Ceylon's State hospitals may now prescribe only from an approved for-

mulary, and a committee meets regularly to amend its contents if necessary. The next step, as the authors see it, is to have the formulary committee deciding on a list of drugs for the whole country, private as well as State practice.

In choosing which drugs to approve and which to reject the committee's evidence "came largely from British publications." The well-conducted clinical trials held in this country together with the critical look often cast on prescribing practices owing to the particular character of our health service make that understandable. Furthermore, Britain too has not always been able to import as much of a drug as she would wish: streptomycin soon after the second world war is a case in point. But whether the complete replacement of phenacetin by paracetamol can be confidently supported by reference to the nephropathy associated with the former drug is perhaps debatable and certainly points to the kind of problem the formulary committee must tackle. Which is the best of several comparable drugs must be difficult to decide when the winner is to be the only one that anyone in the country may receive. Only a desperate economic situation could make such a restriction seem reasonable—but that clearly is the plight of Ceylon.

As well as restrictions on the import of drugs and a ban on the advertising of them Wickremasinghe and Bibile advocate the purchase of cheap drugs made by circumventing the patent law. Here again they can draw on Britain for a precedent, for some hospitals in this country were at one time ordering drugs from foreign sources where they were believed to be manufactured without a licence.¹ The Minister of Health of the day instructed them to stop that practice and tried another, equally questionable, approach to economical purchasing by invoking the Patents Act 1949. This Act enables a Government department or a person authorized by it, to "make, use and exercise any patented invention for the services of the Crown" (with various provisos). The Minister then was Mr. Enoch Powell, and the Ministry issued what was intended to be a reassuring statement to the effect that the Government did not believe its action would prejudice patent protection or research. However, in the end little came of this particular economy measure.

Though Ceylon's need to obtain sufficient drugs at a price she can pay is clear, two obvious dangers attend the course advocated. The first is that some of the drugs supplied will be of inferior quality. This was found to be so in Britain, for the fact remains that a well-known firm's brand name on a product is the best guarantee there is of its purity, efficacy, and potency. Government testing, such as is recommended for Ceylon, is not an adequate substitute. Secondly the drug revolution that has transformed medical practice in the last 20 years and given new life and health to millions of people has been largely the work of industrial firms acting under patent law. If evasion of that law is generally encouraged, the consequences are likely to be harmful to medical advance. Yet the drug companies themselves have responsibilities in the service of mankind such as are not laid on the manufacturers of many other commodities, and the richer countries also have responsibilities to the poorer, which they fulfil to a greater or less extent through foreign aid schemes. What each should never cease to consider is whether their contribution to advancing the health of developing countries is enough.

¹ *British Medical Journal*, 1961, 1, 1521.