in 1953 and is still functioning—a follow-up of nine years. Also in the homograft group there are 10 patients whose major homografts have been functioning successfully for six years or more. Of the three types of procedure used the stored arterial homografts and the rebore types of operation have given the best results. The group of cloth grafts (18 cases, Table III) have also given acceptable results, but with a higher incidence of late occlusion than the others. At the present moment, therefore, when dealing with aorto-iliac disease we prefer a rebore type of operation, with use of either a homograft or cloth graft on certain cases which for technical reasons are unsuitable for rebore.

Summary

A survey of the long-term results in 230 patients with peripheral ischaemia and claudication treated by direct arterial surgery is presented.

There were 90 cases of aorto-iliac occlusion, with an overall mortality of 10%. The best long-term results here were achieved by homograft replacement or by total rebore of the aortic bifurcation and a variable length of the common and external iliac arteries. The results of cloth grafts were not quite so good in our hands.

There were 140 cases of femoral artery occlusion. When this occurs alone in the 50–60 age-group it carries a good life expectancy.

The results of end-to-end homografts, by-pass homografts and vein grafts, crimped cloth (teflon and dacron) grafts, and thromboendarterectomy or “rebore” operation are reported and the follow-up results compared.

End-to-end grafts and cloth grafts are the worst, and are considered as not worth doing below the inguinal ligament in our experience.

Long by-pass tissue grafts (preferably homograft or autograft vein) give much better results.

However, the best long-term results of all are given by the recently evolved “total rebore” operation on the femoral artery, sometimes with terminal vein graft. Eight-seven cases operated on without mortality are reported, 54 of which were total rebores.

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EARLY RESULTS IN 95 PATIENTS UNDERGOING FEMORO-POPLITEAL BY-PASS GRAFT

BY

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Angioplastic techniques are now well established in the treatment of occlusive disease of the vessels of the trunk and limbs. Although the use of endarterectomy and porous grafts is highly successful in the aorta and common iliac arteries, similar procedures in the smaller vessels below the inguinal ligament have given less gratifying results. Obstructions in the leg treated by endarterectomy alone, or graft replacement with end-to-end anastomosis, were often followed by a prohibitive incidence of early thrombosis (Linton, 1955). Kunlin (1951) suggested a by-pass graft with end-to-side anastomosis to the host vessels because of the wider anastomosis that could be made with these smaller vessels and the smaller disturbance of the established collateral vessels. This technique was soon found to have fewer failures than the excision of the obstructed segment with end-to-end anastomosis (Linton, 1955; Crawford *et al.*, 1955). Since then many reports on this operation have confirmed the original findings (Morris *et al.*, 1959; Whitman *et al.*, 1960; Roberts and Hardesty, 1961). In spite of the improved results it became clear at the very outset that the successful insertion of a femoro-popliteal by-pass graft was followed by a higher incidence of late graft thrombosis than in the larger and more proximal vessels (Shaw and Wheelock, 1955), and the reasons for this have been under study during recent years (Edwards, 1960). Meanwhile with the increasing study of the results of these operations certain facts have emerged which have clarified and narrowed the selection of patients for this procedure. In this report many of these points are discussed.

Clinical Material

This paper is based on the study of 95 patients (7 females, 88 males) who underwent a total of 106 femoro-popliteal by-pass procedures. All these patients suffered from atherosclerosis and had thrombosis or stenosis of the superficial femoral artery. The mean age-group of the patients was 64 years. The incidence of related disease has been assessed with regard to those conditions that are known to be associated with peripheral atherosclerosis. Three patients suffered from diabetes, a surprisingly low incidence of this disease. Six of the 95 patients had a previous history of myocardial infarction or E.C.G. changes of myocardial ischaemia. No patient, however, was suffering from angina at the time of operation. Twenty-six patients (27.5%) had a diastolic pressure greater than 95 mm. Hg. Only one

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patient had had symptoms of cerebral ischaemia, and this patient had already undergone a successful carotid endarterectomy. In the early stages of this series routine serum cholesterol estimations were not carried out, but in the last 50 patients of the series 18 (36%) had a serum cholesterol of 300 mg. or more.

Selection of Patients

There were two major indications for operation in this series—intermittent claudication and various degrees of nutritional insufficiency including gangrene. The remaining patients were operated on for replacement of aneurysmal homografs. The distribution of patients in these groups is shown in Table I. In 74 limbs intermittent claudication was the indication for operation, and in selecting these a number of factors were considered. In the majority of cases the

TABLE I.—Primary Indication for Operation

Intermittent claudication	..	..	..	74 (70%)
Gangrene	..	..	..	18 (17%)
Rest pain and ulcers	..	..	..	10 (9.4%)
Aneurysmal grafts	..	..	..	4 (3.8%)
				106

claudicating distance was less than 200 yards (182 metres) and was decreasing. Patients with static or improving claudication were treated conservatively, since the natural history of many patients with superficial femoral artery occlusion is one of spontaneous improvement. Claudication affecting the working capacity of the patient was often the most important factor in selecting patients for surgery. Where claudication was of less severe degree, or was associated with severe angina or cardiac dyspnoea, operation was not advised.

In 28 limbs the indication for operation was nutritional insufficiency, and approximately one-third of these had claudication as well. The major indication was, however, incipient gangrene, often with severe ischaemic rest pain, ischaemic ulceration, or established gangrene. The alternative to by-pass operation here was amputation, and the selection of patients was therefore less critical. Finally, four limbs in this series underwent surgery to replace aneurysmal homografs.

Examination of Patients.—Most patients suitable for a femoro-popliteal by-pass graft have a good femoral pulse with absent or weak popliteal and ankle pulses. A weak femoral pulse or a bruit above the inguinal ligament may warn the clinician that there is more proximal disease, and thigh and buttock claudication will indicate this possibility.

Radiology

Radiological investigations are of considerable help in assessing the patient, and the appropriate investigation can be chosen from consideration of the history and clinical findings. If these suggest that the obstruction is below the inguinal ligament alone, a femoral arteriogram is the investigation of choice. Where the clinical findings or history suggest more proximal obstruction, a translumbar aortogram should be performed. If this fails to show the distal vessels adequately an additional femoral arteriogram may also be required.

The general policy has been to treat proximal obstruction—that is, aorto-iliac disease—before attempting femoro-popliteal by-pass. It is illogical to by-pass a block below a more proximal obstruction, particularly as the poor inflow predisposes to thrombosis of the graft. The profunda femoris generally remains patent

and the removal of the proximal obstruction often achieves a sufficient increase in flow down this vessel to improve the symptoms even in the presence of a thrombosed superficial femoral artery. Lastly, direct arterial surgery in the aorta and iliac vessels appears to achieve a higher percentage of long-term successes than procedures below the inguinal ligament. An alternative method of handling these multiple blocks is an ilio-popliteal or aorto-popliteal by-pass. In this series two patients with multiple blocks underwent aorto-iliac endarterectomy and femoro-popliteal by-pass simultaneously, both with primary success.

Femoro-popliteal By-pass Graft

There should of course be no evidence clinically or radiologically of obstruction above the common femoral artery if femoro-popliteal by-pass is to be performed. It is also self-evident that the distal segment of the popliteal artery must be patent, and preferably free from gross disease, in order that the lower anastomosis can be performed. In most patients with an absent popliteal pulse the artery in fact remains patent, filling from collateral vessels. This can be demonstrated radiologically prior to operation. The arteriogram will also show the state of the three terminal branches of the popliteal artery—the anterior and posterior tibial and the peroneal arteries. For improvement of the peripheral circulation these vessels should obviously be patent to accommodate the outflow from the graft. In this study we have classified this factor into two groups: in group 1 the popliteal artery appeared smooth and had an adequate lumen on arteriography, and at least two of its major branches were of reasonable calibre. In group 2 the popliteal artery appeared severely diseased or two of the three major terminal branches of the artery were thrombosed.

The Operation.—In most cases the operation was carried out by two surgeons working simultaneously, with the patient in the lateral position. The femoral and popliteal arteries were exposed and an introducer was passed from the popliteal incision to the femoral triangle via the adductor canal for introduction of the graft. The graft was then joined to the femoral and popliteal arteries by end-to-side anastomosis. In a number of patients it was necessary to endarterectomize the femoral or the popliteal artery prior to anastomosis. The graft materials used in the 106 operations were: "teflon" in 42, "dacron" in 6, and homografs in 58.

Post-operative Care.—On the fifth post-operative day anticoagulation with phenindione was begun, and on approximately the tenth post-operative day the patient was allowed to start walking about the ward. Most patients were discharged from hospital about the fourteenth day and maintained on long-term anticoagulation with phenindione. This was controlled by regular estimations of the prothrombin time, which was maintained at least at twice the normal control time.

Operative Mortality.—The overall mortality in this series of 106 operations was 5. One patient died of myocardial infarction, two died of bronchopneumonia, one had a massive pulmonary embolus, and the remaining death was due to renal cortical necrosis following a period of severe hypotension during and immediately after the operation.

Operative Morbidity.—The non-fatal post-operative complications are shown in Table II. Of the five with secondary haemorrhage from sepsis, four had ischaemic

limbs—two with gangrenous ulceration and a third with acute popliteal arterial thrombosis and an acutely

TABLE II.—*Post-operative Morbidity*

Sepsis { Groin ..	7 (6.5%)	Cardiac arrest ..	1 (1%)
Popliteal ..	1 (1%)	Lateral popliteal nerve	4 (3.5%)
Deep-vein thrombosis	12 (11%)	Popliteal vein lacerated	2 (2%)
Pulmonary embolus	1 (1%)	Staphylococcal enteritis	2 (2%)
Coronary ..	2 (2%)		

ischaemic foot. It is possible that lymphangitis was a contributing factor at least in the cases of open ulceration. One of the five, however, who lost his limb from wound infection was a claudicant with no nutritional insufficiency, the organism being a coagulase-positive staphylococcus. Deep-vein thrombosis in the operated limb was the commonest complication, and occurred in 12 patients. Since the popliteal vein has to be dissected free from the popliteal artery this is presumed to predispose to popliteal-vein thrombosis and explains the frequent incidence of this complication. In only one of these patients did permanent oedema result, and this patient ultimately developed gravitational ulceration of the limb. Lateral popliteal-nerve palsy occurred in four patients and all recovered function with conservative management. These are presumed to be neuropraxias occurring at the time of the popliteal-artery dissection. The remaining complications are listed in Table II and require no further mention.

Primary Patency of Graft

Only when the graft could be felt pulsating in the popliteal fossa was it considered to be patent. In the vast majority of these functioning grafts one or more of the ankle pulses returned, or, if already present, became stronger. This change in the ankle pulses did not always occur immediately after the operation, it was sometimes delayed for a few days. Improvement in the symptoms or apparent improvement of the skin temperature alone were not recorded as primarily patent grafts.

The incidence of primary patency in these 106 grafts is shown in Table III. The results are classified according to the graft material used. It will be seen that 88% of the homografts functioned immediately after the operation. The cloth grafts gave slightly lower primary success rates, but the differences are not significant statistically. On the other hand, the outflow capacity of the arterial tree distal to the popliteal artery is an important factor in determining the percentage of successful grafts. This is demonstrated by Table IV, which shows that the primary success rate in those with a good distal arterial tree was 91%, against 45% where the outflow was poor. It therefore seems that the calibre of the distal vessels is the most important factor in deciding graft patency immediately after operation.

TABLE III.—*Primary Patency Related to Graft Material*

Graft Material	Patent	Thrombosed
Homograft	51 (88%)	7 (12%)
Teflon	31 (74%)	11 (26%)
Dacron	5 (83%)	1 (17%)
	87 (82%)	19 (18%)

TABLE IV.—*Primary Patency Related to Pre-operative Grading*

Pre-operative Grading	Patent	Thrombosed	Total
Grade 1	49 (91%)	5 (9%)	54
.. 2	8 (45%)	10 (55%)	18

In this series 15% of the homografts were known to have a grade 2 outflow, while 30% of the limbs in the teflon grafts were in this group. This difference perhaps accounts for the primary patency in the teflon grafts being 14% lower than in the homografts.

Effect of a Functioning Graft on Symptoms

The effect of a patent graft on the symptoms of 72 patients is shown in Table V. Of the 56 patients operated on for claudication, 53 (94.5%) received considerable improvement—that is, their claudication distance was at least doubled. In the majority the

TABLE V.—*Effect on Symptoms in Patent Grafts*

	Nutritional	Claudication
No better	1 (6%)	1 (2%)
Worse	1 (6%)	2 (3.5%)
Improved	14 (88%)	53 (94.5%)
Total	16	56

improvement was much more than this and many with claudicating distances of 50–100 yards (45–90 metres) were able to walk an unlimited distance at a normal speed after the operation. In one patient with claudication the symptoms failed to improve in spite of a graft which was certainly patent. This was presumably due to disease distal to the popliteal artery. Finally, the remaining two claudicant patients with patent grafts deteriorated after the operation and suffered from severe ischaemic pain, although their claudication was improved.

In the group of 16 patients with severe nutritional deficiency including gangrene 14 (88%) were improved and the limb was saved; in the remaining two the graft, though patent, failed to improve the symptoms. In one of these who presented with early gangrene there was apparent nutritional improvement, but continuing ischaemic neuritis led to amputation on account of the intractable pain. The other patient had an ischaemic ulcer which failed to heal in spite of the functioning graft.

Effect of Primary Failure on Symptoms

In 26 limbs the graft failed to function, and these are shown in Table VI. Of the 15 patients with intermittent claudication, seven showed no change in the

TABLE VI.—*Effect on Symptoms in Thrombosed Grafts*

	Nutritional	Claudication
No better	0	7 (47%)
Worse	11 (100%)	5 (33%)
Improved	0	3 (20%)
Total	11	15

symptoms following the operation, while three claimed definite improvement. In the remaining five claudicants three required above-knee amputation owing to nutritional deficiency developing immediately after the failed by-pass operation. In the other two there was no evidence that the operation accounted for the falling claudicating distance. Eleven patients with nutritional insufficiency had failed grafts, and in none of these were the symptoms improved. Ten required above-knee amputation and one required below-knee amputation in the immediate post-operative period. All of these patients, however, would have required amputation anyway.

Late Patency of Grafts

This is considered only for the homografts and teflon prostheses as the follow-up for other materials has not been long enough.

The state of the teflon and homografts at follow-up is illustrated in Figs. 1 and 2 respectively. Study of the homograft results shows that by the end of six months of follow-up three of the grafts had thrombosed—that is, 7% of the 42 grafts at risk during this period. By the end of the first year of follow-up no further grafts are thrombosed, while at the end of the second year one further graft had thrombosed—that is, 15% of the 26 grafts followed up for this period. Nineteen grafts were followed for three years and during this time 5 (26%) had thrombosed. It is thus seen that 74% of the grafts that were patent on discharge and followed for three years were still patent at the end of this period.

Of the 24 teflon grafts that were functioning on discharge from hospital, 10 (42%) had thrombosed at

FIG. 1.—Progress of patients with patent teflon grafts.

FIG. 2.—Progress of patients with patent homografts.

the end of six months. After one year of follow-up 12 had thrombosed—that is, 60% of the 20 grafts at risk during this period. This incidence of delayed thrombosis was so high that teflon prostheses have now been abandoned in favour of dacron or autogenous vein graft.

Of the patent homografts that were followed for two years, two had become aneurysmal (9%), whereas at three years 7 (50%) had developed aneurysms. Aneurysmal dilatation of the graft was not confined to those grafts which remained patent, and three of the grafts which thrombosed during the first two years developed aneurysms at their upper end. Aneurysms were not found with any of the other graft materials.

Discussion

When it is remembered that the mean age of the patients in this series was 64 years and that many had evidence of diffuse atherosclerosis the operative mortality of 5%, which includes all hospital deaths, is not unreasonably high. Of the non-fatal complications wound sepsis stands out as a complication of considerable gravity. Sepsis at the site of an arterial anastomosis led to five amputations out of seven infections in the femoral wound. All but one of these were in the group with nutritional insufficiency which would ultimately have led to amputation. The remaining patient, however, was a claudicant whose limb was not at risk.

For the graft to function there must be good downward flow—that is, no significant proximal obstruction—and a reasonable peripheral vascular bed distally to receive the increased peripheral flow. The first of these factors cannot always be excluded by the presence of equal and apparently good femoral pulses and the absence of murmurs. In the later cases in this series aortography was used more frequently and many cases with considerable aorto-iliac disease were rejected for femoro-popliteal by-pass grafts and had the proximal disease treated alone. Lumbar aortography may not always give enough definition to assess the popliteal artery and its branches, and femoral arteriography may be required as an additional investigation before final assessment can be made. With regard to the outflow, when proximal disease is excluded this appeared far and away the most decisive factor in determining primary success or failure. Indeed, in any series of femoro-popliteal by-pass grafts the overall primary success rate is likely to reflect the distribution between those patients with a good and those with a poor outflow. Good radiographs of the popliteal region and calf are probably the most reliable methods of assessing this factor.

Further information is, of course, obtained at operation, when the popliteal artery can be inspected and palpated; when its lumen is opened the state of the intima can be noted and backflow assessed. On several occasions exposure of the popliteal artery has revealed considerably more disease than the x-ray films suggested and has led to the abandonment of the operation. Backflow proved a poor guide in this series, and since closure of the popliteal artery without a graft means a narrowing of the vessel and an arterial suture line in the presence of poor flow below the blocked superficial femoral artery it is probably better to reach a decision without opening the popliteal artery.

Nor is it a simple matter of limiting the operation to those with the best peripheral vascular tree; the majority of these are in the group with intermittent claudication

alone, and calf claudication from superficial femoral artery thrombosis often runs a benign course (Singer and Rob, 1960). Often these patients will improve with no surgical treatment. Furthermore, in these patients amputation is not an immediate hazard, and one must set against the high likelihood of primary success (91%), with improvement in the claudication, the risks of life and limb from the operation itself. With the patient whose limb is in danger the peripheral vascular tree is almost certainly more diseased and primary success is less frequent (45%). With the risk to life small and night pain and gangrene already precipitating amputation, the local complications of the operation can be discounted against the chance of a successful operation with salvage of the limb. Since many of these older people would never use an artificial limb and as some have already lost one leg, this must be accounted a substantial gain. This leads us to the question of how many limbs this operation has saved in this particular series and how many were unnecessarily sacrificed after the operation.

There were 28 limbs undergoing operation for nutritional insufficiency, and 23 of these had reached a stage where immediate amputation was the only alternative. Thirteen (52%) limbs in which amputation would have been necessary were saved, but 3 of these thrombosed and required amputation in the year following operation. During this period another limb was amputated for unrelieved ischaemic pain. Therefore 9 (40%) limbs were saved for at least one year. Of the remaining 5 limbs with nutritional insufficiency that did not require urgent amputation, 4 were saved and remained viable for at least one year.

In the 84 limbs with claudication alone there were 3 amputations due to thrombosis of grafts after operation. A further 3 required amputation during the next year owing to gangrene which occurred after graft thrombosis.

In the final analysis it is the permanence of the improvement gained that must decide the usefulness of this procedure. From this series it can be seen that teflon grafts have a significantly higher rate of thrombosis than homografts. On the other hand, the late changes in the homografts with aneurysmal dilatation are clearly shown in this series, and this has been the finding of others (Szilagyi *et al.*, 1956; De Weese *et al.*, 1959). This has led to an increasing reluctance of surgeons to use homografts and a further intensive search for the ideal vascular material. It has now come to be realized that, as well as non-toxicity and durability, the physical property of porosity is important and correlates well with the histological fate of the grafts. The means of attaining a suitable porosity for better long-term functioning have already been found (Wesolowski *et al.*, 1961).

Meanwhile the lack of long-term success with the early synthetic fabrics ("ivalon" and "teflon") below the inguinal ligament has turned attention back to the patient's own tissues, and the long saphenous vein has enjoyed a return of popularity. This structure, initially employed by many workers (Guthrie, 1912), is technically more difficult to use, is tedious to obtain, and its calibre is often unsatisfactory or the vein diseased. Nevertheless, if obtainable, it may yet prove to have a significantly longer life as a functioning by-pass graft than any of the synthetic substitutes; also it avoids the implantation of foreign material in the patient's tissues.

Certain important technical improvements in the operation have improved the incidence of primary success with autogenous vein grafts (Linton and Darling, 1962) and the long-term results are proving very satisfactory. They will be the subject of a separate communication. Thus the use of better synthetic materials or the use of the patient's own saphenous vein is likely to extend the life of a functioning by-pass graft and make improvement more lasting.

In conclusion, it would appear justified to do this operation in certain patients with superficial femoral artery thrombosis and no gross proximal arterial obstruction. Where gangrene and night pain make amputation a certainty the decision is clear, and, though the likelihood of success is only 52%, the risks to life are small and the use of a limb for even a few years is desirable.

Where claudication is the only symptom the decision is more difficult. The local complications, though small, are real enough and can be serious. Thus with relatively mild and improving or static symptoms surgery should be avoided. Where the symptoms are severe and interfere with the patient's way of life, or the claudicating distance is rapidly decreasing because of the failing of the collateral system, operation should be advised. Many cases show a spectacular initial success, and with the use of better synthetic materials and the more frequent use of autogenous vein this improvement may be of considerable duration.

Summary

Ninety-five patients who underwent 106 femoro-popliteal by-pass procedures are reviewed. They were followed up for periods of between six months and three years. The indications for operation were intermittent claudication (74), nutritional changes (28), and replacement of a previously failed by-pass graft (4). The assessment of the patients clinically and radiologically and their selection for operation are discussed. The operative procedure and post-operative management are summarized. The operative mortality was 5%.

Post-operative morbidity is considered in detail; the most important complications were deep-vein thrombosis in 12 cases, wound infection in 8 cases, and lateral popliteal nerve injury in 4 cases. The danger of wound infection is emphasized, and five of these patients required amputation for haemorrhage. The patency of grafts in the immediate post-operative period was 82%.

The incidence of thrombosis at this stage is related to the radiological assessment of the distal arteries. Where the outflow was good 49 out of 54 grafts were patent, but where outflow was poor only 8 out of 18 grafts were patent. The long-term patency of the arterial homografts and teflon prostheses is considered. The homografts were found to be unsuitable because 7 of the 14 grafts patent after three years of follow-up were aneurysmal. The teflon grafts were also unsuitable, as 12 grafts of the 20 followed for one year were thrombosed at the end of this period.

The results of operation on patients with nutritional deficiency are reviewed. For 23 of these immediate amputation was the only alternative treatment. Nine of these limbs were saved for one year or more. In 84 with claudication alone graft thrombosis necessitated amputation in six limbs during the first year. In view of the poor long-term results of both the teflon prostheses

and the arterial homografts, possible alternative materials are discussed.

We would like to thank Professor Charles Rob for permission to include some of his patients who were treated at St. Mary's Hospital. All the long-term cases fall into this category.

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TUBELESS GASTRIC ANALYSIS WITH AZURE A AND MAXIMAL HISTAMINE STIMULATION

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In an effort to avoid the unpleasant procedure of obtaining gastric contents for analysis, Segal *et al.* (1950) devised a practical "tubeless" method which depends on the dissociation of a cation-exchange resin by the hydrochloric acid in the stomach. This cation is absorbed and appears in the urine, where it is easy to estimate the quantity excreted.

The first exchange resin used, "diagnex," contained quinine hydrochloride, which requires an ether-sulphuric-acid extraction of the urine and is therefore rather inconvenient for routine use. More recently, Segal and Miller (1955) simplified their tubeless technique by combining an indicator dye, azure A, with the resin (azuresin; "diagnex blue"). The azure A released by the acid is absorbed by the small intestine and excreted in the urine: the amount of dye in the urine may be measured by spectrophotometry or, more simply, by comparison with colour standards. The results of the azuresin tubeless test have been checked previously against the results of intubation following caffeine (Segal *et al.*, 1957), submaximal histamine (Fentress and Sandweiss, 1957; Poliner *et al.*, 1957; Dior *et al.*, 1957), and maximal histamine stimulation (Denborough *et al.*, 1958; Marks and Shay, 1960; Bock and Witts, 1961). Patients with a positive azuresin test almost always secrete "free" acid when tested by one of the above intubation procedures, but a negative azuresin test does not necessarily imply that the patient tested is

unable to secrete "free" acid. The high incidence of false-negative tests reported in the literature (Bock and Witts, 1961) suggests the need of certain changes. The fact that histamine is a potent gastric stimulant in man provided the opportunity to investigate the possibility of its superiority to caffeine or betazole hydrochloride ("histalog") as the gastric stimulant in the detection of achlorhydria by the tubeless gastric analysis technique.

The present study was undertaken to evaluate the azure A test with "maximal" histamine stimulation as a possible method for the quantitative assessment of acid secretion. In spite of involving two injections, it was very seldom necessary for the patients to lie flat. Above all, the method does not involve passing a tube, which is, in our opinion, the major obstacle to gastric analysis.

We were also interested in determining the value of azuresin with maximal histamine stimulation as a test of acid secretion in gastrectomized patients.

Material and Methods

We studied 100 patients, the majority of whom were in-patients. A high incidence of hyperchlorhydria was expected, for most of the patients selected were being investigated as part of a study of the augmented histamine test in peptic ulcer. The series was divided into two groups. The first group included subjects with duodenal ulcer (40 patients) and gastric ulcer (10 patients), the remainder being patients with gastric cancer, gastritis, pernicious anaemia, and other miscellaneous disorders. The second, a selected group, was made up of 20 patients who had undergone subtotal gastrectomy for duodenal ulcer.

The azuresin test was performed as described by Segal and Miller (1955) with two important modifications: (1) histamine was used as the gastric stimulant, in the dose proposed by Kay (1953) for the augmented histamine test, and (2) azuresin was given 30 minutes after the injection of histamine, following our own observations that the output of hydrochloric acid in response to the augmented histamine dose is maximal during the 20 to 40 minutes after stimulation (Carneiro de Moura, 1961).

Test Procedure.—After an overnight fast the bladder was emptied, the urine was discarded, and the patients were given an intramuscular injection of 200 mg. of antazoline ("antistin") followed 15 minutes later by a subcutaneous injection of 0.04 mg. of histamine acid phosphate per kg. body weight. The control specimen of urine was collected half an hour later, and the patients were then given 2 g. of azuresin granules with a glass of water. The total volume of urine passed during the two hours following the administration of the resin was kept for the measurement of azure A. All medication was discontinued at least 12 hours before the test.

Methods of Estimation.—The control and two-hour urine collections were diluted to 300 ml. Two 10-ml. aliquots were taken from both specimens for estimation of diagnex-azure-A content of the urine. Each aliquot was acidified with two drops of 6N HCl and then placed in a boiling water-bath for 10 to 15 minutes. This procedure converted the dye (present in a colourless conjugated form) into blue azure A compound (Segal *et al.*, 1957). The aliquots were allowed to cool at room temperature for two to four hours and their colour was compared with two standards supplied by the manu-

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