The presence of a pancreatic tumour should be suspected in patients with atypical ulceration or repeated perforations of the stomach and in those who fail to respond to accepted medical and surgical measures, especially if there is a history of diarrhoea. As to treatment, Zollinger advocates total gastrectomy as well as removal of the tumour on the grounds that nearly two-thirds of the patients whose cases have been reported in the literature had a recurrence of symptoms after either local removal of the tumour or radical gastrectomy and partial pancreatectomy. He postulates a vicious circle of islet hyperplasia leading to hyperchlorhydria, production of secretin in the duodenum and further pancreatic stimulation, which can only be broken by removing all acid-secreting cells. Many of the earlier patients, however, had already been subjected to repeated operations before the presence of a tumour was recognized, and there is no doubt that local treatment alone may be strikingly successful.[6] Careful follow up is essential, for a return of symptoms is likely to be due to metastases.

The hope that this unusual syndrome might provide an insight into the problem of peptic ulceration has not yet been fulfilled. Many questions remain unanswered. Islet cells as well as acinar tissue are concerned in the control of gastric and duodenal secretion, and there may be some form of balance between the two. The effect of insulin and glucagon has been widely studied, but no substance having the properties of the tumour extracts has yet been isolated from normal islets. Is it possible that the tumours arise not from islet cells but from ectopic tissue? Further experiments are needed to define the exact role of the damaged pancreas in inducing ulceration, and tests of acid secretion in patients with pancreatic disease would be helpful. It would also be interesting to know whether partial pancreatectomy would relieve recurrent ulceration in patients who do not conform to the Zollinger–Ellison syndrome.

INHERITANCE OF ENZYMES

The paper by Dr. H. Lehmann and his colleagues on suxamethonium sensitivity at page 1116 of the *Journal* this week introduces us to a remarkable genetic situation with the minimum of technicalities and the maximum of emphasis on what we can understand—namely, patients and their families. Occasionally patients are found who cannot inactivate the drug suxamethonium, and this defect is genetically controlled. These patients have an abnormal pseudocholinesterase in the plasma—not simply less of the normal enzyme. A second type of abnormal enzyme has also been detected,[1] and then very rarely it has been shown that the enzyme can be absent altogether. The net result is the same—patients with a double dose of one or other of the abnormal genes are liable to prolonged periods of apnoea when given suxamethonium as a muscle relaxant. (The apnoea is readily reversible by administering plasma from a normal subject, since the enzyme is stable.)

The normal and the two abnormal enzymes can be inhibited by certain antagonists of pseudocholinesterase —namely, dibucaine and sodium fluoride, the former being the stronger inhibitor. Usually the inhibition percentages in the two tests are in concord, but sometimes anomalies occur, and it is these which led to the discovery of the second abnormal gene. The same inhibitors can also be used to identify most of the heterozygotes, but it seems likely that all those who possess the normal gene together with any of the abnormal genes show no signs of sensitivity. However, with the discovery of the second abnormal gene it was clear that there must be individuals heterozygous for this and the first abnormal one, and also people homozygous for the second. It is precisely these (three of the former and one of the latter) who are now described for the first time. Not unexpectedly, the new heterozygotes show a moderate degree of undue sensitivity to suxamethonium and the same is true of the new homozygote. Investigation of the first-degree relatives of the index cases shows that their sensitivities are consistent with the hypothesis that three pseudocholinesterase genes are distinguishable in these families. A survey of the sibships will be of interest, particularly any children that may be born to patient number 2. Whoever she marries, she will not be able to produce homozygous normal children if the genes are allelic (i.e., alternative to each other at the same locus of the chromosome). The data of Lehmann and his colleagues are consistent with allelism but do not prove it.

As the authors point out, the pseudocholinesterases resemble the haemoglobins in certain respects. Patients heterozygous for sickling and another abnormal haemoglobin (such as haemoglobin C) are anaemic, whereas the heterozygotes for sickling and normal haemoglobin are unaffected. They suggest that we may in fact be discovering a general pattern in the inheritance of abnormal proteins and in the pathological states which result.

Considerably more remains to be done. First, there are probably still other pseudocholinesterase genes to be discovered, and family studies should always be carried out when a sensitive individual is found. Secondly, the frequencies of the genes in the population are so far known only for the homozygote and for the heterozygote for the first abnormal gene discovered. The rest have still to be determined, and one heterozygote (that between the "silent" and the second abnormal gene) has yet to be observed. Thirdly, only analysis of suitable families will show whether the genes are in fact allelic (though there is no contradictory evidence in these particular pedigrees). Fourthly, the possibility that disease (or treatment) may influence the pseudocholinesterase level needs further consideration. Lehmann and his co-workers[1] have pointed out that liver disease, malnutrition, and anaemia can all produce

[1] Lehmann, H. and Liddell, J., The Cholinesterases, Chapter 8 in *Modern Trends in Anaesthesia*, 2nd ed., Evans, F. T., and Gray, T. C., 1961. London.

low levels of enzyme. The present paper reports that apnoea had not occurred in patient number 3 when he was given the standard dose of suxamethonium for an operation in 1959: but a pre-operative transfusion (of which there is no mention) might have accounted for this. Clearly the field is still wide open for research-minded anaesthetists who have liaison with a good chemical pathologist.

OCULOPHARYNGEAL MUSCULAR DYSTROPHY

In 1915, E. W. Taylor[1] reported an unusual familial form of dysphagia associated with bilateral ptosis. The symptoms in the cases he described were slowly progressive, leading in the end to death from starvation, and he attributed the condition to a degenerative process involving the cells of the vagus, glossopharyngeal, and oculomotor nuclei, though he had no pathological proof of this assertion. J. Hutchinson,[2] in 1879, described a form of progressive paralysis of external ocular muscles which he called external ophthalmoplegia, and in 1890 E. Fuchs[3] described five similar cases, in two of which the abnormality was familial. Despite the fact that Fuchs examined sections of the levator muscles in one of his cases, which led him to conclude that the weakness of the ocular muscles was probably myopathic, similar cases occurring subsequently were generally referred to as examples of progressive nuclear ophthalmoplegia, and a degeneration of cranial nerve nuclei was postulated. It was not until L. G. Kiloh and S. Nevin[4] wrote their comprehensive review of the subject of ocular myopathy in 1951 that it was generally accepted that the syndrome of progressive external ophthalmoplegia was, in fact, due to a muscular dystrophy of the external ocular muscles.

In a recent report, M. Victor, R. Hayes, and R. D. Adams[5] have described three cases of a progressive disorder characterized by the association of severe bilateral ptosis with dysphagia. One of the cases was sporadic, but the other two were members of a family in which the disease had been transmitted through three generations. The pattern of inheritance suggested the action of an autosomal dominant gene. Examination of muscle sections obtained by biopsy in two of the three cases confirmed that the muscular weakness was myopathic. In two of the patients there was some associated weakness of the orbicularis oculi, but in none of them, despite the presence of severe drooping of the eyelids, was there any obvious restriction of external ocular movement. Dysphagia was sufficiently severe in one of the patients to necessitate tube feeding, but in the other two it was comparatively mild. The authors point out that their cases resemble closely that described by Taylor[1] in 1915, and that they show certain affinities with the progressive dystrophy of the external ocular muscles as classified by Kiloh and Nevin.[4] They consider, however, that this syndrome deserves nosological identification as a separate variety of restricted cranial myopathy. It is, however, doubtful whether this conclusion can be justified, since dysphagia is a common accompaniment of classical ocular myopathy.[6] It would seem to be more satisfactory to regard this condition as being a variant of ocular myopathy rather than to accept it as a distinctive clinical entity. But it is important to bear it in mind in patients over middle age suffering from progressive ptosis and dysphagia, when these symptoms are not improved by injections of edrophonium or neostigmine.

[1] Taylor, E. W., *J. nerv. ment. Dis.*, 1915, **42**, 129.
[2] Hutchinson, J., *Med.-chir. Trans.*, 1879, **62**, 307.
[3] Fuchs, E., *Arch. Ophthal.*, 1890, **36**, 234.
[4] Kiloh, L. G., and Nevin, S., *Brain*, 1951, **74**, 115.
[5] Victor, M., Hayes, R., and Adams, R. D., *New Engl. J. Med.*, 1962, **267**, 1267.
[6] Walton, J. N., *Ann. Phys. Med.*, 1961, **6**, 116.

STOP SMOKING!

When Lord Newton, Joint Parliamentary Secretary to the Ministry of Health, came to B.M.A. House on Monday to open an exhibition of anti-smoking posters organized by the Central Council for Health Education and by the B.M.A.'s magazine *Family Doctor*, he said that 26,000 people in 1962 had died from lung cancer, 1,000 more than in 1961. "We know why the figure is so high and how it can be brought down," he stated. It could be brought down by persuading people not to smoke cigarettes, but what are the best methods of persuasion? Some, particularly doctors, may be impressed by the evidence. Lord Newton mentioned that more tobacco per head of population is used in Jersey than anywhere else in the world and it also has the highest lung-cancer death-rate for males in the world, and an exceptionally high rate for women, perhaps exceeded only in Mexico. The air of Jersey is free from pollution; and no case of lung cancer was recorded in a non-smoker in Jersey during the period covered by the Annual Report for 1960 of the Chief Medical Officer of the Ministry of Health. "Every human ostrich," said Lord Newton, "should put that in his pipe and smoke it before burying his head in the sand."

Lord Newton also offered some advice to those wishing to stop smoking. He himself stopped because it suddenly dawned on him that smoking was a ridiculous waste of money. He gave a tip which others have found useful. Stop smoking during an illness and don't start again: after even a bad cold cigarettes do not taste good, and one has to persevere before one starts to enjoy them again.

There has been argument for years about the value of posters as a means to improve health or prevent disease. They are probably more effective than lectures, and the best posters may have a lasting effect. Many of the posters at the exhibition in B.M.A. House played upon fear, but the poster winning the first prize (see p. 1173) by Mr. B. Bartholomew was more subtle in suggesting that in some circles at any event those who smoke are not with it.