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RESULTS OF AMNION IMPLANTATION IN PERIPHERAL VASCULAR DISEASE

BY

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Troensegaard-Hansen (1956) states that the implantation of human amnion into the thigh, in patients with peripheral vascular disease with intermittent claudication, brings great improvement—for instance, in 60 cases, 49 had complete cure of the claudication, 7 were much better, and there was 1 failure. The cause for the improvement was obscure. Some of the amnion was prepared by Mr. Troensegaard-Hansen himself, but most was supplied by the research department of Messrs. Smith and Nephew.

Although the rationale of the treatment was obscure, the excellent results quoted and the lack of any other treatment for claudication seemed to justify a trial. The results in seven cases are therefore given. The amnion was prepared locally for the first patient; the remainder was supplied by Messrs. Smith and Nephew. The implants were placed in the thigh of the worst side, deep to the fat, using local analgesia; the patients were not kept in bed at all.

Case Reports

Case 1.—A man aged 65 was seen in August, 1956, complaining of typical intermittent claudication coming on after walking 30 yards, with occasional rest pain in the right calf. The trouble had begun on the right side in 1955, and appeared on the left side in 1956. His feet were cold and clammy and there were no pulses to be felt below the groins. B.P. was 180/100. An arteriogram on the right side showed that the femoral artery was occluded from the profunda to the adductor opening. September 24: Amnion graft implanted. There was no improvement. September 26: Amnion graft repeated. After this the patient stated there was gradual improvement, that his feet were warmer and that he could walk up to one mile, but this did not last. On February 9, 1957, his feet were cold and the distance he could walk was lessening. On February 27 the claudication was at least as bad as before graft; his feet were cold. Next day bilateral lumbar sympathectomy was performed. After this the patient claimed steady improvement in the distance he could walk and in the warmth of his feet. Further progress is awaited with interest.

Case 2.—A woman aged 65 was seen on May 7, 1955, complaining of typical intermittent claudication for two

years, which was becoming gradually more severe and was worse on the right side, the pain beginning after walking 100 yards. Her B.P. was 240/110; her feet were fairly warm, but no pulses were palpable below the femorals. May 10: Left femoral arteriogram showed irregular narrowing and short blocks in the femoral artery as far as the knee, where it was entirely blocked; anterior tibial artery patent at its origin but occluded distally. The other leg vessels were not shown. May 11: Bilateral lumbar sympathectomy. In September claudication was much better. In August, 1956, the claudication was still present, but she said it was better—but difficult to ascertain how much better. Amnion graft implanted in September. June, 1957: Has shown no improvement of any sort following the graft.

Case 3.—A man aged 37 was seen in October, 1956, complaining of aching pain in the left calf when he walked rather less than half a mile; this used to pass off after a few minutes' rest. He had had this for six months, but had had similar trouble in both feet for five years, for which he had been treated with heel lifts, etc., with temporary improvement. November 2: Left arteriogram showed complete block of the femoral artery as far as the adductor opening. Amnion graft implanted. November 14: Patient felt claudication distance had increased up to 1,000 yards or more. December 12: Claudication distance 250/300 yards—not so severe as previously; able to carry on slowly; foot pain absent. February 9, 1957: Walking distance diminished—feet cold and blue. February 27: Bilateral lumbar sympathectomy.

Case 4.—A man aged 60 was seen in November, 1956, complaining of typical intermittent claudication in both legs, but worse on the right side. He had had this trouble since June, 1952. Left lumbar sympathectomy in June, 1954, had given a good result, but operation on the right side had not. His B.P. was 220/140. All the pulses were palpable in the left leg, but only the femoral on the right side. November 30, 1956, arteriograms showed that the right femoral artery was occluded as far as the adductor opening; the left femoral was patent but most irregular in outline. Amnion graft implanted. December 9: Patient stated that his feet were warm for the first time for four years and that there was some improvement in the claudication. February 20, 1957: Patient stated that his feet were warm but claudication was worse. April: Patient stated that the claudication was becoming worse.

Case 5.—A man aged 67 was seen on August 4, 1955, complaining of typical intermittent claudication in the left calf for six months. Walking now reduced to 50 yards. No symptoms in right leg. There was obvious arterial deficiency of the skin of both legs. There were no pulses below the femorals. B.P. 200/120. Heart enlarged. August 23: Bilateral lumbar sympathectomy. November 15: Patient thought his condition was better; but the skin blood supply was obviously most precarious, and he had night pain. January 11, 1956: Patient stated he was much better. June 27: No change. December 19: Right foot satisfactory; left foot still precarious, but no worse. January 3, 1957: Patient stated claudication distance was now 500 yards. January 4: Arteriogram—left—showed that the whole length of the femoral artery was occluded. Amnion graft implanted. February 9: Patient stated claudication definitely better, but skin obviously unchanged. February 23: Patient said he was back to pre-amnion condition. May, 1957: Patient considered there was no improvement—there was certainly no improvement in the skin.

Case 6.—A man aged 59 was seen in May, 1956, with a history of discomfort in the right big toe for two years and discomfort in the right little toe for 18 months, becoming worse. The foot became very cold and he occasionally had discomfort at night. There was no apparent claudication, but it was difficult to be sure, as he could not walk far because of his toes. On examination the right foot was cold and all the toes were rather blue—first and fifth worst. Popliteal and femoral pulses palpable—nil below. Left foot: no symptoms, foot cold, big toe slightly cyanotic,

all pulses palpable except anterior tibial. Right lumbar sympathectomy performed on June 4, 1956. August: Good result—no claudication. January, 1957: Some soreness under big toe and increasing discoloration. February 5: Arteriogram showed localized block at about the adductor opening. Amnion graft carried out. May 18: No improvement at all.

Case 7.—A woman aged 65 was seen in February, 1957, with a history of typical intermittent claudication which had begun in November, 1956, on the left side—the claudication distance was 25 yards. She complained also of cold feet, particularly on the left side. Dyspnoea, orthopnea, and angina also limited walking. B.P. 200/150. On left side only femoral pulse palpable. On right side popliteal and dorsalis pedis pulses could also be felt. Left foot cold. April 5: Left arteriogram showed that the femoral artery was patent as far as the adductor opening, but was grossly irregular, and below this there were only poor collateral vessels. Amnion graft implanted. June 13: No improvement of any sort.

Summary and Conclusions

Seven patients with arterial deficiency of the lower limbs were treated by the implantation of "amnion grafts."

The results of the trial were judged by subjective findings only for the claudication—that is to say, the patient's account of any changes which occurred—and by the effects on the skin, judged clinically.

Some of the patients claimed temporary relief of the claudication, but all returned to their previous state quite soon.

None showed any improvement in the skin.

This trial therefore showed no benefit in any patient as a result of the amnion graft.

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Medical Memoranda

Agranulocytosis and Anaemia Associated with Disseminated Tuberculosis

Blood changes associated with disseminated tuberculosis have been reviewed by Fountain (1954), who reported four fatal cases. A further case, presenting with pyrexia, anaemia, and granulocytopenia, and treated with streptomycin, is here reported.

CASE REPORT

A farmer aged 54 was admitted to hospital on July 16, 1954, with a three-weeks history of increasing weakness, lassitude, dizziness, dyspnoea, oedema of the ankles, anorexia, and constipation. There had been slight loss of weight. He had never been ill before and there was no relevant family history.

Examination showed a well-covered man weighing 13 st. 9 lb. (86.6 kg.). The temperature was 101.3° F. (38.5° C.) and pulse 80. He was flushed, sweating, and rather drowsy, with a dirty furred tongue. There was clinical evidence of anaemia and the lower pole of the spleen was palpable 2 in. (5 cm.) below the left costal margin. The liver was also palpable, but there was no adenopathy. No abnormality was found in the cardiovascular, respiratory, and nervous systems.

Investigations.—X-ray examination of the chest on admission showed no evidence of miliary tuberculosis or lung disease. Blood examination was as follows: Hb, 50% (Haldane), 7.4 g. per 100 ml.; red cells, 2,250,000 per c.mm.; C.I., 1.13; P.C.V., 25 vols.%; M.C.V., 113 cubic microns;

reticulocytes, 1%; white cells, 3,200 per c.mm. (neutrophils 33%, lymphocytes 66%, monocytes 1%); bleeding-time, 2 minutes. A blood film showed well-haemoglobinized red cells, macrocytes being prominent. There was a relative lymphocytosis, but no immature cells were seen. Sternal marrow examination revealed intense hypoplasia, the granulocytic series being more seriously affected than the erythroid. Erythropoiesis was normoblastic. A test meal showed the presence of free hydrochloric acid. Red cell fragility was normal and there was no urobilinogen in the urine. Blood cultures were sterile and agglutination reactions negative for *Brucella abortus* and *Leptospira icterohaemorrhagiae*. *Salm. typhi* O and *Salm. paratyphi* B O were positive to a titre of 1/80 and 1/20 respectively. There was no further rise in titre. The stools were repeatedly negative for occult blood and pathogenic organisms.

These investigations did not give any indication of the nature of the underlying disease. The diagnosis was obscure, enteric fever, atypical Hodgkin's disease, aplastic anaemia, aleukaemic leukaemia, and tuberculosis being regarded as possibilities.

The pyrexia continued with a remittent temperature up to 102° F. (38.9° C.), and five days after admission the white cells had fallen to 400 per c.mm., 85% being lymphocytes. There was no appreciable change in the haemoglobin level or red-cell count.

In view of the rapid development of granulocytopenia, treatment with penicillin was started, and blood transfusions were given. There was no response to treatment with penicillin and subsequently chlortetracycline. The patient remained gravely ill, with a persistent pyrexia, anaemia, and granulocytopenia.

Three weeks after admission there was still no firm diagnosis. A further x-ray examination of the chest showed no abnormality, and no choroidal tubercles were visible in the fundus oculi. A blood count showed: Hb, 60% (Haldane); red cells, 2,430,000 per c.mm.; white cells, 400 per c.mm., granulocytes being absent. The patient's condition was critical owing to anaemia, exhaustion, and toxæmia from developing agranulocytic angina.

On suspicion that undiscovered disseminated tuberculosis might be responsible it was decided to start treatment with streptomycin, 1 g. twice daily. Penicillin was restarted at the same time in view of the agranulocytic angina. This treatment, with further blood transfusions, was continued until the patient's death 10 days later.

During the short time that streptomycin was given there was no improvement in the blood picture, the pyrexia, or the patient's condition. Death resulted from toxæmia and terminal bronchopneumonia.

Necropsy Findings and Histology.—The lungs showed terminal oedema and bronchopneumonia. No areas of caseation or follicular reaction were present. The liver showed multiple small areas of caseation with, in some instances, a fibroblastic reaction in the margin. The histological picture was dominated by caseation. The spleen showed very large numbers of tubercles undergoing caseation. Fibrous tissue was present around some of these tubercles, and the lesions varied in age. It was thought that none was older than six weeks. Tubercle bacilli were found in the spleen. The bone marrow showed marked inactivity with greater depression of the granulocytic series than of the erythroid cells. A few tubercles were present, but they showed little caseation and appeared very recent. There was no evidence of tuberculosis in the kidneys or adrenals, and the primary focus of infection was not discovered.

The post-mortem diagnosis was miliary tuberculosis of the liver, spleen, and bone marrow.

COMMENT

The problem presented by this case was largely one of diagnosis, and, with potent chemotherapeutic agents available for the treatment of tuberculosis, early diagnosis is essential.