Many cases, however, are the children of parents similarly affected, and here, knowing the risk, the clinician has scope for early prophylactic treatment. For example, in the largest series of families reported with familial intestinal polyposis, that of C. E. Dukes[2] from St. Mark's Hospital, in 13 of 33 families the mutant gene had affected three or more generations of a family. Similarly, 10 of 23 families reported from the State of Michigan[3] affected three or more generations. In one of the families whose members had intestinal polyposis with epidermoid cysts, fibromata, and osteomata, 15 individuals in four generations were affected.[4]

Prophylactic surgery is not needed in Peutz's syndrome, in which the risk of carcinoma is not high.[5-7] But when the polyps are confined to the colon and rectum, as is the case with both forms of familial intestinal polyposis, total colectomy soon after the polyps are recognized is the correct treatment. This anticipates the development of cancer. The only point at issue is whether all the rectum should be removed and the patient left with an ileostomy, or whether the lower rectum should be kept and the ileum anastomosed to the stump of the rectum, after any polyps in the latter have been removed.[8-11] There are obvious advantages in the latter procedure, if the number of rectal polyps does not make it impracticable; but there is the risk of malignant change developing in the rectal stump, and so this treatment should not be given where it is not possible to continue to keep the patient under supervision for the rest of his life.

While polyposis may develop as early as the age of 2, carcinoma is very seldom recorded before the teens (only one patient in 91 dying from cancer of the colon before the age of 10 in the St. Mark's Hospital and Michigan series combined[3]), and so it is reasonable to start the routine examination of the children of affected individuals at about the age of 10. This should be repeated about every two or three years, and the majority of those who have inherited the gene will have developed polyposis by the age of 20. These examinations should, Dukes considers, be continued at about five-yearly intervals at least until the age of 40,[11] by which age it is probable, but not certain, that those still without polyps have not inherited the gene. As a piece of practical eugenics, those affected should be told as young adults of the risk to their children, so that they may decide for themselves whether to have children or not.

It would obviously be helpful if there were some way by which the children who have or have not inherited the gene could be distinguished before the development of polyposis. In the families in which neoplasia of skin and connective tissue occur, these will serve as useful pointers, since the tumours are usually present from early childhood. In the uncomplicated cases of familial intestinal polyposis, it would be useful to have a marker gene on the same chromosome as, and close to, the mutant gene responsible for the condition. In one large family from New Zealand, in which probably no fewer than six generations are involved, a preliminary report indicates a linkage with the genes determining the MN blood types.[12] If this is confirmed it will be fortunate, since by testing for the Ss antigens as well, four varieties of the chromosome may be recognized, of which only NS is uncommon, and in many instances it will be possible to recognize soon after birth those patients who have inherited the gene for intestinal polyposis by determining the MNSs blood type.

RHEUMATOID NEUROPATHY

Though the aetiology of rheumatoid arthritis remains stubbornly hidden from us at the present time, nevertheless the increasing amount of attention being paid to this disease is producing valuable information which can often have immediate and practical clinical application. In 1957 F. Dudley Hart, J. R. Golding, and D. H. Mackenzie[1] reported a study of 10 patients with rheumatoid arthritis who had developed a peripheral neuritis, and a year later R. M. Mason and V. L. Steinberg[2] described a further six cases of a similar nature. While a number of studies had been done on the histology of peripheral nerves and small blood vessels in rheumatoid arthritis during previous years, clinical reports describing peripheral neuritis were almost entirely lacking before this apart from two accounts in the last century.[3,4] Since 1957 some 38 further cases have been reported in the European and American literature, and on pages 1594 and 1600 of the *Journal* this week Drs. Dudley Hart and Golding add to these a further 42 cases, and Dr. Steinberg another 18—a total of 60 additional cases. As a result, the clinical features of this syndrome seem to be clearly established.

The syndrome is seen in men with rheumatoid arthritis at least as frequently as in women. Patients usually have active severe disease associated with nodules, often with arteritic changes in the hands or feet, and a strongly positive test for the rheumatoid serum factor. Usually, but not invariably, these patients will be on corticosteroid therapy, probably in high dosage, and this may recently have been altered for one reason or another, or abruptly discontinued. Sensory symptoms predominate with numbness, paraesthesiae, or hyperaesthesiae, affecting the feet rather than the hands; all types of sensation are lost, often with the

[1] Hart, F. D., Golding, J. R., and Mackenzie, D. H., *Ann. rheum. Dis.*, 1957, **16**, 471.
[2] Mason, R. M., and Steinberg, V. L., *Ann. phys. Med.*, 1958, **4**, 265.
[3] Pitres, A., and Vaillard, L., *Rev. Médecine*, 1887, **7**, 456.
[4] Bannatyne, G. A., *Rheumatoid Arthritis*, 2nd ed., 1898. Wright, Bristol.
[5] Pepys, S., *Diary*, 1662 (August 31).

exception of position sense. The loss is of stocking or glove distribution, tending to be symmetrical but occasionally occurring as a mono-neuritis in the lateral popliteal or ulnar regions. Occasionally a median neuritis may suggest a carpal tunnel syndrome. Later motor weakness—usually foot drop—may follow in severe cases, but even with this development tendon reflexes may be retained. The prognosis is bad. Of Hart's 25 personal cases four died (16%), and five of Steinberg's series of 18 (28%) were dead within one year. The cause of death varies, but cardiac failure, especially from coronary thrombosis, predominates. The clinical course in the survivors is very variable and unpredictable, though motor weakness is a bad sign and there is so far no suggestion that any treatment influences it favourably. The best advice at present is that if the patient is on corticosteroid therapy the dose should be kept constant and the temptation to alter the dose (upwards or downwards) in an effort to "do something" should be resisted, except perhaps when the patient is obviously suffering from severe hypercortisonism; even then changes in dose should be very gradual and cautious.

Necropsy studies have usually revealed evidence of a generalized arteritis with damage to the vasa nervorum, and it is tempting to accept the view that it is this which accounts for the neuropathy. But this is not an invariable finding, and comparison with polyarteritis nodosa, in which an arteritis is the cause of peripheral neuritis, does reveal certain differences to which Hart and Golding refer. Notable among them is asymmetrical damage to motor nerves in polyarteritis nodosa, which contrasts with the symmetrical damage to sensory nerves in rheumatoid neuropathy. And, as they also point out, it was at one time readily accepted that the neuritis of diabetes mellitus was vascular in origin also—a view which is no longer tenable, though no alternative explanation has been found.

Clearly one important question arises: Is the apparent increase in the frequency of peripheral neuropathy in rheumatoid arthritis a real increase, and, if so, is it related to more frequent treatment with corticosteroids? Both series reported here contained examples of patients who had never been given these substances, so this is probably a feature of the disease itself. It may well be that many cases have been missed in the past—the symptoms of neuritis being misinterpreted as being due to the arthritis itself. This should no longer occur if this possibility is borne in mind, and if the other possible causes of these symptoms can be reasonably excluded—such as diabetes, subacute combined degeneration of the cord, chronic alcoholism, avitaminosis, malignant disease, amyloidosis, and pressure on nerve roots from various causes.

It seems likely, however, that excessive dosage, change of dose, or abrupt withdrawal of corticosteroids may precipitate or at least exacerbate the process, and this provides yet another reason for insisting that all alterations of dose of these substances should be under strict supervision. In severe cases with multiple rheumatoid nodules and a strongly positive test for the rheumatoid serum factor the risk that corticosteroid therapy may produce this complication must be weighed in the balance before a decision to begin it is made. In all such cases a full trial should be given to drugs not likely to be associated with neuropathy—aspirin, phenylbutazone, or gold, for example—before running the risk of being faced by the very distressing picture of an arthritic Mrs. Bennett so aptly quoted by Drs. Hart and Golding from *Pride and Prejudice*, and of having to reply like Samuel Pepys, "God preserve us! For all these things bode very ill."[5]

INCIDENCE OF PEPTIC ULCERS IN BRITAIN

One of the few established facts relating to the aetiology of gastric and duodenal ulcers is that the incidence varies in different communities and at different times. It is therefore reasonable to believe that environmental factors are important in their production and that a close study of the conditions under which the diseases become more or less frequent might give a clue to their cause. Many investigators have followed this path; but their conclusions have often been disputable, because their diagnostic criteria have not been sufficiently uniform.

One way of overcoming this difficulty has been to study the incidence of acute perforated ulcers. This has the advantage that in areas where the medical services are adequately developed every case will come to medical attention and the diagnosis will be established with certainty—whatever the method of treatment. Moreover, affected patients will not travel far for treatment, and it may be relatively easy to collect all the cases occurring in a particular population by studying a small number of institutions. With this technique B. Bager[1] in Sweden and C. F. W. Illingworth and colleagues[2] in Glasgow established that there had been an increase in the incidence of perforations and that this increase had exclusively affected duodenal ulcers. The technique, however, has the disadvantage that a difference in the incidence of perforations may reflect a difference in the liability of an ulcer to perforate rather than a difference in the incidence of the underlying conditions.

Examination of necropsy material eliminates this difficulty. But, unless a high proportion of deaths occur in hospital and a high proportion of subjects come to necropsy, it is hardly possible to know whether the results obtained are representative of the population at large. The best necropsy index is, probably, the incidence of ulcers in patients dying of other conditions—that is, all subjects being excluded in whom the ulcer was the cause of death. Using this index, G. Watkinson[3] showed that duodenal ulcers were found more often in the North of England than in the South, whereas the incidence of gastric ulcers was practically the same in both areas. Watkinson[4] also showed that

[1] Bager, B., *Acta chir. scand.*, 1929, **64**, suppl. 11.
[2] Illingworth, C. F. W., Scott, L. D. W., and Jamieson, R. A., *Brit. med. J.*, 1944, **2**, 617 and 655.
[3] Watkinson, G., *Schweiz. Z. allg. Path.*, 1958, **21**, 405.
[4] ——, *Gut*, 1960, **1**, 14.
[5] Pulvertaft, C. N., *Brit. J. prev. soc. Med.*, 1959, **13**, 131.
[6] Registrar General, 1958, *Decennial Supplement England and Wales, 1951, Occupational Mortality*, Part II, London.
[7] Doll, R., Jones, F. A., and Buckatzsch, M. M., 1951, *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, No. 276, H.M.S.O., London.

the incidence of duodenal ulcers found by a department where there was a specialized interest in the stomach and duodenum was higher than elsewhere; so it is evident that necropsy data are, in this respect, subject to a substantial observer error.

No one method of estimating the ulcer incidence can provide a satisfactory estimate free from all objections; firm conclusions can be reached only by concerting the results of different studies carried out by different methods. C. N. Pulvertaft's study[5] of the incidence of peptic ulcer in York and the surrounding countryside is therefore of particular interest, as his data are derived from clinical diagnoses. The populations of York and of a rural area on three sides of the city are served exclusively by the local city and county hospitals, and nearly every fresh ulcer is diagnosed at one or other hospital. Cases first diagnosed elsewhere—for example, on holiday abroad—would also be recorded through the co-operation of local consultants and general practitioners, and it seems likely that Pulvertaft's figures provide a good estimate of the frequency with which fresh ulcers are diagnosed. A positive diagnosis was made only if the ulcer was seen at laparotomy or gastroscopy, was demonstrated radiologically, or, if it had been suspected previously, was found at necropsy; ulcers found incidentally at necropsy were excluded. The estimates are therefore conservative and comparisons with other clinical series may be misleading. But comparisons can be made confidently between subgroups of the population studied.

Altogether during the years 1952–7 the annual incidence of duodenal ulcers among persons aged 15 years and over was 2.15 per 1,000 men and 0.62 per 1,000 women; the corresponding figures for gastric ulcers were 0.53 and 0.31 per 1,000. The general pattern of distribution of ulcers by sex and site is similar to that reported in other clinical series. Pulvertaft's data also provide confirmation for the belief that the incidence of both gastric and duodenal ulcers is higher in urban conditions than in rural. Among women the urban excess was small (duodenal ulcers 1.2 : 1 and gastric ulcers 1.5 : 1). Among men it was larger (duodenal ulcers 1.7 : 1 and gastric ulcers 2.3 : 1), and it is notable that the ratio for all duodenal ulcers was identical with that for perforated duodenal ulcers alone. It is therefore unreasonable to suppose that the higher urban incidence was artificial and due to the greater ease of access to hospital in towns. The data also agree with those obtained in the Registrar General's occupational mortality study[6] and in the survey reported by R. Doll and colleagues[7] in the south of England in showing that gastric ulcer is predominantly a disease of the semi-skilled and unskilled labourer. Duodenal ulcer is more evenly distributed among the social classes, but it was also somewhat commoner in the lower economic groups —an observation which weighs against the common belief that it is characteristically related to responsibility.

Comparison of the figures for perforations alone with those reported for other cities shows that the incidence in York was 15–20% lower than in Glasgow, and that the incidence of perforated duodenal ulcers was more than 50% lower than in Aberdeen, while perforated gastric ulcers were somewhat commoner. The explanation for these differences is unknown. Speculation has been inhibited in the past by a gnawing doubt about the validity of the available data. Such doubts are no longer justified.

MEDICAL MECHANICS AT LOUVAIN

How often, one may ask, is useful research held up, or even prevented altogether, because necessary apparatus cannot be got? How much time is wasted by experimentally minded clinicians and medical scientists in peddling their ideas before the scrutineers of research organizations, charitable trusts, and the like? Scrutiny is of course essential, but is our whole machinery for putting at the right moment the right tools in the right hands too cumbersome and creaky? Some would say emphatically it is.

At Louvain University in Belgium they have found a novel answer to this problem. This ancient Catholic university (founded in 1425), with its very large faculties of medicine and science, is in a phase of rapid expansion. Since 1950 the number of students there has risen from 7,500 to over 12,000: with this there is of course a heavy demand from the various departments for research and other specialized equipment. To meet the demand the university has established its own University Technical and Experimental Centre (U.T.E.C.), staffed by university engineers, where apparatus wanted by the departments and not readily available commercially can be designed, developed, and produced up to the highest industrial standards. U.T.E.C. is of course remarkably well placed to do this. It can call on the research experience of the whole university; if a chemical problem arises there is a chemist to answer it; if the advice of an electronics engineer, a metallurgist, or physiologist is wanted it can be speedily obtained, and so on. There are experienced administrators to look after the Centre's finances, and a whole faculty of lawyers to safeguard the patent rights of new inventions.

Some idea of the diversity of the equipment designed and made by U.T.E.C. can be gleaned from a bare catalogue of items shown to invited representatives of the *Journal* at the Centre this month. At the university library, with its 800,000 volumes, there is a "continuous belt" machine to speed the delivery of books from one floor to another. At the teaching hospital, apparatus from U.T.E.C. ranges from a palatial multiple-cabinet morgue, with powered lifting to assist the attendants and full refrigeration, and an electronic control system for the heating of the whole ten-acre hospital site, to highly mechanized stereotactic equipment for brain surgery and a room for cancer research with luxuriously precise control of temperature and humidity. (The temperature in this room, it was said, can be kept constant within one-tenth of a degree centigrade.) Other hospital equipment includes a specially designed bath for paralysed patients and an air-conditioning system for the operating theatres.

At the U.T.E.C. workshops themselves the anatomical specimens are specially notable, as befits a foundation which numbers Vesalius among its sons. Chief among these are the plastic skeletons cast from flexible moulds of human bones. Their construction is remarkably good and their accuracy sufficient for most undergraduate purposes; they are more than adequate for teaching medical auxiliaries. The bones are put up as articulated skeletons, mounted skulls with the bones separated, "half-sets" for students, and separately. It is hoped that samples will be on view at the summer meeting of the Anatomical Society of Great Britain which is being held this year at the Royal College of Surgeons on July 1 and 2. At the workshops they are also developing suitable processes for making soft-tissue specimens, and some of these muscle-and-nerve preparations seem very promising. Pathological, biological, and botanical specimens are embedded in clear plastics for museum purposes. Other apparatus includes electronic equipment for the continuous recording of blood pressure, Geiger counters, an E.C.G.-monitor for use during surgical operations, small climatic chambers for the study of tropical plant physiology, and tilting, stainless-steel operating tables for rats and mice, tailored to the experimenter's requirements. This is just a sample of the activity that goes on.

The benefits to Louvain University—and to the outside research units, hospitals, and commercial firms who on occasion go to U.T.E.C. for equipment—are definite enough. The dangers of such a set-up are, on the one hand, that the unit may get bogged down by large routine jobs of little intrinsic research merit, though at Louvain the U.T.E.C. directors seem well alive to this; and, on the other, that the natural inventiveness of designers may progress too far in the direction of push-button machines for every occasion.

ULNAR NERVE LESIONS IN THE PALM

Wasting of the small muscles of the hand unaccompanied by sensory loss always raises the suspicion of motor-neurone disease. It is therefore as well to remember that lesions of the ulnar nerve in the palm of the hand can produce just such a picture. When the nerve is injured after curving round the pisiform bone, it has already given off its sensory branch to the palmar aspect of the ulnar two fingers, and usually its supply to the hypothenar muscles also. The result is thus a purely motor loss affecting the interrossei, the medial two lumbricals, and the adductor pollicis muscle. If the lesion is a little more proximal, the hypothenar muscles are also affected without sensory loss.

This syndrome was originally described by Ramsay Hunt,[1] and similar cases were reported by W. Ritchie Russell and C. W. M. Whitty.[2] More recently P. Ebeling and colleagues[3] have discussed a further nine cases and have shown that measurement of nerve conduction can be a useful aid to diagnosis. Not only can this procedure suggest a local nerve lesion, but it can sometimes indicate its site with some accuracy, and further help in assessing the beginning of recovery before clinical evidence is available. The cause of these lesions is almost always traumatic, and this can usually be discovered in the history. Sometimes the amount of trauma may be slight, because there is some source of internal pressure on the nerve. H. J. Seddon[4] described cases in which a palmar ganglion caused compression of the nerve, and similar lesions were found in four of Ebeling's patients. In such cases operation may hasten recovery, though recovery often occurs simply from protecting the nerve from further external pressure with a properly placed foam-rubber pad in the glove. Careful serial studies of nerve conduction may also help to establish the need for operation. It is important to bear in mind this diagnosis, which is a neat vignette of applied anatomy, and not to condemn the patient unnecessarily to the gloomy diagnosis of motor-neurone disease.

[1] Hunt, J. Ramsay, *J. nerv. ment. Dis.*, 1908, **35**, 673.
[2] Russell, W. R., and Whitty, C. W. M., *Lancet*, 1947, **1**, 828.
[3] Ebeling, P., Gilliat, R. W., and Thomas, P. K., *J. Neurol. Neurosurg. Psychiat.*, 1960, **23**, 1.
[4] Seddon, H. J., *J. Bone Jt Surg.*, 1952, **34B**, 386.

PREVENTION OF INJURY IN ROAD ACCIDENTS

Would improvements in the design of cars lessen the number of serious injuries arising from road accidents? Only research can provide the answer, and the Automobile Association has generously agreed to sponsor an investigation which, in the long run, should benefit the National Health Service by reducing the number of beds occupied by casualties from the roads. Announcing the plan after the annual meeting of the Automobile Association in London last week, the Duke of Edinburgh, who is President of the A.A. as well as of the B.M.A., said that a road injuries research group will work in conjunction with the Institute of Accident Surgery at the Birmingham Accident Hospital. One of the main objects of the group will be to find out the extent to which injuries are related to the design of vehicles, and the sum of £30,000 has been set aside to finance research on these lines for the next seven years.

Mr. W. Gissane, surgeon-in-chief at the Birmingham Accident Hospital, will supervise the research there. One of its purposes will be to compare engineers' reports on damage to vehicles with surgeons' reports on the injured, whether inside or outside the cars. Among the many points of design to be examined will be the steering assembly, which, as Mr. Gissane[1] says, can cause irreparable damage to vital organs. In his view the traditional design of the steering wheel is the most unnecessary single hazard in present-day car design. But brakes, headlamps, bodywork, tyres, and so on, will all be under close scrutiny in this research, which it is to be hoped the motor industry will wholeheartedly support.

The half-yearly indexes to Volume II of the *Journal* and *Supplement* for 1959 are now being despatched. Members who have not previously asked for the indexes to be sent regularly to them can obtain copies, post free, from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

[1] *Birmingham Post*, May 20.