separate from an integrated N.H.S. This sentiment seems to pre-empt the outcome of any inquiry. Indeed it could be thought, perhaps unjustly, that the local authorities see an inquiry as much a means of delaying Government action as a way of achieving the most effective school health service. It is quite understandable that local authority associations should wish to get in an early bid about the future of this service for by all accounts the amount of time available for discussion of the third green paper will be severely limited, a situation that everyone concerned with the future of the N.H.S. will deplore. So even though many doctors will disagree with its objective at least the recently publicized statement from the local authorities should alert the medical profession to the need to give to the Government as soon as possible its own views on the future role and organization of the school health service within an integrated N.H.S.

[1] Ministry of Health, *The Administrative Structure of the Medical and Related Services in England and Wales*. London, H.M.S.O., 1968.
[2] Department of Health and Social Security, *The Future Structure of the National Health Service*. London, H.M.S.O., 1970.

Peptic Ulcer after Burning

Burned patients are specially liable to acute ulcers of the duodenum and of the stomach.[1-4] The pathogenesis remains obscure, but so is that of other peptic ulcers. Therefore the understanding of post-burn ulceration might make the causation of other peptic ulcers clearer.

Necropsy studies have shown duodenal ulcers in 5 to 10% of burned patients and acute gastric lesions rather more frequently.[5 6] The duodenal lesions are usually single or double ulcers in the first stage. The gastric lesions vary, but multiple tiny disseminated erosions are not uncommon and occasionally also involve the proximal duodenum. In Great Britain most of the ulcers are clinically silent and are first discovered at necropsy, though severe haemorrhage occasionally occurs and perforation less often. Gastroduodenal symptoms rarely follow burning, so that healing must be effective. A high frequency of acute haemorrhage, often severe and necessitating large blood transfusions and even gastric resection, has been reported from Texas.[7] The difference there from the experience in Britain is not clearly understood, though it may reflect the higher incidence of haemorrhage in the United States from other peptic ulcers than in this country, or it might be a consequence of differences in treatment.

Acid-peptic digestion following local necrosis or haemorrhage of the mucosa is the most likely precipitating mechanism, but the nature of the initiating local lesion and its causes are obscure. Localized foci of necrosis without ulceration in the first stage of the duodenum have been found at necropsy and may represent the pre-ulcer stage.[6] Experiments in rabbits suggest that focal haemorrhages in the gastric mucosa following focal ischaemia induced by haemorrhagic shock[8] are possible sources of gastric erosions. Other explanations offered include haemoconcentration, through its lowering the mucosal vitality[9]; infection[10]; and the vague concept of stress-ulceration related in some way to adrenocortical hyperactivity. Hyperacidity has not generally been found in burned patients with or without ulcers, and the frequent colonization of the ulcers by bacteria and yeasts indicates either a lack of free hydrochloric acid or protection of the ulcers from its action.[6 7]

Differences in the protective effect of gastroduodenal mucus may be important. Qualitative differences related to ABO blood groups might account for the higher frequency of duodenal ulcers in burned O patients than in A patients.[6] And quantitative changes are in accord with the reduction in the secretion of gastric mucus found in burned rats and dogs and with the associated histochemical changes detected in mucosa by the periodic-acid Schiff method.[11] Local absence of mucus may leave the stomach and duodenal linings vulnerable to acid-peptic digestion.

Nevertheless, the duodenal and gastric lesions are not necessarily identical in pathogenesis. In 1939, J. L. Keeley[12] thought they were distinct pathological types. More recently S. Sevitt[6] reported a variety of differences in their frequencies respectively in adults and children, their relationship to the extent of the burned area, their times of onset, the patients' ABO blood groups, and other factors. Only different factors in pathogenesis can explain why ulcers occur either in the stomach or duodenum and why lesions in both organs are uncommon, why ulceration may be early or delayed, and why delayed duodenal ulcers are particularly common in burned children. Such differences may be relevant to those reported in various forms of experimental ulceration.[13] Neurogenic ulcers (Cushing's) are associated with hyperacidity but not with depletion of gastric mucus, while the reverse is claimed for "stress-ulcers." Further, stress-ulcers and steroid-ulcers are probably separate entities, since the former are said to be prevented experimentally by precursors of cortisol, and cortisol itself is particularly inhibitory.

Thus in the analysis of ulcers in burned patients the use of the umbrella title of Curling's ulceration[7] is unfortunate, for it may hide essential differences. If proper names are needed, the gastric erosions might be termed Dupuytren's ulcers, as suggested by M. Thomsen and B. Sørensen,[14] and the term Curling's ulcer restricted to lesions in the duodenum.

[1] Dupuytren, A., *Leçons orales de clinique chirurgicale*, Vol. 1. Paris, Bailliére, 1832.
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[3] Cooper, S., *London Medical Gazette*, 1839, **23**, 835.
[4] Curling, T. B., *Medico-Chirurgical Transactions*, 1842, **25**, 260.
[5] Sevitt, S., *Burns. Pathology and Therapeutic Applications*. London, Butterworths, 1957.
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Gastric Mucin

The mucous membrane of the human stomach is normally covered by a continuous film of mucin. In view of its macromolecular composition and gel-like structure it must influence the movement of molecules into and out of the epithelium itself. The analysis of this component of gastric juice is difficult because of these very characteristics.

Fortunately many of the bonds responsible for the maintenance of the gel structure are so-called hydrogen bonds, which can be broken by high concentrations of urea or guanidine. By making use of this property D. Waldron-Edward and S. C. Skoryna[1] have succeeded in obtaining gastric gel mucin in solution, to which modern techniques for the fractionation of macromolecules could be applied.

Gastric juice obtained from fasting individuals was treated and analysed. From it a fraction was obtained which had a molecular weight of about 2×10^6. It showed distinct blood group activity consonant with that of the person from whom the sample came, and like the blood group substances obtained from ovarian cysts it was composed of about one-third amino-acids and two-thirds sugar residues.

The present view of the structure of this type of molecule is that it has a central protein or peptide core from which numerous polysaccharide chains project. They are linked to the core by glycosidic linkage to the hydroxy groups of serine and threonine.[2 3] Gels formed from such molecules show two features which must largely influence their biological effects. Since no two bodies can occupy the same space at the same time, solutions, and of course gels, of these molecules exhibit the phenomenon of excluded volume.[4] This means that large molecules are prevented from entering whereas small molecules are unhindered. Secondly, even molecules small enough to enter the interstices of the gel may have their movements hindered by entanglement with the relatively rigid polysaccharide side-chains, and hence a sieving effect is exerted on them as they pass through the gel.[5] These properties must influence the interchange of molecules between the mucous membrane and the gastric contents. The movement of hydrochloric acid would be unimpeded but macromolecules in the food would be effectively barred from direct contact with the epithelium. Pepsin, a relatively small protein of molecular weight 36,000, is presumably within the range of substances capable of traversing the mucin gel. It is tempting to assume that the film of mucin exerts a protective action against potential ulcerating agents, but in the present state of ignorance of the pathogenesis of peptic ulceration the mechanism of such protection remains entirely speculative.

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Ovarian Ablation for Breast Cancer

Destruction of ovarian function was the first endocrine measure used successfully to treat breast cancer, and in premenopausal women it is now accepted as the best primary treatment for the advanced disease. About a quarter of those so treated will be helped, the exact proportion depending on how a successful response is defined. Treatment can be effected either by removal of the ovaries or by destroying their function by x-irradiation. The results are probably the same from either method, though the effect of oophorectomy is more immediate.

A continuing source of controversy has been the question whether ablation of the ovaries also has prophylactic value after treatment of the primary disease. Two controlled clinical trials[1 2] have shown that prophylactic ablation probably gives some benefit in prolonging survival and delaying recurrence. But the results of each trial have been criticized —in one case[1] because the dose of irradiation was thought to be too small and in the other[2] because of the unusual selection of cases. Moreover, the degree of improvement was not impressive, and many surgeons thought it was unreasonable to ablate the ovaries of so many women after mastectomy when the return was so small.

In the United States R. G. Ravdin and his colleagues[3] have now reported the result of another clinical trial carried out to investigate the use of prophylactic oophorectomy. Patients aged under 50 were randomly allocated after mastectomy either for oophorectomy or for no prophylactic therapy. A third option, in which patients operated upon received thiotepa, was also included in the study. The investigation began in 1961, and the present report describes the recurrence rate and survival of over 350 patients analysed at least 36 months after primary treatment. No significant differences were noted between the results of the three groups. In particular, oophorectomy conferred no increase in survival time or in time between mastectomy and recurrence. The report concludes that "there would seem to be no further justification for the use of prophylactic oophorectomy in the treatment of operable breast carcinoma".

The question remains how this result and recommendation should be interpreted. About 30% of British surgeons ablate the ovaries after mastectomy.[4] Should this practice be abandoned? Unfortunately this new trial poses almost as many questions as it answers. The most important arises from the remarkable finding (in direct contrast to that of the previous two trials) that the patients having an oophorectomy apparently derived no advantage whatever from it. If it is accepted that ablation confers considerable benefit on many patients with the advanced disease in that deposits may regress—sometimes for many years—then it is almost inconceivable that the same effect would not happen if the oophorectomy follows mastectomy, when distant deposits must often be present, though smaller in size and symptomless. Thus those patients having viable cancer cells remaining after mastectomy, and who have responsive tumours, logically must have the progression of their disease altered by prophylactic ovarian ablation. This alteration should affect the time when recurrence becomes manifest and also, possibly, survival. The results of the present trial suggest that such patients form a very small proportion of the whole—so small in fact that the benefit conferred on them did not show up in the numbers analysed.

Thus, although many surgeons would agree with the conclusions reached in this trial, in that it may be improper to ablate the ovaries as a routine prophylactic measure after mastectomy, this should not be taken to mean that the treatment is totally ineffective. It is reasonable to presume that some patients must benefit, though the measure of their improvement is lost when analysed with the majority in whom the treatment is ineffective. If only these few could be identified beforehand, ablation might still be used to their advantage. It is to be hoped that other current investigations,[5] in which this particular aspect is being studied, will throw more light on the problem.

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