They were very uncertain in their action. One never knew whether the whole or only part of a structure would be impregnated. One part of a section might stain beautifully, while similar tissue near by might be only partly coloured or not at all. Much concerning the minute structure of cells was still obscure. A combination of morphology and staining reactions was needed in deciding histological questions. Another point against Dr. Robertson's theory was that there was no constant relation between the site of inoculation and the site of the tumour. Scarification of the ear did not, for instance, explain the occurrence of a tumour in the mammary gland or uterus. Dr. Murray thought that the failure of the site of the tumour to correspond in all cases with the site of inoculation, together with the variability in the incubation periods, was strong evidence that Dr. Ford Robertson's bacillus was not a specific cause of cancer.

Mr. McADAM ECCLES (Surgeon, St. Bartholomew's Hospital, London) said that Dr. Ford Robertson's paper was of the greatest importance, and was another link in the chain of evidence of the infective origin of carcinoma. As an operating surgeon frequently dealing with carcinomata, such scientific investigation of the cause of carcinoma was of particular and practical importance. All the material investigated appeared to have been from a neoplasm which might have been infected from the surface, the mamma through the ducts in the nipple, the rodent ulcer, etc. If similar results were to be obtained from a carcinoma which had arisen in a "buried" organ, say a testis, it would be a very striking fact.

The infection of and subsequent development of an epithelial growth in so many mice was of the greatest value. He ventured to throw out the suggestion that because mice were the animals most easily infected with later growths, might they not be a possible source of the bacteria which infect the human, seeing also that they were with us everywhere, and did not hesitate to run over and help themselves to our food? Had any of the tumours arising "spontaneously" in the mammae of mice shown any of these distinctive bacterial-like structures?

Dr. FORD ROBERTSON, in reply, said he desired to acknowledge the kindness with which Dr. Murray had criticized views that were completely at variance with those advocated by him for many years. The evidence he had put before them, and that of the twenty-one microscopical preparations laid out in another room, remained, however, untouched by anything that had been asserted.

THE PATHOLOGY OF GASTRIC AND DUODENAL ULCER.*

BY

ALEXANDER G. GIBSON, M.D., F.R.C.P.,

HONORARY PHYSICIAN TO THE RADCLIFFE INFIRMARY, OXFORD, AND LECTURER ON MORBID ANATOMY IN THE UNIVERSITY.

[With Special Plate.]

ONE aspect of the production of gastric ulcer has recently come before me in doing experimental work with an organism mildly pathogenic for monkeys. The organism, a streptothrix of the species *actinomyces*, was obtained from a case of acholuric jaundice, and has been described in the *Journal of Pathology and Bacteriology*, Edinburgh, 1920, xxiii, 357. If a culture in broth be injected intraperitoneally into a monkey (preferably not rhesus) the animal suffers no inconvenience for a month or two; subsequently, however, it becomes less active, tends to sit crouched in a corner, and gradually fails in health during a period which may be as much as a year. There is not, so far as my observations go, any anaemia, but the animal is certainly paler in the late stages, may be puffy under the eyelids. The appetite is preserved throughout. Rigors are sometimes seen. There is usually some tenderness elicited over the spleen, and this may be enlarged and tender.

* A paper read in the Section of Pathology and Bacteriology at the Annual Meeting of the British Medical Association held in Newcastle-on-Tyne, July, 1921.

One of these monkeys, a male callithrix of moderate size, was injected on three occasions intraperitoneally with a broth culture of the streptothrix. The animal preserved its condition and kept up its weight for seven months, after which it quickly failed, and was killed thirty-two weeks (224 days) after the first injection. During the period of observation the animal was more apathetic than the controls, and for the last four months sat crouched in one corner of the cage. On palpation of the abdomen tenderness was first noticed six weeks after the first injection, and, except on one occasion, could always be elicited, more usually over the spleen, sometimes over the liver, and once or twice elsewhere. The spleen was felt throughout, but could never be said to be enlarged.

Blood counts, taken several times during the experiment, showed a gradual increase in the red cells and a slight increase in haemoglobin, not in excess of the control animals. An increase in the mononuclear count was also shown in this and the controls. The fragility was not raised. The necropsy, made immediately after death, showed no peritoneal abnormality. The spleen was extremely small and shrunken. On opening the gut the contents were black and pultaceous, mostly in the caecum and first part of the colon. There were several circular ulcers of the stomach with sharp borders not confined to any area, measuring up to nearly a centimetre across, showing blood altered by gastric juice. The black substance in the colon gave the reaction for occult faecal blood. The small intestine showed several hyperaemic and haemorrhagic patches, and a similar patch on the point of ulceration was found in the appendix. There was ulceration of the first part of the ascending colon. The spleen was in a marked condition of fibrosis with thrombotic changes in some of the veins. The liver was very pale and fatty, and showed towards the edge in one part two small areas suggesting contracting infarcts, and on the under surface were two shrunken, slightly haemorrhagic patches suggesting an area of ischaemic atrophy. On section the liver showed general fatty change and much bile staining near the bile passages. The lungs showed numerous haemorrhagic areas, and small haemorrhagic areas were also to be seen in the mesentery. Cultures made from the spleen, liver, and lung, heart blood and pericardial fluid, were negative. Shortly, this animal showed a chronically inflamed and fibrotic spleen with thrombo-phlebitis, multiple gastric ulcers, and haemorrhagic embolic lesions of the liver and lungs.

The venous blood from the spleen may return to the portal vein by two channels, either by the splenic vein or by the vasa brevia of the stomach wall; this latter channel is probably the normal one for a large amount of splenic blood. In fact, Mayo quotes 30 per cent. as the proportion of splenic blood that returns in this way (W. J. Mayo, *Contributions to Medical and Biological Research*, dedicated to Sir William Osler, ii, 991). The gastric veins must therefore be freely open to any substances, embolic or not, that may emerge from the spleen. If emboli are infective, it is not difficult to imagine that some may attach themselves to the wall of the vessel and produce a weakening and haemorrhage from it.

Acholuric jaundice is a condition that usually gives rise to no gastric symptoms beyond vomiting, and I have only been able, so far, to find one reported case that suffered from haematemesis (Box, *Proc. Roy. Soc. Med.*, Clin. Sect., 1913, vi, 8); but acholuric jaundice is very nearly related to splenic anaemia, and both are undoubtedly due to an infective agent whose site is the spleen. Why in the one type we should see progressive inflammation of the spleen with anaemia and jaundice, while in the other there is anaemia and haematemesis is not known. Be that as it may, the facts are that from an inflammatory lesion in the spleen both types follow, for splenectomy in the earlier stage cures both diseases. In the clinical group of cases known as splenic anaemia there is an enlarged inflamed spleen and a tendency to periodic gastric haemorrhage which may be so great as to be fatal. The origin of the bleeding is sometimes from dilated oesophageal varices, sometimes from lesions in the stomach which are described as erosions; such lesions, however, give rise to such blanching haemorrhages that we must presuppose a leakage from one of the large vessels of the stomach wall. It is curious that clinically such haemorrhages are seldom followed by the symptoms that we have come to look upon as characteristic of gastric ulcer, and must be related to

the fact, now sufficiently well observed, that in an otherwise healthy stomach ulcerative lesions produced by destruction of the mucous membrane quickly heal.

The gastric ulcers commonly met with clinically have very different causation in different cases; experimental work has shown that ulcers arise in the stomach in a variety of ways. In bringing the present observations before your notice I do not wish it to be thought that even a small proportion of clinical gastric ulcers are produced in this way. For this we must suppose a general or an intestinal infection or some such mechanism as Charles Bolton has so admirably worked out for a specific gastro-toxin. But we know rarely of the origin of ulcer in septicaemia, pyaemia, endocarditis, and a large number of other infective processes, both general and local, in which emboli or metastatic infective material may be brought to the stomach wall and produce an amount of necrosis of the mucous membrane that may give rise, after action of the gastric juice, to macroscopic ulceration.

In the instance here described we have a similar process. The spleen in the experimental animal, as in the human disease, shows a thrombo-phlebitis, as has been drawn attention to especially by Dock and Warthin in human cases of splenic anaemia. In some cases of the human disease this phlebitis is so massive as completely to obstruct the portal vein. In other cases, however, it is merely sufficient to thicken the efferent channels. The presence of thrombo-phlebitis in the splenic venules produces from time to time emboli which, travelling by the main splenic vein, are held up by the liver. That this is so is proved, first, by the evidence of what appear to be minute infarctions in the liver of the monkey. Unfortunately, I have so far not been able to get definite evidence of recent phlebitis in the radicles of the portal vein in the liver, owing to my desire to obtain as much material as possible for culture. But in Fig. 1, a section from the liver of a monkey the subject of a similar experiment, there is seen a localized area of phlebitis in a venule in the liver almost blocking the lumen. In this last experiment I have obtained a pure culture of the streptothrix from the spleen pulp.

On these grounds, remembering also that 30 per cent. of the splenic blood returns via the vasa brevia of the stomach, the assumption cannot be avoided that the same process evident in the liver is present in the stomach, a thrombo-phlebitis and inflammation of the neighbouring parts of the inner lining membranes of the stomach, with necrosis and consequent erosion by gastric juice of the area so affected. Histologically the gastric ulcers show the ordinary appearance of acute ulcer with a few minute thrombi in the veins of the periphery which might be seen in ulcer from other causes.

The lungs bear out the view of the presence of a shower of emboli leading to haemorrhages. We know that minute emboli are not stopped by having to pass through a capillary system, and the minute anatomy of the lung shows a marked degree of arteritis of the pulmonary arteries, with obliteration of their lumina (Fig. 2). The spleen in this case is atrophic and shows in a marked degree fibrosis and absence of Malpighian bodies, with phlebitis of the venous channels (Fig. 3). Patches of intense inflammatory reaction are to be found here and there. The difference between this and the spleen of a control animal may be seen by reference to Fig. 4, where the fibrosis is not evident and the Malpighian bodies of normal aspect may be seen.

In conclusion, I submit that in this experimental animal an inflammation of the spleen with thrombo-phlebitis has given rise to infective emboli, evident in their effects in the stomach, producing ulcers and haemorrhage, in the liver and lungs producing haemorrhagic lesions, and that in splenic anaemia, and more rarely in acholuric jaundice, the gastric haemorrhage may be due in a proportion of cases to septic embolism and consequent inflammation of the branches of the vasa brevia.

DISCUSSION.

Mr. D. P. D. WILKIE (Edinburgh) believed that the type of ulcer described by Dr. Gibson was probably that due to retrograde venous embolism. Attention was first directed to this type by von Eiselsberg, who suggested that the

haematemesis which occurred some days after abdominal operations in which portions of omentum had been ligated was due to the separation of a small portion of thrombus in an omental vein, the embolus thus produced being side-tracked into a gastric vein and arrested in the venous plexus of the gastric submucosa, causing there a zone of thrombosis, a devitalized portion of mucosa and thus an ulcer. Experimentally he himself had found that such a succession of events was possible, but in the human subject he had only met with two cases in which this appeared to be the cause of gastric ulceration. The cause of the ordinary peptic ulcer of the stomach and duodenum was now considered by most surgical pathologists to be due to arterial embolism, and the researches of Rosenow would indicate that streptococci borne by the blood stream from a primary focus in the teeth or tonsils were the causal organisms. Whilst he had failed in his efforts to confirm Rosenow's results experimentally he had repeatedly confirmed the presence of streptococci in such ulcers. The difficulty of isolating and growing on culture these strains of streptococci made the close co-operation of surgeon and bacteriologist a necessity in this line of investigation.

THE BONE GRAFT.*

BY

MARCUS MAMOURIAN, F.R.C.S.ED.,

SURGEON TO THE DISTRICT INFIRMARY, ASHTON-UNDER-LYNE.

THE bone graft is now universally recognized as a most effective means of bone repair and the most important modern development of orthopaedic surgery. The subject has been taken up with great keenness and enthusiasm by many, both from its practical and experimental aspects, with the result that the literary output has attained formidable dimensions.

The question of the part played by the bone graft remains undetermined, and Ollier and Macewen may still be considered as leading counsel for the claims of the periosteum and bone respectively. Both sides believe in the survival and growth of the graft, differing only in their interpretation of the process of its development. In England, Groves and Wheeler, while supporting Macewen in theory, are Franco-American in practice, as they advocate whole-piece, autogenous, periosteum covered grafts and rigid fixation. The success of the "inlay" technique and the claims of Albee, McWilliams and others seemed to silence all opposition until Murphy advanced the view that the graft was "osteo-conductive," acting as a scaffolding.

In July, 1918, in a short paper contributed to the BRITISH MEDICAL JOURNAL, I expressed the opinion that all that the graft did was to supply the biochemical stimulus or irritant which had been abolished by trauma or infection, the new bone being formed by the diaphyseal ends, by periosteal and bony remains in the shaft zone, and, in the young, by epiphyseal lengthening, and I supported Murphy's contention that the graft becomes absorbed. I adhere to that opinion, which has been strengthened by my recent work, the radiographic record of which shall be submitted to you.

I do not intend to weary you with lengthy descriptions of various histological and experimental observations, as they are mostly inconclusive and often contradictory. Suffice it to say that they veer in the direction of proving that growth—whether from periosteum, cambium or bone—is mainly subperiosteal, the rest of the graft showing atrophic changes.

We must admit that when a piece of tibia is used as a graft, logically speaking, we cannot expect it to grow, either in length, thickness, or density, to a greater extent than the parent bone, especially when we bear in mind the precarious nature of its blood supply. But it does grow, so we are told, and it grows by virtue of Wolff's law, which conveniently also explains the absorption of a graft when implanted in a region where there has been no bone before. In every contribution on the bone graft Wolff's law is the pivotal argument. Wolff has laid down the law and the bone conforms! And what is this law? It is nothing else than the universal law of organic strengthening under

* A paper read in the Section of Surgery at the Annual Meeting of the British Medical Association held in Newcastle-on-Tyne, July, 1921.

FIG. 1.—Rod-shaped micro-organisms in serum salt solution culture from a cancer of the breast. Ziehl-Neelsen staining. ($\times 1,000$).

FIG. 2.—Mouse showing tumour of buttock, seven months after subcutaneous injection with anaerobic diphtheroid bacillus isolated from a cancer of the breast.

FIG. 3.—Section of tumour shown in Fig. 2.

FIG. 4.—Spreading ulcer on back of mouse, eight weeks after inoculation (by scarification) with culture of an anaerobic diphtheroid bacillus isolated from a rodent ulcer.

A. G. GIBSON : PATHOLOGY OF GASTRIC AND DUODENAL ULCER.

FIG. 1.—Section from the liver of a monkey the subject of an experimental infection, showing a patch of endophlebitis in one of the branches of the portal vein.

FIG. 2.—Section of the lung of a monkey the subject of an experimental infection, to show the almost complete obliteration of one of the branches of the pulmonary artery in the neighbourhood of one of the haemorrhages.

FIG. 3.—Section of the spleen from a monkey the subject of an experimental infection, to show the great increase in the number and size of the trabeculae and a vein (a) showing endophlebitis.

FIG. 4.—Section of the spleen from a normal monkey to compare with Fig. 3.