rheumatoid arthritis to which we have now given insulin. It may be significant that in both cases the attacks followed a second course of insulin: we have now given second courses to 12 patients.

In Case 1 the attacks did not begin until 12 days after the last insulin treatment, the patient having suffered meanwhile from gastro-enteritis. The investigations done when she was readmitted did not elucidate the mechanism of the hypoglycaemia. It may be noted, however, that the glucose-tolerance curve suggested slow absorption; that the adrenal response to hypoglycaemia, as judged by subsequent eosinophil depression, was normal; and that the serum colloidal gold reaction was positive (3), thymol turbidity, alkaline phosphatase, and plasma bilirubin being normal.

In Case 2 the spontaneous hypoglycaemic attacks started on the day after the last insulin treatment and must be wholly attributed to the therapy. Evidence of undue sensitivity to the hypoglycaemic action of insulin was sought three days after the first spontaneous attack. In fact, five units intravenously produced no depression at all of the very low fasting blood sugar; neither did adrenaline, given later, produce any rise. Glucose tolerance on the following day was apparently normal, though the curve was pitched at a low level owing to the subnormal fasting blood sugar. One day later 25 mg. of A.C.T.H. produced normal depression of circulating eosinophils.

Several liver-function tests were done between 10 and 15 days after the first spontaneous attack. The oral hippuric-acid synthesis test was probably normal, laevulose tolerance was at the outside limit of normal, and galactose tolerance was distinctly abnormal. A second insulin-sensitivity test was also done at this time. This showed a normal blood-sugar depression 20 minutes after 5 units of insulin intravenously; the depression had, however, been abolished 10 minutes later. Adrenaline was again without any effect at all.

One month after the first attack the fasting blood sugar was normal and the glucose-tolerance curve was of the "lag" type.

From the clinical aspect, the attacks were easily controlled by the institution of a high-protein diet with a "snack" at bedtime. It would seem wise to insist on these measures for three weeks after any course of insulin therapy, for the attacks, though not serious, are distressing to patients and their relations.

Summary

Two cases of rheumatoid arthritis developed attacks of spontaneous hypoglycaemia in the early morning shortly after the end of second courses of insulin hypoglycaemic therapy. The attacks were controlled by a high-protein diet with a feed at bedtime, and the tendency to them disappeared within two weeks.

In six other patients who had received similar treatment, daily fasting blood-sugar estimations for 12 days after stopping insulin administration showed that the lowest blood sugars occurred about the tenth day.

We would like to express our appreciation to Dr. H. J. Gibson and his laboratory staff for some of the pathological investigations, and to Dr. P. Woolf for assistance.

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THE NEUROLOGICAL ORIGIN OF PEPTIC ULCER

FRONTAL-LOBE LESIONS AND GASTRIC ULCER

BY

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There are many reasons, mainly experimental, for belief in the existence of a cortical relation to visceral sensitivity. As Fulton (1943) has said, in the vegetative nervous system, just as in the somatic nervous system, there exist suprasegmental levels capable of influencing intersegmental autonomic reflexes.

The work of Watts and Fulton (1934) and of Davey (1949) has shown the existence of areas in the cerebral cortex whose stimulation or ablation causes changes in the behaviour of the gastro-intestinal tract. These changes are in the motility and secretions of the stomach and intestinal tract.

Cortical relationship to the alimentary tract is confined to the frontal lobes. Stimulation of the sixth area of the frontal lobes in monkeys (Watts and Fulton, 1934) has resulted in an increase of intestinal peristalsis to the extent of obstruction due to intussusception. Davey (1949) obtained similar results with operations on this area, but according to him it is the ocular region of the cortex which reacts best, producing more active changes in the behaviour of the stomach and intestines.

Anatomical evidence has also furnished further proof of these facts. Gastric or intestinal ulceration is often found in experimental animals subjected to cerebral operations. Mettler *et al.* (1936) frequently found gastro-intestinal ulceration in decorticated animals. The earliest account in the literature is that of Brown-Séquard (1876), who reported a perforated gastric ulcer in a dog whose frontal lobes he had cauterized.

There is plenty of clinical evidence to support the relation between the cerebral cortex and the digestive tract. It is well known that in some subjects strong emotions can produce intestinal disturbances due to disorders of motility; the alimentary character of the aura of some epileptic attacks; and the digestive disturbances, usually intestinal, which occasionally occur in leucotomy cases. Among the most significant observations on this subject is a case described by Cushing (1932). Despite the fact that he maintained the view that in those cases in which the gastric lesion had a neurological origin this was to be referred to the hypothalamus, as it is here that vegetative functions are represented and integrated, his case may well be cited. In Cushing's case there were found at post-mortem examination multiple superficial bleeding ulcers in the stomach and duodenum, and in the brain the remainder of a meningioma, previously removed, situated in the olfactory groove, together with a large area of softening in the frontal lobe caused by ligation of the anterior communicating cerebral artery.

Bodechtel (1935) in one of his cases found a glioblastoma multiforme of the frontal lobe and multiple acute bleeding ulcers of the stomach.

I have been able to study post mortem two cases of frontal-lobe lesions associated with multiple acute ulcerations in the stomach and duodenum that may be

brought forward as further proof of the relation between the cerebral cortex and the digestive tract.

Case 1

A 25-year-old man came to necropsy with the diagnosis of pneumococcal meningitis bacteriologically confirmed. There was a purulent meningitis localized to the frontal region. Both frontal lobes were completely covered by a creamy exudate, greenish-yellow in colour, which spread over the anterior half of the brain and filled the sulci (Fig. 1, A). The rest of the brain was quite free of exudate. In addition to the purulent exudate there was a circular depression (shown in the photograph) with well-marked borders which

FIG. 1.—Case 1. A, Frontal lobes covered by exudate. B, Section showing circular depression and haemorrhage.

FIG. 2.—Case 1. Duodenum immediately beyond the pylorus, showing seven ulcers.

was surrounded by an indefinite area of dull colour, dark blue in the fresh specimen. On section this was seen to be due to a haemorrhage in the anterior portion of the frontal lobe. The stomach contained a little dark-brown fluid and "coffee-ground" material, and in the duodenum immediately beyond the pylorus there were seven ulcers (Fig. 2). These varied in size, and had well-defined edges and dark bleeding bases. Some were very superficial, merely erosions, others deeper and funnel-shaped. There were no other important findings.

Case 2

A man aged 35 died with signs of a haemorrhage into a cerebral frontal tumour. There was no history of digestive trouble. Necropsy revealed swelling of the anterior half of the left cerebral hemisphere with well-marked signs of raised intracranial pressure and marked flattening of the convolutions. The brain was hardened, and on subsequent section the whole of the left frontal lobe was seen to be invaded by a tumour, in the centre of which were several areas of haemorrhage, softening, and necrosis (Fig. 3). The tumour filled the whole of the frontal lobe and obliterated the anterior horn of the ventricle, which was represented by a small groove towards the posterior end of the tumour. The lateral ventricle and frontal lobe on the right side were deformed and displaced by the tumour. There was also displacement of the caudate and lenticular nuclei, both limbs of the internal capsule, and the optic thalamus on the left side. There were haemorrhages into the lenticular nucleus and the thalamus on this side, and there was hydrocephalus, all of which is well shown in Fig. 3. The tumour was proved to be an ependymoma, using the silver carbonate method of Rio-Hortega.

FIG. 3.—Case 2. Showing left frontal-lobe tumour in the centre of which are several areas of haemorrhage, softening, and necrosis.

In the stomach there were four ulcers very similar to those in the previous case (Fig. 4). It should be pointed out that these ulcers were situated in the upper part of the greater

FIG. 4.—Case 2. Showing four stomach ulcers.

curvature and not on the line of the lesser curvature, as is the rule in chronic gastric ulceration. The stomach contents consisted of the typical coffee-ground fluid with some supernatant small clots of blood.

From their shape, their number, and their bleeding character, we may accept these as acute ulcers similar to those in the previous case, and more especially as there was in Case 2 no history of any previous subjective or objective gastric disturbance.

Discussion

These two cases demonstrate the close relationship between gastric ulceration and localized lesions of the cerebral frontal lobe.

The nature of the ulceration does not correspond to that of the chronic gastric or duodenal ulcer. The haemorrhagic character, number, site, and funnel shape of these ulcers are typical of acute ulcers due to haemorrhage. The primary cause is a local vascular disturbance, possibly related to alteration of the gastric motility, which produces haemorrhages that separate the epithelium from the submucosa. The devitalized epithelium is then digested away by the gastric juice and a superficial erosion produced. The funnel shape and the depth of some of these ulcers are, similarly, evidence of their vascular origin.

The regulating action of the cerebral cortex—in particular certain areas of the frontal lobe—has been firmly established experimentally, so that in these two cases we may accept the evident relationship between the cerebral lesions and the gastric and intestinal changes.

As for the anatomical pathways which take part in the transmission of regulating impulses from the cortex, at present three are accepted as connecting the frontal area to the primary subcortical centres—one to the anterior thalamic nucleus, another to the dorso-medial nucleus of the thalamus, and a third to the hypothalamus, though this latter has no firm anatomical basis, its existence being accepted only through the physiological observations of Ward and McCulloch (1947).

It is possible that in addition to these direct and indirect connecting pathways to the hypothalamus other extrapyramidal tracts may regulate the primary and autonomic centres, as may be deduced from the work of Spiegel and Hunsicker (1936).

Summary

Two cases of frontal-lobe lesions with acute multiple ulceration of the stomach and duodenum are described.

In one case there was a purulent pneumococcal meningitis localized to the frontal area, together with seven acute ulcers in the duodenum. In the other case there was an ependymoma of the frontal lobe with four acute ulcers in the greater curvature of the stomach.

The possible mechanism in the production of these ulcers is discussed along with their relation to vascular changes and alterations in gastric motility of cerebral origin.

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THE TREATMENT OF BLEPHARITIS

BY

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Blepharitis, though sometimes dismissed lightly as a minor complaint, is in fact one of the most distressing afflictions met with in ophthalmic practice. Even with the wide range of antibacterial substances now available some cases prove very obstinate, causing prolonged suffering to the patient. The majority can be cured, however, if appropriate antiseptics or antibiotics are used before the disease has become chronic.

The mildest form—squamous blepharitis, manifests itself by a scaliness of the lid margins. It is merely dandruff of the eyelashes, associated with seborrhoea elsewhere. Dandruff of the scalp is an almost constant accompaniment. Squamous blepharitis is itself not serious except in so far as, if neglected, it is likely to pass on to the more severe condition of ulcerative blepharitis in which pyogenic infection of the skin of the lid margins has supervened. Shallow ulcers then form near the bases of the lashes and become covered by a thick yellow crust. By far the commonest infecting organism is *Staphylococcus aureus*, but any pyogenic organism may be found.

Ulcerative blepharitis is serious, for if not cured at an early stage it will become chronic and lead to a deep folliculitis. After this has happened even the most assiduous treatment may fail to eradicate the infection, and scarring of the lid margins with trichiasis, epiphora, and dermatitis of the surrounding tissues will ensue. It is important, therefore, that the action of the different classes of antibiotic and antiseptic substances should be understood so that each may be used to best advantage.

Treatment

As with any inflammatory lesion, the results of local treatment will be disappointing if general measures are not employed when necessary. Particularly in the case of children it is found that sufferers from ulcerative blepharitis are debilitated. A holiday in the fresh air, good food, and preparations containing the vitamin-B complex may be of the greatest value.

An uncorrected error of refraction is often blamed as the cause of blepharitis. While this is never the true cause, the ocular discomfort and asthenopia which result play their part in undermining the general constitution. Refractive errors should therefore be meticulously corrected.

Squamous Blepharitis.—As with dandruff of the scalp, the scaliness of the lids in squamous blepharitis is the result of epidermal irritation following infection by pityrosporum. Treatment consists in frequent bathing with a 2% solution of sodium bicarbonate in order to remove the scales, followed by the application of 1%