The Relationship between Haemagglutination and Opsonic Action.

It does not, however, follow that reagents which agglutinate the red cells always prepare them for ingestion. This latter effect depends on a mutual reaction between the red cells and the phagocytes by which the two become mutually adhesive.

Some reagents, like mercury perchloride, which in dilute solution agglutinate red cells are themselves toxic to the leucocytes. Others, like acriflavine, which in dilute solution are not markedly leucotoxic, do not seem to promote the ingestion of the red cells. It is a suggestive fact that those reagents which do promote the ingestion of red cells by leucocytes—for example, liquid paraffin and dilute gum solution—are mostly inert substances; they both, in different degrees, protect the shed leucocytes from rapid divitalization. They both stimulate the elaboration of iodophil substances by the leucocytes, and they check the rapid diffusion of this substance from the cells into the surrounding medium. They both affect the density of the serum and alter the surface tension of the cell bodies which they envelop. They are not erythrocidal or haemolytic in character. Thus a 5 per cent. gum solution in normal saline agglutinates washed red cells, but cells so agglutinated are not disintegrated, they can be washed free of the agglutinin in normal saline, and can then be reagglutinated by the gum solution. Reagents, on the other hand, which haemolyze and destroy the red cells prevent ingestion, possibly because they bring about a rapid diffusion of the liberated endotoxin in sufficient volume to poison the leucocytes.

Factors Concerned in the Haemagglutination and Phagocytosis of Red Blood Corpuscles.

The foregoing observations suggest that the phenomena of haemagglutination as it affects the cellular elements of the blood should be described in terms of both red and white cells. Three factors are probably involved in the process:

1. An erythrocytic agglutination in which the red cells agglutinate *inter se*. This process does not necessarily bring about ingestion, but in some cases seems to favour it.
2. A leucocytic agglutination in which the leucocytes themselves clump together irrespective of any action on the red cells. This is seen when leucocytes are acted on by certain animal blood serums and will be described in a subsequent paper.
3. An erythro-leucocytic agglutination in which the red cells and the leucocytes become mutually adhesive. This occurs when opsonic blood serums prepare the red cells for ingestion.

General Conclusions.

It may be that in our search for chemical reagents with which to sterilize wounds we have relied too much on bactericidal capacity and have not sufficiently considered the influence exerted by these substances on the natural defensive mechanism in its humoral and cellular aspects. We should probably do well to regard antiseptics (when effective) as co-operating with the physiological defence in bringing about an agglutination and opsonization of the invading organisms and thus rendering them vulnerable to phagocytic attack.

I am not without hope that the foregoing observations on the artificial agglutination and opsonization of red blood cells by chemical means may throw some light on an allied problem—namely, the mechanism by which the agglutination and opsonization of pathogenic organisms is brought about naturally, and the possibility of aiding this process by chemical means. It would, for example, be of considerable advantage to know what chemical reagents, if any, are capable of agglutinating bacteria and cocci, and whether organisms so artificially agglutinated are also opsonized and rendered easier of ingestion and digestion by phagocytes. The mechanism by which organisms and phagocytes are rendered mutually adhesive, before phagocytosis can take place, is also one of great importance.

ADMIRAL WILLIAM C. BRAISTED, Surgeon-General of the United States Navy, reports that the naval casualties of the war, exclusive of the Marine Corps and of deaths from disease, amounted to 1,233. Practically all the deaths were due to submarine attacks.

CANCER OF THE TONGUE.

ABSTRACT OF THE BRADSHAW LECTURE DELIVERED
BEFORE THE ROYAL COLLEGE OF SURGEONS
OF ENGLAND.*

BY

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CANCER of the tongue is remarkable in the fact that it is almost entirely a human disease; it is always of one type; it is unknown in children; it is common in men, rare in women; it is not associated with any inherited predisposition to carcinoma.

Cancer of the tongue did not become important surgically until the seventeenth century. The Greek, Latin, and Arabian writers on surgery hardly mention it, and, so far as can be ascertained at present, it was unknown to the Anglo-Saxons.

The first definite notice of cancer of the tongue is the case of Ralph Freeman, who died on March 16th, 1634, whilst serving the office of Lord Mayor of London. He suffered from secondary haemorrhage, and it was the opinion of the physicians and surgeons who were in attendance upon him that a mercurial course might have been of use at an earlier period of the disease. The second recorded case occurred in Germany and was looked upon as a miraculous punishment for cursing the clergy. The story runs that "lately a certain baron spoke abusively to all and sundry, but kept his most venomous shafts for the clergy and for those who devoted themselves to God's service. One day a holy brother of good repute, whom he had just lashed, said: 'Your foul tongue has overlong deserved that punishment from an offended God which it will shortly receive.' The baron rode off undismayed, but a few days later a small swelling began to grow at the side of his tongue. Little by little it increased in size until it became an inoperable cancer, and the baron, penitent and confessed, died miserably afflicted." From the middle of the seventeenth century onwards cancer of the tongue became so frequent that it was no longer necessary to invoke a miracle to account for its production.

The zoological distribution of lingual carcinoma was considered in the light of the experience of Sir John McFadyean, principal of the Royal Veterinary College, of Dr. J. A. Murray, Director of the Imperial Cancer Research Fund, and of Dr. Anton Sticker. At the present time cancer of the tongue is known to have occurred in one horse, three cats, and one dog. All these animals were aged, and in each the cancer was of the squamous-celled variety.

It appears fair to assume, therefore, that lingual carcinoma has always occurred in men and domesticated animals; that originally in man it was no more frequent than it now is in animals, but that from the seventeenth century onwards it has increased out of all proportion in man whilst the incidence has remained stationary in animals.

The rate at which cancer of the tongue has increased in man is well shown in the returns of the Registrar-General. Dr. Stevenson, superintendent of statistics, wrote in 1909: "The increase amongst males of deaths from cancer of the jaw, and especially of the tongue, is remarkable, and can scarcely be explained by improved diagnosis. Although cancer of the tongue presents little difficulty of diagnosis in its later stages, the recorded mortality has increased amongst males by no less than 228 per cent. in forty-one years. The increase, moreover, is entirely confined to the male sex."

The possible factors causing this increase in cancer of the tongue were considered. Irritation has long been looked upon as an important factor in causing cancer, and the state of the teeth was therefore passed in review to determine whether pyorrhoea and caries have lately become more common. The virulence, but not the amount, of pyorrhoea seemed to have increased, whilst caries does not appear to be more frequent now than it was in some parts of England during the prehistoric period. It was noted, too, that the Roman skulls found in England had nearly as many carious teeth as there are in the skulls

* The text of the lecture is published in the *British Journal of Surgery* for January, 1919.

of Londoners who died within the last two hundred years. If cancer of the tongue were the direct result of carious teeth the disease should have been as well known to the surgeons at Rome as it now is to us. But neither in Celsus nor in the Latin satirical poets is there any allusion to it.

An examination of the records of St. Bartholomew's Hospital showed that 169 persons were admitted with cancer of the tongue during the years 1909-1916. Nine of the patients were women, the rest were men. The proportion of men to women admitted into the hospital during this period, therefore, was eighteen to one; the true proportion, as shown by the returns of the Registrar-General, being one woman to eight men. Of the women seven were married, one was unmarried, and the social state of the other is not mentioned. Of the seven married women one gave a history of syphilis, two showed signs of syphilis, and one was a widow who had only one child alive out of five; the note adds, "she looks as if she drank." One woman had leucoplakia of the tongue at the age of 17, and stated that her father had suffered from an "abscess of the brain" which was cured by medicine. This was probably a gummatous meningitis. There was no history of syphilis, either acquired or inherited, in the other two married women. The unmarried woman—a nurse—said that her father died of aneurysm, and that she herself had suffered from an abducent paralysis, which came on suddenly and was cured by medicine. None of the women smoked, but all had bad teeth.

In the case of the men 93 out of the 160 were syphilitic, 62 of these gave a history of syphilis, and the remaining 31 showed signs of the disease. The syphilis was invariably of long standing, and taking a few cases in the series without selection the primary infection was said to have been 26 years, 30 years, 29 years, 40 years, 28 years, 23 years, and 43 years previously. Twenty-six patients stated definitely that they had never had syphilis, but one of these had suffered from gonorrhoea, and two had a positive Wassermann test. Many of the patients had drunk to excess, but did not as a rule acknowledge that they had taken spirits freely. A Wassermann test had only been performed 26 times, with the result that it was negative in twelve and positive in six cases; in five it was doubtfully negative, and in three doubtfully positive. These results were compared with those obtained by Captain Arnold Renshaw, R.A.M.C., of the Manchester University Medical School, and Captain Archibald Leitch, R.A.M.C.(T.), of the Cancer Hospital, Brompton. The evidence brought forward pointed to a close association between syphilis and cancer of the tongue. The syphilis may be active, it is more often quiescent or even extinct, and the conclusion arrived at was that, as in some cases of tuberculosis, "syphilis makes the bed upon which cancer is born." It appeared further that an increase in the number of deaths from lingual carcinoma has occurred after periods when mercury has temporarily fallen into disuse in the treatment of syphilis. Such insufficient treatment was the rule in the later years of Queen Elizabeth's reign, when guaiacum, sarsaparilla and the "vegetable" cures displaced the original mercurial methods; during the Regency period when some of the army medical officers nearly succeeded in abolishing the use of mercury; and again in the early Victorian era, when the value of potassium iodide was unduly exploited. It is interesting to notice that many of the patients whose cases are recorded at St. Bartholomew's Hospital stated voluntarily that they had only been treated with mercury for a fortnight or three weeks, after which they considered themselves cured.

Syphilis cannot be considered as more than a predisposing cause of cancer of the tongue, because lingual carcinoma occurs in animals. An exciting cause, therefore, must be looked for, and that cause must have become more prevalent during the last fifty years if the increase in cancer of the tongue is to be attributed to it. The cause must also be one which acts in men more than in women. The increased consumption of tobacco seems to fulfil these conditions. Cancer of the tongue did not become frequent until some years after the introduction of smoking in the last quarter of the sixteenth century. The habit spread slowly during the seventeenth, eighteenth, and nineteenth centuries, until cigars could be smoked openly in the streets by the upper and middle classes, though pipes were taboo in public. Cigarettes

were introduced about 1877, and from that time onwards the smoking of tobacco has steadily increased, until it is now an almost universal habit with both sexes from adolescence onwards. Smoking acts in two ways as an irritant to the tongue, partly through the nicotine and partly by the increased heat in the mouth, which is measurable by the thermometer. In the latter respect it may bear the same relation to cancer that heat does in kangri cancer, where the thermal irritation appears to be a definite factor in the production of epithelioma. Although the predisposing and the exciting causes of cancer may be known, the actual cause has yet to be discovered; but if two factors are recognized, it ought not to be impossible to discover the third.

In conclusion the lecturer thought that it was theoretically possible to reduce cancer of the tongue to the subordinate position it occupied in man before the seventeenth century, and which it still holds in the domestic animals. This could be effected by a thorough treatment of syphilis in its initial stages. Persons who were being treated for syphilis should be told never to smoke, not to drink to excess, and to pay regular visits to the dentist. Such advice should be given whilst the patient was still under treatment, and should not be deferred until the tongue had become sore. Failure to follow this advice or a continuance of the treatment of syphilis on ineffective lines would be followed in all probability by a very large increase in the number of patients with cancer of the tongue. This increase should begin about 1950, and should affect women as well as men, for syphilis is now more widely spread amongst the younger generation than it has been for many years past, and both sexes smoke much larger quantities of tobacco than ever before.

A NOTE ON A CASE OF ACUTE FEBRILE POLYNEURITIS.

BY

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(From the Neurological Department, British Salonica Force.)

UNDER the title "Acute febrile polyneuritis" Gordon Holmes has described a type of polyneuritis presenting a characteristic combination of symptoms which had not previously been described. This series of cases, some twelve in number, occurred among men from all parts of the territory occupied by the British armies in France, and other observers, French and German, have since reported similar cases appearing on the Western front. The case which we describe below appears to belong to this type, and, so far as we are aware, is the first which has occurred in the British Salonica Force, and therefore, we think, worthy of record.

History of Case.

Lieut.-Cpl. N., M.G.C., came to Macedonia from France in November, 1915, and with the exception of one trivial attack of diarrhoea, remained free from malaria or dysentery, and in good health until the onset of his illness on March 4th, 1918. He awoke feeling quite well, but in the course of the forenoon developed severe pain in the back of his neck. In the evening this was present in both lower limbs, and he had considerable difficulty in walking, his gait resembling that of a drunken man. He felt slightly feverish, but had no shivering, vomiting, or sweating. For the first two days of his illness he had no control over his bowels.

On admission to hospital, on March 6th, both lower limbs were weak, but slight pain was now only present in the small of the back and legs. Two days later he complained of being unable to open his mouth sufficiently wide to eat solid food. Articulation was altered, and some weakness of the upper part of the face noted.

On admission to a general hospital on March 10th his condition was as follows: Higher mental functions normal. Paresis of the left external rectus, and complete paralysis of all muscles supplied by the facial nerves; face expressionless, and drooping of both lower eyelids. Articulation difficult and slightly indistinct. Difficulty in swallowing, especially solids; other cranial nerves normal.

Sensory Functions.—Slowness of perception to rough tests (finger and pin) for tactile and painful stimuli over both lower limbs.

Motor Functions.—Trunk and abdominal muscles normal. Paralysis of diaphragm. Hand grasps weak. Both lower limbs can be lifted a few inches from the bed. Movement at ankles good; flexion of knee and extension of limb against resistance very weak. Gait staggering and greatly enfeebled. No definite inco-ordination of limbs. Sense of posture good.