Pathophysiology of Raynaud’s phenomenon

Raynaud’s phenomenon is episodic digital ischaemia provoked by stimuli such as cold,1 emotion,2 trauma,3 hormones,4 and drugs.5 It is manifested by pallor of the affected digits, followed by cyanosis and then redness; these changes reflect, respectively, the underlying arterial ischaemia, venostasis, and reactive hyperaemia. In some cases the underlying episodic vasospasm is severe enough to close the digital arteries completely,6 but the precise mechanism is still not fully understood.

Primary Raynaud’s disease is found in otherwise normal healthy individuals. The anatomy of the digital arteries of these patients shows no variation from normal.7 Raynaud’s phenomenon is secondarily associated with a whole host of diseases, including occlusive arterial disease, neurovascular entrapment syndromes, and many of the connective-tissue diseases. Of these, the strongest association is with systemic sclerosis, where up to 90% of patients may have Raynaud’s phenomenon. A disease closely related to systemic sclerosis and identified by the presence in the serum of an antibody to ribonuclear protein is mixed connective-tissue disease.8 Patients with this disease may show features of systemic lupus erythematosus, dermatomyositis, or systemic sclerosis. Most have severe Raynaud’s phenomenon. The aetiology of this disease is unknown, whereas in systemic sclerosis the lesions in the small vessels are well described and, indeed, the vascular tree may be seen as the main target organ.9 What these associated diseases have in common is that their pathophysiological changes affect blood flow—through changes in pressure gradient, vessel calibre, or blood viscosity.

Apart from any structural changes that may reduce their calibre, the diameter of the digital arteries depends on the physiological mechanisms that regulate vasomotor tone. These arteries play a vital part in regulating body temperature, and blood flow through them may vary up to 200-fold.10 Blood flow is reduced in both primary Raynaud’s disease and secondary Raynaud’s phenomenon under basal and “cold”-provoked conditions.11–12

Vasomotor tone is influenced reflexly by the sympathetic nervous system and directly by local factors including chemical mediators such as serotonin13 and prostaglandins.14 The adrenergic sympathetic fibres constict the digital arteries, but since these arteries have vasoconstrictor fibres supplying them reflex vasoconstriction occurs when the sympathetic influence is removed. Raynaud himself considered that his phenomenon was due to excessive sympathetic activity; but over 120 years this theory has never been substantiated and the many treatments directed towards minimising sympathetic control of the vasomotor tone have given disappointing results. Sir Thomas Lewis3–16 later proposed the “local-fault” theory, suggesting that the vessels themselves were abnormal. Our understanding of these “local” factors has made little progress but discovery of the prostaglandins may have helped. The vasodilatory action of the E and F classes of prostaglandins has long been recognised, but only relatively recently have thromboxane A2 and prostacyclin (PGI2) been identified. Thromboxane A2 produced largely in platelets, is a potent vasoconstrictor and platelet aggregator.17 Prostacyclin is synthesised in and released from vascular endothelium18 and is a potent vasodilator and inhibitor of platelet aggregation.19 The interaction of these two compounds is thought to control the laying down and clearing of platelet thrombi within the vasculature. Lewis performed some very elegant studies on the digital arteries from patients with Raynaud’s disease and Raynaud’s phenomenon, Those patients who had had tissue necrosis and ulceration were found to have thrombi in the small digital vessels,2 a finding later confirmed by Pickering.20 Most probably prostaglandin and thromboxane A2 will prove important factors in the process.

Finally, blood viscosity may play a part in Raynaud’s phenomenon. Pringle et al21 and Goyle and Dormandy22 reported that the viscosity was raised in patients with both Raynaud’s disease and Raynaud’s phenomenon. This increase in viscosity was more definite at 27°C than at body temperature —yet another factor impeding blood flow in the cold. Thus each of the factors that influence blood flow may be abnormal in both Raynaud’s disease and Raynaud’s phenomenon —though we still do not understand the roles of these abnormalities in the pathogenesis of this reversible digital ischaemia.

1 Raynaud AGM. De l’aphysie locale et de la gangrène symétrique des extrémités. Paris: Rigo, 1862.
An appalling Panorama

The Panorama television programme on brain death (BBC 1, Monday 13 October) was a disgrace. Its inevitable effect will be to alarm the relatives of dying or dead patients and dissuade them from agreeing to the kidneys being removed for transplantation. That damage would be done to the transplant programme was made clear to the BBC before the programme was screened: Sir Ian Tretethan was left in no doubt that patients with endstage renal failure will die as a result. Such serious effects could be justified only by clear evidence that the programme raised new issues of grave public importance. No such evidence was presented. Detailed criticisms by a neurologist appear at p 1064.

Panorama's film centred on four American patients said to have been declared brain dead who subsequently recovered. Advance publicity on BBC radio and in the Radio Times was alarming, with statements such as “transplant surgeons have got their colleagues into a fix, because they've put them under pressure to diagnose death in the potential donor sooner than they want to, perhaps sooner sometimes than it is safe to do.” The programme itself took a sensationalist approach with graphic descriptions by patients of their being conscious while they were assumed dead. In no case were the criteria for certifying brain death set out by the Conference of Medical Royal Colleges and their Faculties 1 satisfied or even approximated. The first patient was “thrashing about” at the time he was pronounced dead: he was apparently breathing spontaneously when seen to be alive by the transplant surgeon. The second had muscle-relaxant apnoea (the British criteria specifically warn against this mistake). The third was a neonate, and the fourth, who had taken a massive drug overdose, was apparently declared “dead” in the ambulance before she arrived at the hospital. Only one of these four had even been considered as a transplant donor.

Little was said in the programme of the safeguards built into the British system for certifying brain death—in particular, that all the tests for absence of the brain stem reflexes should be repeated later. Instead, the report argued that without a mandatory electroencephalogram the British criteria are unsafe, basing much of its evidence on a collaborative study 2 carried out in the United States in the early 1970s. Whether or not an electroencephalogram would strengthen the British criteria is a valid topic of medical controversy and one that could quite reasonably be discussed in a radio or TV programme. No attempt was made to mount a reasonable discussion of that point: the two British experts interviewed were cut off in mid-sentence. Doctors are not infallible; the diagnosis of death is sometimes made haphazardly and—as in any human activity from piloting airliners to felling trees—mistakes are possible. The Royal Colleges' criteria are designed to make such mistakes as close to impossible as human fallibility allows. The Panorama team produced no evidence—not even a hint—that the British system produced anything like the catalogue of disasters they filmed in the United States.

In Britain most kidneys are obtained from patients with subarachnoid haemorrhage or head injury—conditions in which the electroencephalogram is considered unnecessary by other countries with good quality neurologists. 3 Clearly the British doctors cannot prove they are infallible: but what justification had Panorama for questioning the integrity of British doctors in such a snide, aggressive way?

The BMJ has criticised television in the past, and the medical profession has met with the BBC to try to agree a basis for reasonable co-operation. Panorama went its own way. We suggested two years ago that the prime question should be, “Is this programme likely to confuse, worry, or misinform patients?” This programme seemed designed to cause the maximum disquiet. The reporter interviewed a whole galaxy of American and three British doctors, cutting and editing to serve his own purposes. Asked his opinion about the value of the electroencephalogram in determining brain death, the British neurologist got as far as, “That is always a very difficult point,” and was then cut. Little wonder that the doctors concerned are aggrieved. 5

In a single night Panorama has virtually destroyed all the efforts of the past two years to re-establish trust between television and the medical profession. But it is not only medical amour propre that will suffer. By the end of this year the transplant surgeons will be able to count the patients denied treatment for endstage renal failure. Already one unit has found—for the first time for many months—that relatives are refusing to consent to organs being removed. When, as is inevitable, patients die the BBC will have those deaths on its conscience.

Annie Elias

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17. Lewis T. Experiments relating to the peripheral mechanism involved in spasmoxic arrest of the circulation in the fingers. A variety of Raynaud's disease. Heart 1929;i7:107-11.

18. Lewis T, Landis EM. Observations upon the vascular mechanism in acrocyanosis. Heart 1930;i5:229-46.


