HEREDITY AND LEG ULCERS

BY

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Accurate knowledge of the aetiology of any disease is necessary for its rational treatment. This applies equally to preventive treatment, and it was with this in mind that the present investigation was carried out to learn more about heredity in relation to gravitational ulcers of the leg.

Its place in the aetiology of these ulcers has never been soundly established, though many authors have expressed the opinion that it may be important. Weber, Rast, and Lutterotti (1930) described chronic ulceration of the legs following pneumonia in a man aged 25 with thromboangiitis obliterans whose father had suffered from similar ulcers, and Carleton (1948) reported a striking family history in two sisters with leg ulcers. Weber (1948) wrote that there certainly is a constitutional tendency to *ulcus cruris* in some families. Heredity undoubtedly plays a part in ulceration of the legs associated with purpura haemorrhagica, sickle-cell anaemia, congenital haemolytic icterus, splenic anaemia, Gaucher's disease, and Cooley's anaemia (Weber and Dörner, 1910; Weber, 1930; Taylor, 1939; Cummer and LaRocco, 1940; Witts, 1942; Woofter, Dick, and Bierring, 1945; Estes, Farber, and Stickney, 1948), but these conditions account for few of the leg ulcers seen here.

There is more evidence of the importance of heredity in the aetiology of varicose veins. Virchow (1855-61) recognized this, and Gay (1868) reported two affected families. Curtius (1928) published several pedigrees and Čičováčki and Stöger (1939) recorded one which showed that the condition is inherited as a dominant character. Ottley (1934) examined a series of 50 patients, and found that the inheritance was of a simple dominant type in 26 families; in another 10 either a recessive character was concerned or the usual dominant type was masked in predisposed individuals.

In patients with varicose veins a positive family history was found in 50-75% by Magnus (1921), 55% by Nicholson (1927), 65% by de Takats and Quint (1930), 56% by Jensen (1932), over 50% by Payne (1936), 43% by Larson and Smith (1943), only 6-10% by McPheeters and Anderson (1946), and 80% by Pratt (1950). A positive family history of varicosis might therefore be expected in many patients with leg ulcers resulting from varicose veins, and this has been noted by Bauer (1948).

Present Investigation

A series of 525 patients examined personally has been investigated to try to determine more precisely the place of heredity in gravitational ulceration.

Here the term "positive family history" indicates that ulcers or varicose veins are known to have been present in one or more parent, sibling, child, uncle, or aunt. Varicose veins rarely appear before the age of 20 (McPheeters and Anderson, 1946; Roberts, 1949), and in the present series ulceration before that age developed in only 17 patients (3.2%). Because of this and the difficulty in obtaining information about grandparents, pedigrees dealing with many generations are rarely obtained. Eighty pedigrees have been determined, but in many of them

accurate information is limited to parents, siblings, and children.

It is not easy to discover the complete family history of patients with leg ulcers unless several members of the family can be examined, and this has seldom been possible here. Although the presence of ulcers and varicose veins in parents, siblings, and children may be known by the patient, accurate pedigrees which include other relations are difficult to obtain, as these conditions are not commonly disclosed.

Of the 525 patients (360 women and 165 men) examined, 29 were unable to give a family history, and of the remaining 496 a family history of ulcers or varicose veins was present in 256 (51.6%). As, however, the variety of causes of gravitational ulcer makes such figures of little value, an

Details of Family History

Cause of Ulcer	No. of Patients	Family History Known	Negative Family History	Positive Family History					Total	%
				Without Details	History of V.V.	History of Ulcers Only				
Thrombotic:										
Post-partum thrombosis ..	111	103	48	15	30	10	55	17	53.4	
Ante-partum thrombosis ..	28	28	11	9	5	3	17	3	60.7	
Disease of leg:										
Injury without fracture ..	101	97	48	15	26	8	49	5	50.5	
Injury with fracture ..	22	22	17	1	4	0	5	22	22.7	
Infection of leg ..	20	19	15	2	2	0	4	22	22.2	
Treatment of varicose veins ..	28	28	11	5	10	2	17	60.7		
Operation on leg ..	9	8	3	2	3	0	5	62.5		
Burns of leg ..	5	4	4	0	0	0	0			
Thrombosis — unknown cause ..	39	35	13	7	13	2	22	62.8		
Recumbency:										
Medical illness ..	34	32	20	2	5	5	12	37.5		
Operation—not on leg ..	19	18	9	2	7	0	9	50.0		
Other causes ..	4	4	1	1	2	0	3			
Miscellaneous causes ..	5	5	1	0	3	1	4			
"Silent" thrombosis ..	9	9	6	1	1	1	3	33.3		
Non-thrombotic:										
Varicose ulcers ..	32	29	3	2	22	2	26	89.9		
Arteriosclerotic ulcers ..	6	6	2	0	0	4	4			
Arthritic ulcers ..	5	5	2	0	3	0	3			
Doubtful cause (with varicose veins) ..	44	40	24	4	8	4	16	40.0		
Doubtful cause (without varicose veins) ..	4	4	2	1	1	0	2			
Total ..	525	496	240				256	51.6		

attempt has been made to break up the series into different aetiological groups. The accompanying Table shows the number of patients with a positive family history in each of these groups.

In considering the incidence of positive family histories in the various groups in the table it must be remembered that varicose veins are common, and leg ulcers not uncommon, in the general population of this country. Roberts (1949) found, in the examination of 10,000 candidates applying for Post Office appointments, a mean incidence of 1.57% of men and 1.68% of women with varicose veins. All age groups were included, though most males were under 45 and most females under 25. In a social survey conducted in 1947 (General Register Office, 1950—personal communication) of 30,843 men and 38,503 women of all ages over 16 years, varicose veins were found in 1.03% of men and 3.13% of women. The highest incidence (4.18%) occurred in the 11,440 women aged 45-64 years. Less is known about the incidence of leg ulcers, but it has been stated (Annotation, 1950) that about 5 per 1,000 of the population are affected.

It has not been found possible, from these figures, to estimate the incidence of positive family histories to be

expected in the general population, and the determination of this incidence by questioning a random group has not been carried out.

The Thrombotic Group

However, ulceration from thrombosis after fracture, burning, infection, or operation affecting the leg would seem to result from causes less susceptible to hereditary influences than some, and more likely to result from chance. (The group with injury of the leg without fracture has not been included, as it is heterogeneous, the degree and mode of injury being very variable.) Of the 56 patients concerned, 25% gave a positive family history. As hereditary factors may have played some part in causing the thrombosis which occurred in these patients (and this seems to have been so in the operation group), it cannot be argued that this incidence of positive family histories represents that to be expected in the general population, yet it provides a useful comparison with the incidence found in other groups of patients with ulcers.

In the thrombotic group, 53.4% of patients with ulcers caused by post-partum thrombosis gave a positive family history. This incidence is significantly higher than that expected (25%), and it is worthy of note that the mothers of 10 of these patients and the sisters of 2 of the 10 had also suffered from post-partum thrombosis. Special precautions to prevent thrombosis seem to be indicated in parturient women with a family history of varicose veins, leg ulcer, or thrombosis, especially if the confinement be difficult (Anning, 1949).

Among the other patients in the thrombotic group, those with ante-partum thrombosis, and thrombosis due to treatment (especially injection) of varicose veins, to operation on the leg, and to unknown causes, had a significantly higher incidence of positive family histories than that expected, and this is possibly also true of patients with thrombosis due to injury without fracture. In thrombosis from recumbency and in "silent" thrombosis, heredity seems to play a doubtful part.

The Non-thrombotic Group

In the non-thrombotic group heredity is clearly of major importance in varicose ulcers—that is, ulcers due to varicose veins alone—a positive family history being present in 89.9%. A family affected in this way is shown in pedigree 1. Here gross varicose veins were present, but ulceration occurred only in two members, probably because most of the affected members wore elastic supporting bandages or stockings. Sitting back on her heels, kneeling, caused thrombosis in one member (III, 2).

In varicose ulcers it is possible that not only congenital weakness of the wall of the veins but congenital absence of valves may also play a part (Eger and Casper, 1943; Curtis and Helms, 1947). The importance of defective valves in the deep veins in this type of ulcer has been stressed by Warwick (1931), Luke (1941), and Bauer (1948).

The number of patients with ulcers thought to be due primarily to arteriosclerosis is small, but of these a large proportion gave a family history of ulcers of the legs (without varicose veins), and such a family is shown in pedigree 2. Only the three youngest women in the second generation were examined. They each had cold extremities, cyanosis of the toes, tortuous radial arteries, impalpable dorsalis pedis arteries, and radiological evidence of calcification of arteries in the leg. There was hypertension.

PEDIGREE 1.—Ulcers due to varicose veins alone. (Key on Pedigree 3.)

PEDIGREE 2.—Ulcers of the legs (without varicose veins) due primarily to arteriosclerosis.

PEDIGREE 3.—Varicose veins, thrombosis from various causes, and ulcers.

It will be noted that, apart from the arteriosclerotic group, the proportion of patients with a family history of ulcers only is small compared with that of patients with a family history of varicose veins. A tendency to thrombosis occurs in some families, occasionally without primary varicose veins, but more commonly in association with them. (Here primary varicose veins must be distinguished from those appearing secondarily to the thrombosis.) Primary varicose veins seem to be the common factor in the family history, when positive, of most patients with leg ulcers of the post-thrombotic and the varicose types. A family with varicose veins, thrombosis from various causes, and ulcers is shown in pedigree 3. Here, in the first generation, the husband had a leg ulcer and his wife varicose veins; of their 10 children the eldest fractured her left tibia and fibula at the age of 46; thrombosis followed while the leg was in plaster-of-Paris and an ulcer appeared when she was 48; the second had a post-partum thrombosis followed by ulceration; the third had varicose veins; the fourth had thrombosis for no known cause and ulceration later; the sixth and seventh had varicose veins which were operated upon, an ulcer appearing after the operation in the seventh; of the third generation, one had an ulcer.

Conclusion

The presence of a familial tendency to ulceration, except in the arteriosclerotic group, is usually associated with the inheritance of varicose veins; this applies to post-thrombotic as well as to varicose ulceration. It must not be assumed, however, that varicose veins are present in an individual before thrombosis occurs, as this is not usually so. It means merely that thrombosis, unless caused by fracture or infection of the leg, seems more likely to occur in individuals with a family history of varicose veins.

Where thrombosis may occur, as in parturient women, patients recumbent for medical or surgical reasons, and those with fractures of or undergoing operations on the leg, special efforts should be made to prevent it if there is a family history of varicose veins, thrombosis, or ulcus cruris.

Summary

The influence of heredity in gravitational ulceration of the leg has been investigated in a series of 525 patients.

The significance of the family history has been considered in various groups of patients with ulcers from different causes.

The implications of the family history in regard to prevention of thrombosis are mentioned.

I am grateful to Dr. John T. Ingram and Dr. F. F. Hellier for allowing me to carry out this investigation on their patients, and to Dr. Percy Stocks and Miss Eileen M. Brooke for providing me with information from the General Register Office.

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The London Area Mobile Physiotherapy Service (L.A.M.P.S.) is a voluntary society founded in May, 1948, to provide physiotherapy at home to those who cannot afford to pay, since it became clear that the National Health Service would, for some years at least, be unable to provide such a service. About 30,000 members of the Home Nursing Scheme have automatically come into the society, and some 250 private physiotherapists are providing the treatments, which in the year 1949-50 amounted to nearly 4,000.

TREATMENT OF POST-PHLEBITIC LEG AND APPLICATION OF VENOUS-PRESSURE MEASUREMENT*

BY

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Homans (1941) was the first to champion ligation of the superficial femoral vein in the treatment of the post-phlebitic leg. He argued that the condition was due to valvular incompetence in the main leg veins as a result of the thrombus recanalizing, and that ligation of the superficial femoral vein, harmless when performed for other conditions, was likely to do good. His lead was followed by Buxton *et al.* (1944), who recorded 21 cases, later increased to 26 (Buxton and Collier, 1945). Linton and Hardy (1947) published 34 cases (58 legs), later raised to 49 (84 legs) (Linton and Hardy, 1948), in which they stripped the long saphenous vein as well. Glasser (1949) and Sandegård (1949) published 91 (40 cases followed up) and 32 cases respectively, the latter selecting his patients for operation by the retrograde phlebogram method of Bauer (1948).

Bauer in his paper advocated the ligation of the popliteal rather than of the femoral vein and published the result of 24 cases, later increased to 196 (Bauer, 1950). I have set out the results claimed by these authors in Table I. Ulcers are claimed to remain healed in 70-100% of cases, bursting pain is usually cured, but oedema persists in a disappointingly high proportion of those treated, except in Bauer's hands.

Impressed by Bauer's arguments and results, we have employed his methods at St. Bartholomew's Hospital on a series of 30 legs. This paper presents the results of this treatment, and the application of venous-pressure measurements in the selection of cases. The division and ligation of the vein is done through a 3-in. (7.6-cm.) vertical incision in the upper half of the popliteal fossa. Afterwards the knee is kept extended for five days to aid healing, but early walking with a crêpe bandage is allowed. Rapid healing is ensured if the joint crease is not transgressed.

Material

Twenty-six patients were treated, 4 of the 30 ligations having been done bilaterally. Four patients, accounting for six of the ligations, showed no evidence of previous thrombosis, and these must be included in Bauer's (1948) and Luke's (1941) group with primary valvular incompetence of the deep veins. The histories varied from 2 to 50 years in duration, and the ages from 24 to 72. Four patients were older than Buxton's upper limit of 55 years, and I agree with Glasser (1949) that this upper limit is meaningless.

The chief symptoms were ulceration or eczema—usually painful—bursting pain, and oedema. Less common were coldness and cyanosis, nocturnal cramps, and varicose veins. Ulceration occurred in 15 instances (50% of total). In 12 cases the ulcers were notably painful, a feature which helped to distinguish them from varicose ulcers. The medial malleolus was the common site, and a varying

*A slight amplification of a paper read to the Section of Surgery at the Annual Meeting of the British Medical Association, Liverpool, 1950.