Peripheral vascular disease (PVD) is an atherosclerotic disease of the distal arterial system typically affecting the lower limbs. This syndrome encompasses a wide range of patients from those with asymptomatic arterial narrowing to those with intermittent claudication, and at the extreme end of the spectrum, patients with critical limb ischaemia and gangrene. The common pathophysiological mechanisms underlying the development of PVD and other atherosclerotic diseases are reflected in the fact that patients often have concomitant coronary artery and cerebrovascular disease. Over the last 20 years, a number of studies have established the importance of birth weight as a determinant of both coronary heart disease and cerebrovascular mortality. By contrast, there has been very little work investigating the possible influence of the prenatal environment on the later development of peripheral vascular disease. In this review, we will summarise the epidemiological work conducted on peripheral vascular disease. In addition, we will appraise the evidence that birth weight is associated with the development of this disease. Finally, we will analyse the possible mechanisms underlying such an association using the information gained from both human and animal studies.

**Epidemiology of Peripheral Vascular Disease**

Symptomatic PVD is a relatively common condition with a prevalence of around 7% in adults over the age of 55 years. This disease has a relatively benign course—only one quarter of patients with intermittent claudication experience deterioration of symptoms and the annual risk of amputation for those with intermittent claudication, and at the extreme end of the spectrum, patients with critical limb ischaemia and gangrene. The common pathophysiological mechanisms underlying the development of PVD and other atherosclerotic diseases are reflected in the fact that patients often have concomitant coronary artery and cerebrovascular disease. Over the last 20 years, a number of studies have established the importance of birth weight as a determinant of both coronary heart disease and cerebrovascular mortality. By contrast, there has been very little work investigating the possible influence of the prenatal environment on the later development of peripheral vascular disease. In this review, we will summarise the epidemiological work conducted on peripheral vascular disease. In addition, we will appraise the evidence that birth weight is associated with the development of this disease. Finally, we will analyse the possible mechanisms underlying such an association using the information gained from both human and animal studies.

**Animal Models**

The concept that adult disease may be determined by prenatal factors has led to the development of a number of animal models to analyse the pathophysiological effects of the fetal environment. The focus of these studies has, however, been on the importance of maternal nutrition on the development of systemic hypertension. Recently, however, there have been some studies examining the role of the fetal environment on specific vascular beds. Ozaki et al have demonstrated that in rats, global undernutrition during gestation causes enhanced thromboxane induced contraction in the femoral arteries of the male offspring. Koukou et al have also reported that mothers fed a high fat diet produce offspring whose femoral arteries show reduced endothelium dependent vasodilatation. In addition, further work by the same group has demonstrated that the aortas of these offspring have an altered fatty acid content. Using a sheep model, Nishina et al have shown that protein and global nutrient restriction in early gestation produce offspring with impaired endothelium dependent and independent femoral artery dilation, and that this dysfunction is most pronounced in the protein restricted group. Although these animal models provide indirect evidence that maternal nutrition may contribute to the development of lower limb vascular dysfunction in humans, it is important to inject a degree of caution in reviewing these data. After all, the relative calibre of the femoral artery in humans is far larger than that of rats and sheep, and it is questionable whether data from a quadruped species has relevance to a bipedal human.

So what evidence, if any, is there from human studies on the effects of uterine environment on peripheral vascular
Is there a fetal origin of peripheral vascular disease?

O A Khan and C Shearman

*Heart* 2005 91: 869-870
doi: 10.1136/hrt.2004.047373

Updated information and services can be found at:
http://heart.bmj.com/content/91/7/869

These include:

References
This article cites 14 articles, 3 of which you can access for free at:
http://heart.bmj.com/content/91/7/869#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections

- Drugs: cardiovascular system (8839)
- Epidemiology (3766)
- Diabetes (841)
- Metabolic disorders (1029)
- Tobacco use (635)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/