in their home environment; (3) they are sent to a sanatorium; (4) they are, in only a few instances, treated by artificial pneumothorax.

Treatment of Symptomless Adolescent Pulmonary Tuberculosis

For those who can afford the time and treatment it is probable that with rest at home, followed by gradually increasing activity and then by years of sheltered life, healing may take place. It is, however, only a favoured few who can afford this; for the majority a more rapid return to work is necessary. Moreover, it is unusual to find any person who, while apparently in good health, will submit to this treatment and at the same time retain a healthy outlook on his "illness," also the capacity to return to a normal life at the end of it.

For the majority, therefore, some other course is advised. Sanatorium treatment is the usual one adopted for these patients. Owing to the healthy condition of the patient on admission to the sanatorium and the constant urge to get home and back to work, it is usually impossible to keep him or her at the institution long enough to hope to effect a cure. There may be a temporary improvement in a few cases, but in the majority there is no material change in the x-ray picture, and the expected spread of the disease comes sooner or later after a variable interval.

It seems that artificial pneumothorax provides a more satisfactory prospect; we believe that this is the correct treatment for these cases, and it is the one which has been adopted. These symptomless patients should be ideal subjects for such treatment. As they have no constitutional disturbance it does not seem that they require prolonged bodily rest at hospital or sanatorium. Some measure of local rest to the lung is provided by a pneumothorax, and it is not necessary to attempt complete collapse of the lung: a shallow pneumothorax sufficient to control and immobilize the diseased lung, partially or completely, is what is required, and it is suggested that the pneumothorax be maintained for not longer than two or three years, by which time, on the analogy of the tuberculous joints, it is hoped the lesion will have healed. A shallow pneumothorax for a slight lesion of the lung is unlikely to give rise to complications, and causes no discomfort or subjective incapacity.

Once the collapse is established daily supervision is not necessary, and, provided that the home conditions are good, the patient need only stay in hospital for a short period. Where the home is unsatisfactory, or the patient's general condition is below normal, a period in a sanatorium may be necessary. A number of our patients have returned to work or school without any ill effects a short time after the induction of the pneumothorax. If the infiltration is bilateral the position is unaltered and the treatment is the same. A shallow bilateral artificial pneumothorax is tolerated as easily as a unilateral one, and in the case with a unilateral artificial pneumothorax there should be no hesitation in inducing a bilateral artificial pneumothorax should a tuberculous deposit appear in the other lung.

Regular supervision is ensured by the weekly attendance for refills; and this is important, because without such a tie healthy young people will naturally tend to become less and less frequent in their attendance over a period of years.

Here, then, is a form of treatment which offers a reasonable prospect of cure without prolonged exile from normal life and work. We would emphasize that, as yet, it is impossible to assess its value, but we suggest it as a reasonable alternative to other methods in use which, in our experience, are unsatisfactory in their final results or are impracticable for the majority of patients.

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PERIPHERAL ARTERIAL EMBOLISM

BY

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The surgical treatment of embolic occlusion of a peripheral artery has been developing over a long time. In 1907 both Sampson Handley and Moynihan attempted to relieve the condition by operation. In this country little attention was paid to their efforts, but the Scandinavian surgeons, led by Einar Key, developed a satisfactory operative technique, and in 1925 Jefferson performed the first successful embolectomy in England.

The incidence of embolic occlusion it is impossible to assess, but, although the condition is not common, I believe many cases are missed. Griffiths (1938) reports 8 cases in a three-year period in Manchester; and in St. James's Hospital, Leeds, from 1936 to 1939, with approximately 28,000 admissions, there were 7 cases in 5 patients, all of which came under my care.

The embolus may arise from the pulmonary veins, a vegetation on the mitral valve, a mural thrombus of the left auricle, or an atheromatous plaque of the aorta; or from a systemic vein in the presence of a patent foramen ovale. The cardiac origin is by far the commonest, and is often associated with auricular fibrillation. It was the focus in all my cases. Emboli usually become impacted at the bifurcation of an artery, for it is here that the lumen is most suddenly reduced in size. Of 382 Swedish cases (quoted by Riddell, 1937) the embolus was located in the common femoral in 54%, in the common iliac in 17%, in the popliteal in 11%, in the upper limb in 12%, and in the aorta in 4.5%. The few cases operated on in England suggest about the same percentages, and in my series four of the emboli were impacted at the bifurcation of the common femoral artery, two in the popliteal, and one at the bifurcation of the aorta.

Diagnosis

Diagnosis is usually easy, and depends on pain, pallor, paralysis, and loss of arterial pulsation in a limb. It is reported that immediately the artery is occluded the patient complains of sudden severe pain, often located over the site of the embolus. This description is inaccurate, for although pain may be severe it may also be absent. None of my patients complained of severe pain and only four of slight pain. In the case of occlusion of the bifurcation of the aorta the operative findings indicated that most probably the blockage had been sudden and complete; for there was no secondary thrombus, and yet the patient did not complain of real pain but only of abdominal discomfort. Deitch (1936) speaks of "agonizing colicky pain," and Riddell of "intense agonizing pain." The intensity or absence of the pain therefore must not influence the diagnosis.

All my patients did complain of numbness and loss of use in the affected limb. In five in whom the incident occurred while they were in hospital undergoing treatment for auricular fibrillation it was the first complaint to be made to the ward sister. The circulation was probably impaired for a few minutes before nerve symptoms appeared. In a case of occlusion at the bifurcation of the common carotid Griffiths (1938) reports sudden contralateral hemiplegia. A general pallor with some blotchy cyanosis was observed in all the affected limbs and was present within a short time of the first complaint by the patient. The limbs felt colder than the normal, and the area of anaesthesia was of the stocking type but not reaching as high as the site of impaction.

There is always loss of arterial pulsation beyond the blockage, but this may be misleading in the case of obstruction at the bifurcation of the common femoral artery. The common femoral artery is 1½ in. long, and, to the unwary, palpable pulsation below Poupart's ligament may give the impression that the femoral arteries are patent and that the blockage is in the popliteal. I found that if a sphygmomanometer cuff was applied round the mid-thigh no oscillations in the mercury column were visible at any pressure in cases of femoral blockage, but that they were easily seen in cases of popliteal

blockage. A more accurate instrument is the Pachon oscillograph, but it is rarely available.

Whether this group of signs and symptoms occurs rapidly or slowly should not affect the diagnosis, which it is important to make as early as possible.

Leriche, Fontaine, and Friehe in 1933 urged the use of thorotrast in diagnosis and in localization of the embolus, but although this method may be very accurate I feel that it should be rarely necessary.

Treatment

Opinion regarding the best treatment varies from non-operative conservation to removal of the affected part of the artery. Leaving the patient may result in spontaneous recovery, or by chance the embolus moves into a side branch of the artery, but it is more likely that he will die rapidly or after the onset of gangrene. Murray (1936) has experience of 13 cases which were not operated upon; 8 of these patients died before the onset of gangrene, and the others afterwards.

Embolectomy is not universally favoured, the dissenters claiming that it does not restore circulation in a sufficiently large proportion of cases and that too many patients fail to survive. Strömbeck (1935) reviewed 327 operations and found that 63% of the patients died in hospital and only 12% survived for five years. In spite of the failures many cases are outstandingly successful. It is accepted that patients rarely die from the operative intervention; all my cases were suffering from auricular fibrillation, yet there was no operative mortality. The patient with aortic occlusion stood the operation surprisingly well; the circulation in his leg recovered, and he survived for several months. Another patient on whom I performed a femoral embolectomy was doing her full housework one year later. Embolectomy is rarely contraindicated by the poor condition of the patient, and if performed within six hours there is a reasonable chance of success, but if after twelve there is practically none. Surgeons are therefore very largely dependent upon the general practitioner and physician for the successful treatment of the condition.

Anaesthesia was induced by spinal percarine 1/200 for all except the aortic case, for which it seemed better to use the 1/1500 solution so as to make the Trendelenburg position safer. Local anaesthesia is efficient and safe, and is of particular value when operating on the brachial and subclavian arteries. A special advantage is that the patient can describe subjective sensations, which are useful in assessing any recovery of circulation during the operation.

Operative Technique

The affected artery is approached through one of the usual incisions, and I stress that the bifurcation of the femoral is more distal than often imagined. Recent opinion has been that an aortic embolus should be milked down from the bifurcation after retroperitoneal exposure and removed through a femoral artery previously prepared but temporarily closed distally by a rubber band. I approached the aorta transperitoneally and found no difficulty. There was no unusual distension of the gut, and the patient withstood the operation extremely well. This is, I believe, the tenth successful aortic embolectomy, and of these cases four have been approached transperitoneally.

The site of the embolus is located by the cessation of pulsation. A sling of rubber tubing is placed both proximal and distal to the embolus. The proximal one is rendered taut and an incision made in the artery over the embolus. This is gently lifted out, and it usually brings with it a length of secondary thrombus; in one femoral case 8 in. of thrombus was removed. If the distal band is made taut before this stage the secondary thrombus may be broken and part of it pass along to block the artery more distally; this I believe is an important point in technique. For the same reason I think an artery which is being opened distal to the embolus—for example, a femoral in a case of aortic occlusion—should not be lifted by the slings until it is seen to be free from secondary thrombus. I found suction applied through a Eustachian catheter passed into the artery useful in removing distal thrombus. If completely cleared there should be some bleeding from the distal end.

The distal sling is then lifted and the proximal one released, when the blood pressure is usually sufficient to clear this part

of any remaining fragments. Then both slings are lifted, the wound is bathed in sodium citrate 3%, and the artery wall quickly sutured with waxed Chinese silk size 0, the stitches passing down to but not through the intima. It is surprising how few stitches are required.

This was the technique followed in my cases, including the aortic, in which the slings were placed around the aorta and common iliacs while the incision was made just above the bifurcation.

If the distal circulation shows no signs of recovery within one hour a more distal exploration of the artery must be considered, but it should be remembered that circulation may improve without recovery of peripheral pulsation.

Other operations described for the relief include ligation of the artery above and below the incision after removal of the embolus, the intention being to prevent post-operative thrombosis. A more radical device is the excision of the affected part of the artery, it being maintained that complete section of the artery prevents spasms and tends to open up the collateral circulation.

I have no experience of the post-operative use of heparin, but it seems probable that this may prevent post-operative thrombosis in the affected vessel. The dosage recommended is 10 units of heparin to 1 c.cm. of saline given by intravenous drip at the rate of 25 to 30 drops a minute, or 1,500 units four-hourly if given intermittently.

Summary of Cases

Case 1.—Man aged 57, admitted Dec. 18, 1936, with auricular fibrillation and mild cardiac incompetence. Cardiac condition improved but fibrillation persisted. On March 6, 1937, there was a sudden onset of numbness without pain in right leg. Five hours later, when first seen by me, the signs of occlusion of the popliteal artery were typical. Under spinal anaesthesia an embolus was removed through the popliteal artery from the level of the adductor hiatus. No thrombus could be extracted from the distal point and there was no return of blood from it. The artery was closed, but the circulation did not recover and amputation became necessary. There may have been a more distal embolus or the thrombus may have broken away during the exposure of the artery. It might have been better to excise the affected portion of the artery, but the chance of recovery must have been remote.

Case 2.—Man aged 64, admitted Nov. 30, 1938, with auricular fibrillation, palpable liver, and basal pulmonary congestion. On Dec. 5 he developed a typical occlusion of the left femoral artery without any pain. The embolus with three inches of thrombus was removed under spinal anaesthesia three hours later, and the circulation of the limb recovered completely. On Dec. 9 the right popliteal artery became blocked and an embolus was removed from it. The circulation did not recover, and the next day he developed a paralysis of the right arm, followed in twelve hours by a hemiplegia, and he died. The terminal signs were probably due to a blockage with spreading thrombosis in the cerebral circulation. No necropsy was granted.

Case 3.—Woman aged 53; she had several transient attacks of pain and loss of use in the left leg and arm and right leg. Admitted Feb. 5, 1939, fourteen hours after the onset of pain and loss of use in right leg. Auricular fibrillation was present, but the only evidence of failure was albuminuria. A diagnosis of femoral block was made and an embolus was removed, but no thrombus could be extracted and there was no bleeding from the distal end. Gangrene developed, necessitating amputation. The cardiac condition then improved and she went home on April 6. On April 12 she was readmitted with a right femoral blockage of six hours' duration. An embolus with four inches of thrombus was removed. The circulation was almost normal after twelve hours, but became deficient again, with the development of gangrene. A rapidly increasing bacterial endocarditis appeared, and the patient died on May 4. No necropsy was granted, but I think a secondary thrombosis may have caused the failure in the second embolectomy.

Case 4.—Man aged 28, admitted April 5, 1939, because of dyspnoea, cough with blood-stained sputum, and oedema of feet. A diagnosis of auricular fibrillation with failure was made. He was given digoxin 0.25 mg. t.d.s., and his pulse, though still irregular, fell from 110 to 72. On April 13 he suddenly complained of numbness of both legs and a little abdominal discomfort. When seen one hour later there was a blotchy discoloration below the knees, with loss of use of both legs and anaesthesia of stocking type reaching almost to the knees, and no femoral pulsation. A diagnosis of occlusion at the bifurcation of the aorta was made. He was operated on under spinal percarine anaesthesia. The embolus was removed through the aorta, which was approached transperitoneally. There was no post-operative shock and the patient's condition remained good. The

circulation had recovered completely after two hours—i.e., four hours after the blockage—and full use of the legs was regained. His cardiac condition did not improve and he developed a subacute bacterial endocarditis, but he was lost sight of at the time of the forced hospital evacuation in Sept., 1939.

Case 5.—Woman aged 36, admitted April 12, 1939, with auricular fibrillation and slight cardiac failure. She was given small doses of digitalis, and on May 5 developed a right femoral occlusion with the typical signs and slight pain. She was operated on within four hours under spinal anaesthesia, and an embolus together with 8 in. of thrombus was removed. The circulation recovered perfectly and pulsation of the posterior tibial artery at the ankle could be felt after a few hours. She left hospital, and although still fibrillating was doing most of her housework one year later.

I wish to thank Dr. J. Dick, medical superintendent, St. James's Hospital, Leeds, at which hospital I was working, for permission to publish these cases.

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GLOBIN-ZINC-INSULIN: SOME EXPERIMENTS

BY

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The above new delayed-action insulin—a compound of ox globin, insulin, and a trace of zinc—is already on the market in America, where several articles (see Bibliography) have been published on its action on animals and use in diabetics. These reports seem to have been thought so favourable by the British manufacturers and authorities that I gather it is already licensed and may soon appear for sale. It has received no proper clinical trial in this country (not easy in wartime); but even were it proved to be more useful than protamine-zinc-insulin, it seems doubtful wisdom to introduce another new type of depot insulin without withdrawing the old, as this is sure to confuse clinical practice. Moreover, any real new merit in globin insulin is not apparent to me either from the published works or from the following trials of a supply kindly provided by the courtesy of Burroughs Wellcome and Co.

It is generally agreed that soluble insulin is strong but too short-lived in action, and P.Z.I. weak but prolonged and apt to cause serious hypoglycaemia at night if too large doses are given in an attempt to stop glycosuria after meals. It is hoped that G.Z.I. will be intermediate in action and, with one injection before breakfast, will act strongly and control sugar by day,

lished shows many irregularities and contradictions, and, when one discounts the bias in favour of something new, little real difference. I have substituted 20 to 40 units of G.Z.I. for P.Z.I. in 6 mild cases under hospital control, and my colleague Dr. Wilfrid Oakley has tried other cases, without being able to appreciate any difference on blood and urine tests. I have not compared a series of severe cases in this way, as the results from day to day on any depot insulin are so irregular as to make such a study valueless. But the accompanying table shows the results of what is probably the least erroneous clinical method—the effect of equal doses of different insulins on the fasting blood sugar of a severe diabetic followed for 24 hours without carbohydrate food.

A diabetic man aged 35, on insulin five years, feeble-minded but otherwise organically normal, was the subject. His insulin had varied from 40 to 50 units a day, and was kept at 20 and 16 units during the experimental period. Once a week the evening dose was omitted so that the patient was thoroughly diabetic next morning, and after two fasting blood-sugar estimations at 7 and 8 a.m. (a wise precaution) the same test dose, 32 units, of the different insulins was given. The effect on the blood and urine was followed two-hourly, later three-hourly, for 24 hours, during which time no carbohydrate food was given, but some protein—meat, bacon, etc.—was allowed, which I always find does not affect the blood sugar although it probably increases ketosis. The table shows the blood-sugar results and the ketonuria by Rothera's test—more informative than the glycosuria, which ran strictly parallel. The fasting blood sugars are at a fairly uniform level and the comparisons on the whole satisfactory, although some tests (the blood sugars mostly in duplicate) were lost. Perhaps the contrast would have been clearer with a larger test dose; but any risk of hypoglycaemia had to be avoided, as quite small restorative doses of sugar may raise the blood sugar considerably in such protamine experiments and completely spoil the curves.

It is clear that soluble insulin is much the most active, that neither G.Z.I. nor P.Z.I. gives any very active liberation of insulin during the 24 hours, and that there is no practical difference between the general trend of their action. G.Z.I. seems to come into action more quickly (4 to 6 hours after injection), but its maximum effect is shown at 15 to 18 hours—no different from P.Z.I., and still making the night the most likely time of hypoglycaemia.

There are other points against the present introduction of globin insulin which are more obvious from the clinical than from the laboratory angle. It is clear that its action is weak and that it will have to be supplemented, like P.Z.I., in many cases with soluble insulin. At present a large number of cases are treated with a mixed injection of P.Z.I. and soluble insulin, and we know that some of the soluble is converted by the excess of protamine. We do not know if G.Z.I. contains an excess of globin nor what is the result of mixing G.Z.I. and soluble; but this is of great practical importance, and now is the stage when the initial mistake made with P.Z.I. might be

Time in Hours	Globin Insulin at								P.Z. Insulin				Soluble Insulin			
	I		II		III		IV		V		VI		VII		VIII	
	32 Units Globin		32 Units Globin		32 Units Globin		32 Units Globin		32 Units P.Z.I.		32 Units P.Z.I.		32 Units Soluble		20 Units Soluble	
	Blood Sugar (mg. %)	Urine Ketosis Rothera	Blood Sugar (mg. %)	Urine Ketosis Rothera	Blood Sugar (mg. %)	Urine Ketosis Rothera	Blood Sugar (mg. %)	Urine Ketosis Rothera	Blood Sugar (mg. %)	Urine Ketosis Rothera	Blood Sugar (mg. %)	Urine Ketosis Rothera	Blood Sugar (mg. %)	Urine Ketosis Rothera	Blood Sugar (mg. %)	Urine Ketosis Rothera
7 a.m.	164	0	258	+++	263	+++	282	+++	233	—	278	+++	256	+++	265	+++
8 a.m.	260	Sl. tr.	Lost	—	278	+++	267	+++	233	+++	285	+++	241	+++	256	+++
2 hours	250	+	260	—	285	+++	260	+++	256	+++	282	+++	235	+	222	+++
4 "	260	++	215	—	217	+++	263	+++	256	+++	267	+++	180	++	177	+++
6 "	202	++	190	+++	210	+++	244	+++	250	+++	263	+++	137	+	145	++
8 "	210	—	210	—	Lost	+++	210	+++	256	+++	266	+++	91	Sl. tr.	204	+++
10 "	218	+++	183	+++	210	+++	244	+++	244	+++	278	+++	90	+	—	—
12 "	206	+	183	+++	244	+++	227	+++	250	+++	259	+++	133	++	—	—
15 "	167	Trace	167	+++	241	+++	215	+++	217	+++	218	+++	—	—	—	—
18 "	194	+	194	+++	244	+++	169	+++	170	+++	190	+++	—	—	—	—
21 "	190	0	213	++	244	+++	177	+++	187	+++	198	+++	—	—	—	—
24 "	Not done	—	213	—	238	+++	220	+++	230	+++	200	+++	—	—	—	—

especially in the afternoon, but will tail off and avoid hypoglycaemia at night, though retaining enough action to prevent a serious diabetic relapse before breakfast—a worthy ambition but a tall order for any one preparation. On the whole the publications and opinions expressed in America suggest that G.Z.I. has more action in lowering blood sugar near from 4 to 12 hours after injection and less from 12 to 24 hours than P.Z.I. But a close study of the few detailed protocols pub-

avoided. The manufacturers must know the problem of mixed injections, because I have urged them for years to try to produce a P.Z.I. without an excess of protamine (I gather it contains twice as much protamine as is necessary to precipitate the insulin) so that varying mixtures of P.Z.I. and soluble could be injected with more predictable results. Again, the fact that P.Z.I. is cloudy and soluble insulin clear is a great safeguard against mistakes between delayed-action and quick-