

frequently occurs in mitral stenosis. This work is valuable in drawing attention to the influence of respiratory factors on the pulmonary arterial pressure in health and disease, but much has still to be learnt before the story of pulmonary hypertension is complete, and all the factors affecting pulmonary resistance are fully understood.

HAZARDS FROM AGRICULTURAL CHEMICALS

The use of pesticides in agriculture increases at this time of year. In May and June the most dangerous pesticides such as parathion and dinitro orthocresol (D.N.O.C.) are dispersed in the greatest quantities. But on a smaller scale many insecticides, herbicides, fungicides, and rodenticides are applied for a much longer season in food stores, glasshouses, or in the open.

The same pest may be successfully attacked by chemicals ranging in their toxicity to man from the very dangerous to the virtually harmless, though factors other than danger to the user must determine the choice of any particular material in agricultural work. As a result of a co-operative effort by many people, including the manufacturers, distributors, and officials of the Ministry of Agriculture, Great Britain has had in recent years a good record in the safe use of the more dangerous pesticides. Before jumping to the conclusion that the regulations controlling the use of these materials are superfluous, it is as well to consider what happens elsewhere. In Germany W. Reinl¹ has assembled records of 28 cases of poisoning by organo-phosphorus insecticides among agricultural workers in 1950-5. These included 1 fatal, 3 severe, 7 moderate, and 17 mild cases of poisoning. An analysis of the symptoms showed that headache, dizziness, weakness, nausea, and vomiting were most frequently seen. Though contraction of the pupil has often been cited as a characteristic sign of poisoning by organo-phosphorus insecticides, it was noted in less than a third of these cases. There is indeed a recent report² of two patients with severe parathion poisoning who had dilatation of the pupils when first seen, and this led to some hesitation in making a diagnosis. Full atropinization saved these cases, and atropine must be given in large doses to all suspected cases of poisoning by organo-phosphorus insecticides. If a mild case responds well to atropine the patient must be kept under observation for 12-24 hours, because a single dose of atropine may be of only temporary benefit. The chemicals that can reverse the inhibition of cholinesterase caused by these compounds are still being studied,³ but specific recommendations for their use have not yet been made.

There is no specific treatment for D.N.O.C. poisoning. Cases are most likely to occur in hot weather when farm labourers are working long hours with weed-killing sprays on cereals. The chlorinated hydrocarbon group

of insecticides continue to be used with complete safety in agriculture. Endrin poisoned people who ate contaminated flour,⁴ and dieldrin when carelessly used has poisoned public health workers.⁵ Despite dramatic signs of poisoning, such as convulsions, no deaths were reported, and the margin of safety is apparently wide. Fluoroacetamide, a slightly less toxic derivative of fluoroacetate, is now on the market for anyone to buy, but it is sold as a very dilute solution containing acetamide, which is an antidote to the poisonous effects of fluoroacetamide in rats.⁶

Antibiotics, including penicillin and streptomycin, have been used for some years in agriculture as supplements to pig and poultry feeds.⁷ More recently sprays containing streptomycin have been applied to a number of different crops in the United States to control plant diseases due to micro-organisms. It seems to be generally accepted that the hazards of handling these antibiotics as agricultural sprays are negligible, and there have been no reports of ill effects among agricultural workers. But since nurses handling antibiotics may become sensitized to them this might be a risk also run by men handling concentrated sprays for crops. Whether or not resistant strains of bacteria can develop in persons coming into only casual contact with antibiotics remains to be seen. If preparations containing antibiotics of the type used in clinical medicine are introduced into agricultural practice in Britain, bacteriologists might look for evidence of any harmful developments.

The doctor with agricultural workers among his patients would do well to ask about possible exposure to toxic chemicals when cases of vague illness are reported to him. It may be helpful to ask to see the pesticide container, for the labels of all reputable brands contain much useful information on the properties of their contents. These pesticide containers are an obvious hazard if left within the reach of children who cannot read the labels.

HYPERGLOBULINAEMIA

Many pathological states are associated with increased levels of serum globulin, and clinicians have long used the erythrocyte sedimentation rate, which is in part dependent upon the globulin level, as an index of organic disease. Certain disorders, such as multiple myeloma, sarcoidosis, kala-azar, and some collagen diseases, may be associated with striking hyperglobulinaemia, but the question remains, How informative is precise measurement of the degree of hyperglobulinaemia as an aid to diagnosis? Using the salting-out technique of C. Cohn and W. Q. Wolfson,¹ which gives results in close agreement with the electrophoretic pattern,² A. R. Feinstein and R. G. Petersdorf³ have correlated in 394 patients the clinical diagnoses with the degree of hyperglobulinaemia. They found that when hyperglobulinaemia exceeded 5 g per 100 ml. nearly half the patients were suffering from one of the diseases known to be associated with a raised level of serum globulin, and that the chances of the patient

¹ Reinl, W., *Arch. f. Toxikol.*, 1956, 16, 158.

² Dixon, E. M., *J. Amer. med. Ass.*, 1957, 163, 444.

³ Askew, B. M., *Brit. J. Pharmacol.*, 1956, 11, 417.

⁴ Davies, G. M., and Lewis, I., *British Medical Journal*, 1956, 2, 393.

⁵ Blázquez, J., and Biachini, C., *Gac. med. Caracas*, 1956, 63, 1.

⁶ Phillips, M. A., and Worden, A. N., *Lancet*, 1956, 2, 731.

⁷ *British Medical Journal*, 1953, 2, 417.

¹ Cohn, C., and Wolfson, W. Q., *J. Lab. clin. Med.*, 1948, 33, 367.

² Jager, B. V., Schwartz, T. B., Smith, E. L., Nickerson, M., and Brown, D. M., *ibid.*, 1950, 35, 76.

³ Feinstein, A. R., and Petersdorf, R. G., *Ann. intern. Med.*, 1956, 44, 899.

having multiple myeloma, sarcoidosis, or a collagen disease were almost 1 in 2. A moderate degree of hyperglobulinaemia with the level of serum globulin ranging from 4.2 to 5 g. per 100 ml. was attributable to these conditions in only about 1 patient in 10, whereas a third of the patients had liver or neoplastic diseases, and the remainder usually had acute or chronic infections. Lesser degrees of hyperglobulinaemia (3.9 to 4.2 g. per 100 ml.) were found in a wide variety of conditions. Fewer than 1 in 10 had multiple myeloma, sarcoidosis, or a collagen disease, and though all had organic disease more than half had conditions not specifically associated with hyperglobulinaemia. From these findings it can be deduced that, when the diagnosis is not clinically obvious, hyperglobulinaemia exceeding 5 g. per 100 ml. should direct investigations towards confirming the presence or absence of myeloma, sarcoidosis, or one of the collagen diseases. Hyperglobulinaemia of 4.2 to 5 g. per 100 ml. will suggest cancer, liver disease, or infections. Lesser degrees of hyperglobulinaemia give little clue to the best lines of further investigation, and serve only to indicate the existence of organic disease.

POST-MATURITY

It is perplexing to all who practise midwifery that, whereas to some doctors post-maturity poses a difficult and not uncommon problem, others dismiss prolongation of pregnancy as of little or no clinical importance. This division of opinion is reflected in the figures collected by Professor F. J. Browne from 20 hospitals over the last decade, figures which he discusses in an article at p. 851 in this issue. For example, in one hospital in which the total deliveries for 1954 were 1,027, 31 women were induced for uncomplicated post-maturity, while in another hospital there were no such inductions among 4,949 deliveries in 1949-50. The difference was apparently not due to resort to elective caesarean section for post-maturity in the second hospital, for its section rate was less than half that in the first. Indeed, the suspicion arises that the more inductions performed the higher the section rate may be, for 6.2% of all the women induced for simple post-maturity were eventually delivered abdominally.

It seems reasonable to regard the perinatal mortality as a good yardstick by which to measure any adverse effects of prolonged pregnancy, but again opposite conclusions can be drawn from different published reports. In one hospital in Professor Browne's series in which there were no inductions for post-maturity the perinatal mortality was low and there were no stillbirths in pregnancies prolonged beyond 40 weeks; while in the hospital where the induction rate was 3% the total foetal loss was relatively high. Discrepancies might arise partly because conditions in different hospitals are never exactly the same; the logical approach, therefore, would be to compare the results of intervention and non-intervention in a single hospital. This was in fact done

by D. Racker and his colleagues,¹ and their figures showed a lower foetal mortality in the group induced soon after term than in the group allowed to await the spontaneous onset of labour. After discussing the many variables concerned, physiological and clinical, Professor Browne offers certain conclusions. He suggests that many cases of so-called post-maturity are really examples of slow maturation of the foetus and placenta, and that to induce labour in these cases may do nothing to improve the perinatal mortality rate. Others may be due to the occurrence of conception in a very long menstrual cycle; but even when the date of isolated insemination is accurately known the conception-to-delivery interval varies widely—from 235 to 298 days according to E. J. Farris.² Finally, Professor Browne believes that the higher foetal mortality in post-mature babies compared with those born at term can be adequately explained by the larger size of the infants and by the longer average duration of labour in the former group.

The debate continues. And in post-maturity, as in most problems in medicine, the opinion and practice of the individual doctor is likely to be coloured by his personal experiences, and in particular to be influenced by an otherwise unexplained stillbirth or neonatal death, even though such occur also at or before term. For the present, perhaps, an old rule of thumb provides as good a guide to maturity as any: if the cervical canal is taken up and the external os is not closed, the patient is near, at, or after term.

TREATMENT OF PARKINSONISM

The syndrome of Parkinsonism is a challenging problem to the physician. Treatment of this distressing condition began on an empirical basis, and there it still remains. The only real progress has been an increase in the number of drugs available. Solanaceous alkaloids were first given for Parkinsonism so long ago as 1882, but they have never been thoroughly satisfactory because, though they may control the symptoms, their effect is transient, and attempts to extend it by increasing the dose cause severe side effects to appear. The action of many drugs may be prolonged by prescribing them on a form which lengthens the period of absorption from the intestine by several hours, and solanaceous alkaloids have been specially prepared in this way for an investigation into the treatment of Parkinsonism.¹ The preliminary report suggests that this classic treatment may return to favour in modern form.

It has been found that synthetic compounds with anti-acetylcholine and antihistamine activity can favourably influence the Parkinson syndrome. One of the first to be tried was diphenhydramine hydrochloride ("benadryl"). Slight modifications of structure have produced

¹ Gillhespy, R. O., and Ratcliffe, A. H., *Bgham med. Rev.*, 1956, **19**, 115.

² ——— *British Medical Journal*, 1955, **2**, 352.

³ Palmer, H., and Gallagher, D. J. A., *ibid.*, 1950, **2**, 558.

⁴ Bovet, D., and Longo, V. G., *J. Pharmacol.*, 1951, **102**, 22.

⁵ Doshay, L. J., and Constable, K., *Neurology*, 1951, **1**, 68.

⁶ Efron, A. S., and Schultz, W. M., *Amer. J. med. Sci.*, 1951, **221**, 561.

⁷ Porteous, H. B., and Ross, D. N., *British Medical Journal*, 1956, **2**, 138.

⁸ Dunham, W. F., and Edwards, C. H., *Lancet*, 1948, **2**, 724.

⁹ Montuschi, E., Phillips, J., Prescott, F., and Green, A. F., *ibid.*, 1952, **1**, 583.

¹⁰ Doshay, L. J., *J. Amer. med. Ass.*, 1956, **162**, 1031.

¹ Racker, D., *et al.*, *Lancet*, 1953, **2**, 953.

² Farris, E. J., *Human Ovulation and Fertility*, 1956, London, p. 119.

more powerful analogues, the most active of which has the formula β -dimethylaminoethyl-2-methylbenzhydryl hydrochloride ("disipal"). In the clinic where this compound was investigated disipal is regarded as the best drug with which to begin treatment of new patients.² Ethopropazine hydrochloride ("lysivane") has also been shown to produce beneficial results when given by itself.³ Benzhexol hydrochloride ("artane") is more popular in the U.S.A. than in Britain.⁴⁻⁶ Although it has useful therapeutic properties it has been reported to cause severe mental disturbance.⁷ The activity of caramiphen hydrochloride ("parpanit") has been assessed as equivalent to that of the solanaceous alkaloids,⁸ but some clinicians have found it to be one of the least effective of the drugs commonly prescribed. Phenindamine tartrate ("thephorin") has been said to be the most potent of the antihistamine compounds given for Parkinsonism.¹ Another drug for which good results have been claimed is procyclidine hydrochloride ("kemadrin"),⁹ but it has not achieved any great popularity. A recent addition to the range of drugs has been reported from America. It is a synthetic compound named "cogentin," and has the tropine part of atropine united with the benzhydryl part of diphenhydramine. It is said¹⁰ to have a "prolonged potent anticholinergic, antihistaminic action" and was administered to 302 patients with various forms of Parkinsonism. Of those who began treatment four years ago 57% have experienced benefit with few side effects.

The aetiology of Parkinsonism is still obscure, and any classification provides little more than a convenient nomenclature. Similar presenting symptoms may have different causes requiring different treatment, and it is unlikely that maximal improvement will be obtained through the use of any drug by itself. There is no easy road to success; the only way is to persevere with various combinations of drugs until one is found which gives the individual patient the greatest relief. Frustrating as this approach may appear at times to be, there can be few experiences more rewarding to the physician than to see a patient who was helpless from severe Parkinsonism restored to normal activity.

THE NEW ESTIMATES

Total expenditure on the Health Service in Great Britain is approaching £690m. That figure takes into account payments from all sources, rates as well as taxes, patients' charges as well as the contribution from the national insurance fund. A similar gross figure for 1949-50, the first complete year of the Service, was £450m. But as the Minister of Health explained in the House of Commons recently, this increase of 53% is largely due to the rise in prices, of goods and services, in the intervening period. If prices had remained constant, expenditure on the Health Service would have gone up by only 15% in the last seven years. In other words, the real resources used by the Service have increased by 15%; but, as the country's total resources have expanded even more, the proportion taken by the Service has actually dropped slightly.

It is nevertheless the huge gross total of the Service that has prompted the Government to place more of the cost on to national insurance contributions instead of on to the taxpayer or the patient. At present, the share of the contributions from employer and employees that is credited to the Service is £40m., or approximately one-seventeenth of its cost. In 1949-50 the £40m. represented one-eleventh of the cost, and when the Service was being planned it was estimated that one-fifth of the cost should be met by insurance contributions. As the alternatives for meeting the higher cost are increasing the already onerous burden on the taxpayer and raising charges to patients, the Government has proposed instead to double the amount that will come from the national insurance fund. At £80m. this would meet between an eighth and a ninth of the gross total.

Even so, the amount to be met by the taxpayer would be £510m. A year ago, the taxpayer's bill was estimated at £502m., but supplementary estimates in February raised it to £529m. If, therefore, the proposal to increase the insurance contribution goes through, the taxpayer will be saved nearly £20m. in this financial year. Nearly £1m. of this saving will go to meet the 10% increase in the salaries of junior hospital staffs that came into force on April 1.

Within the Service the estimates¹ are remarkable for the comparative stability shown by the individual items—with the one exception of the hospitals. In fact, the pharmaceutical service actually shows a small fall, from £59.4m. to £57.6m., in its net cost. But this reduction has been achieved only by the expedient of charging patients a shilling for each item on the prescription instead of for each form. This has increased patients' payments for drugs from £8.8m. to £13.4m., and had it not been for this increase the pharmaceutical service would have cost nearly £3m. more.

The rise of nearly £3m. in the dental service can be explained by a bigger demand for treatment. But the increase in the cost of the executive council services as a whole—just over £3m.—is completely dwarfed by the rise in the cost of the hospitals. Some of this, £5.6m., is on capital account and represents the carrying out of the hospitals' building programme. But a sum twice as big is needed for the estimated extra cost of maintaining the hospitals in the new financial year compared with the year just ended. The additional £11m. will bring the total advances to hospital boards for hospital maintenance to £371.5m., or about 54% of the total gross cost, compared with 45% in 1949-50. Presumably this growth in the hospitals' share of Health Service resources is largely inevitable. But it is worth emphasizing, as we have done before, what a large proportion of the hospitals' costs is accounted for by the salaries and wages of staffs other than doctors and nurses. Doctors' salaries are estimated at £39m. in 1957-8 and nurses' at £90m. But all other salaries and wages, excluding the central administrative expenditure of management committees and boards, amount to £108m.