

BRITISH MEDICAL JOURNAL

LONDON

SATURDAY NOVEMBER 18 1944

THE RISE IN PEPTIC ULCER

It is difficult to say anything fresh about the clinical aspects of peptic ulceration. Except for having learned the risks of alkalosis and avitaminosis, we know no more about the aetiology and control than when Sippy introduced his treatment by diet and alkalis in 1915. Since that date, however, peptic ulcer has grown from a clinical problem to a social problem, owing to a secular change in incidence. A rise was already suggested by the large number of cases of haematemesis which came under study in the decade preceding this war. It was hardly possible to doubt the fact of this rise when the present army was recruited and large numbers of men were found to be suffering from peptic ulcer. It was officially stated in May, 1942, that 17% of the total discharges for all diseases from the Army and the Royal Air Force and 13.8% from the Royal Navy were on account of digestive disorders. The majority of these men were suffering from peptic ulcers, and 90% of the ulcers had given rise to symptoms in civil life, before the man joined the Services.¹ In wartime industry men have broken down with peptic ulcer under the strain of long hours or changing shifts, and while the Services can discharge the man with a peptic ulcer the industrial medical officer cannot deal with the situation so simply. No such phenomenon was noted in the last war, either in the armed Forces or in industry, and the only explanation seemed to be a considerable increase in the incidence of peptic ulcer in the years between the two wars. Nor is the increase confined to this country, as is shown by the provision of special dietetic facilities for workers with peptic ulcer in Russian factories and the formation of special units for German troops suffering from digestive disorders.

Nevertheless, in the absence of morbidity statistics, it was still possible for sceptics to doubt the increase in peptic ulceration and compare it with the loose talk about the increase in cancer which had not been substantiated on careful investigation. An analysis of death rates from peptic ulcer in Great Britain was published this year by Tidy,² who came to the conclusion that there was little or no rise between 1912 and 1920, but a sharp rise between 1921 and 1930; the curve then flattened out and remained at the same high level. Tidy thought that the rise was almost entirely due to an increased incidence in males over 40. He found certain differences between England and Scotland, more particularly a rather belated increase in the incidence of gastric ulcer in Scotland. When these results were presented at a meeting of the Association of Physicians³ they were criticized on the ground that certifi-

cation is liable to be affected by changing fashions and improved diagnostic procedures. This type of criticism has recently been answered by Stocks,⁴ who points out that death certification is generally more accurate than certification in life, and that the statistician is interested in long-term trends which are unlikely to be gravely affected by mis-diagnoses and mis-statements. In any event it seems impossible to offer any serious criticism of the factual value of the data on perforation which have been presented by Prof. Illingworth and his colleagues in the article of which the second part appears in our present issue. This is a remarkably thorough piece of investigation which was made possible by the circumstance that the Glasgow region forms a natural catchment area from which practically all cases of perforation flow into a small group of hospitals in the city. It was aided by the high standard of surgical records in these hospitals, which will be the envy of other regions which have tried to compile morbidity statistics. It is clear that perforation of a peptic ulcer was almost unknown in Glasgow until the last decade of the nineteenth century. Since then it has increased in almost exponential fashion to attain a sudden peak in 1940-1, since when the rate has fallen. The main analysis deals with the twenty-year period 1924-43, during which the changes almost entirely concern duodenal ulcer, gastric perforation having remained stationary. The sex ratio has undergone little change, having remained at about 19 males to 1 female throughout. Apart from the rise from a total of 191 perforations in 1924 to 615 perforations in 1941, there are two observations to which we may draw attention. The first is that perforation seems to be related to fatigue, being less common after the summer holiday and the week-end, and more common in the late afternoon; the second is that the fatality rate increases sharply with age.

It is difficult to believe that merely the perforation rate has increased in the Glasgow region, and not the total incidence of peptic ulceration. Nevertheless the papers of Tidy and of Illingworth and his colleagues both point to the need for statistics of the total incidence of peptic ulceration in our population and not just of the fraction which perforates or dies. This implies "filling in forms," which is unpopular with men overworked in practice, but it is the only way in which morbidity statistics can be collected. At present it would be fair to say that we do not know how the incidence of peptic ulceration is affected by climate, occupation, or income level. Such knowledge is desirable in view of the two current theories of causation. These may be defined as the psychological and the nutritional, and both ultimately attribute the blame to our so-called civilization. Donnington has described the characteristic diseases of civilization as psychoneurosis, exophthalmic goitre, hyperpiesia, and peptic ulcer. He attributes their increase to the greater emotional strain of civilized life, and the tendency for feelings to be individual rather than communal, and to be pent up rather than exteriorized. He pictures this pent-up emotion welling up, as it were, in the hypothalamus and expressing itself through the autonomic nervous system and the viscera.

¹ Hurst, A. F., *Medical Diseases of War*, 4th ed., London, 1944.

² *British Medical Journal*, 1944, 1, 677.

³ *Quart. J. Med.*, 1943, 36, 260.

⁴ *Proc. roy. Soc. Med.*, 1944, 37, 593.

His theory receives support from Wolf and Wolff,⁵ who have made careful observations on a man with a large aperture in the stomach. They found that prolonged emotional disturbances, and in particular internal conflict with unfulfilled desire for aggression and fighting back, were accompanied by marked and prolonged increases in gastric motility, secretion, and vascularity, with reddening and engorgement of the mucosa. It would be generally agreed that nervous tension and fatigue at any rate favour perforation and haemorrhage, and the results of Illingworth and co-workers are in harmony with this view. The importance of diet in the aetiology of peptic ulcer has been unequivocally demonstrated by McCarrison⁶ both in the field and in the experimental laboratory. Peptic ulcer is very common in the south of India; it is in fact 58 times as common as in the north. On putting groups of rats on the well-constituted diet used by the Sikhs, and on the defective diets used by the poorer classes in Madrassi and Travancore, McCarrison obtained the following results: first group (Sikh diet), *nil*; second group (Madrassi diet), 11%; third group (Travancore diet), 29% incidence of peptic ulcer. These are remarkable findings, and it is obviously desirable that we should have statistics which would enable us to relate the incidence of peptic ulceration to nutritional status. Many would doubt whether the correlation between peptic ulceration and general poverty of the diet in this country is as close as it appears to be in India. Many would doubt again whether fatigue, nervous tension, and unfulfilled aggression have increased to an extent commensurate with the rise in peptic ulceration.

There are of course other important aspects of peptic ulcer when it is viewed as a social problem. Both water-borne and air-borne infections have been declining as a result of improved social conditions, and developments of chemotherapy have greatly increased our control of bacterial disease. During the last few years virus diseases, like yellow fever and typhus, have yielded to new prophylactic measures, and we can probably look forward with confidence to the eventual conquest of infectious disease. The population is shrinking and ageing, and we are coming to the stage where we are getting rid of acute disease, where our patients live to be older, and where their illnesses by the very fact of age are less tractable and of longer duration. The mortality of both haemorrhage and perforation of a peptic ulcer is directly proportional to the age. Changes in type of disease and in age of population are combining with a real increase of incidence to make peptic ulcer one of the most important diseases in this country. Similar morals could be drawn from a study of rheumatism or mental disease. In planning a medical service and making our hospital provision we must make sure that we are providing for the present war against disease and not the past. There is a tendency in some quarters to speak as if "long-term sickness" could be divorced from general medicine; the lesson from peptic ulcer is that long-term sickness may well be the most important problem of the coming years.

MEPACRINE AND MALARIA

After the great researches of Ehrlich and his successors which led to the discovery of the various arsenical and other compounds used in the treatment of syphilis and sleeping sickness the progress of chemotherapy seemed to halt, and during most of the nineteen-twenties no further notable advance took place. One fresh product—pamaquin (plasmoquin)—appeared which promised new things in the treatment of malaria and was remarkably effective in the laboratory infections of canaries with *Plasmodium relictum*. When applied in human malaria it proved to have only slight curative action and to be very toxic; its discovery, although encouraging, was of little real value to clinical medicine. A much more substantial contribution to medical science was made about 1932, when from the I.G. Farbenindustrie came an account of the antimalarial action of a new substance first called "erion," then "atebrin," and now officially designated as "mepacrine" in the *British Pharmacopoeia* and as "quinacrine" in the *United States Pharmacopoeia*. Mepacrine is composed of an acridine nucleus with a long side-chain ending in a substituted amino group; it is strongly basic and acts in many ways like a yellow dye, tending to stain the skin that colour when it has been taken by mouth in large quantities. According to the original statement of the manufacturers' its action against malaria was as powerful as that of quinine, and this was confirmed during the malaria epidemic of Ceylon in 1935, when mepacrine was first tried out on a large scale. From the experience gained in this epidemic and from field trials organized in Malaya and elsewhere, it became generally accepted that mepacrine was about as effective as quinine in the treatment of acute attacks of malaria. It had an advantage over quinine in that it was less apt to cause vomiting and less likely to be followed by blackwater fever; but, on the other hand, its action was rather slower, and in a small proportion of cases it might cause alarming symptoms resembling those of epilepsy or mania. It also had the disadvantage that its prolonged use tended to stain the skin yellow. In the remaining years before the war each compound had its own champions. Some persons and communities relied almost exclusively on quinine and regarded mepacrine with suspicion, but this may have been due mainly to conservatism and tradition. Other groups vaunted the great superiority of mepacrine; but these were mostly German, and their preference often seemed to be based more upon nationalist than upon medical grounds. In parts of the Tropics such as East Africa, where there were large German settlements, a yellow discoloration of the skin began to acquire the significance of a demonstration of patriotism, apparently without any qualms about the resulting non-Nordic appearance. Among more detached observers the general view prevailed that mepacrine and quinine were about equal in their merits and demerits.

With the coming of the second world war and the Japanese onslaught on Occidental possessions in the Far East and the Pacific the problem of the prevention and treatment of malaria became of the utmost importance. The broadcast of the Australian Premier is now well known in which it was stated that 80% of the Australian Forces

⁵ *Human Gastric Functions*, New York, 1943.

⁶ *Nutrition and National Health*, London, 1944.