cell counter and should always be undertaken when the automated count is abnormal—and always by someone experienced enough to recognise what he is seeing rather than by a junior medical laboratory scientific officer likely to punch out a differential count and miss important morphological changes. A blood film should also be examined even if the automated count is normal if there is a good clinical reason—suspected glandular fever is a good example. A differential count should form part of that examination only when such numbers need to be known: when monitoring the effect of chemotherapy, for example, or looking for the toxic effect of drugs. We need, however, to be cautious of the spurious security in numbers that takes no account of variation due to sex,[1] smoking,[2] diurnal changes,[1] and random error in counting.[3] The value of the differential count in establishing the presence of infection when the total white cell count is normal is much less certain. Only five of 106 patients with acute appendicitis studied by Raftery had normal white cell counts with abnormal differentials, whereas four had completely normal blood counts.[4]

Possibly clinicians may request differential counts for less than adequate reasons, such as buying time or simple curiosity,[5] and some laboratories perform them on all blood counts as routine. Such activities are known to epidemiologists as "case findings" and are not particularly profitable.[6] Rich *et al* uncovered no clinically inapparent disease from 475 differential counts done for this reason.[7] Although they are not expensive—depending on who does them, differential counts cost between 25 and 50 pence each—a lot are done. An average sized laboratory might spend £15 000 a year on case finding. In the context of health service economics it is the little things that cost a lot.[8]

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Urticarial vasculitis

Urticarial vasculitis is a diagnosis applied in recent years to patients with urticarial weals which on histological examination have shown leucocytoclastic vasculitis (venulitis).[1-5] The general picture is one of individual weals which tend to persist—many last over 24 hours. Initially these weals were said not to itch, but this is a variable feature. Occasionally purpura may be seen in the centre of the weal, and rarely lesions resembling erythema multiforme may appear. In most cases there are no clinical features that will clearly differentiate vasculitis from ordinary chronic urticaria—angio-oedema and weals at the site of pressure occur in both. Arthralgia is more likely to occur in the patients with vasculitis, and less common features include abdominal pain, fever, lymphadenopathy, and rarely glomerulonephritis.

The histological picture varies but usually shows leucocytoclasis, fibrinoid deposits in and around the vessel walls, and a dense perivascular cell infiltrate, often with neutrophils predominating and present in the vessel walls. There may also be extravasation of erythrocytes and swelling of vascular endothelial cells. Direct immunofluorescence may show deposition of immunoglobulins, complement, and fibrin, but with no distinct pattern. Serological investigations show a raised erythrocyte sedimentation rate in many cases. Hypocomplementaemia is present in less than half the cases, and in a few the reduction of C1q is due to 7 S C1q precipitins. Many patients show evidence of circulating immune complexes.

One unresolved question is the relation of urticarial vasculitis to systemic lupus erythematosus, which has vasculitis as one of its histological features. In some series of patients with systemic lupus erythematosus up to 5-10% have had urticaria; indeed, O'Loughlin *et al*[6] recorded urticaria in 12 out of 54 patients with systemic lupus erythematosus. As with urticarial vasculitis, the weals may last longer than those of ordinary chronic urticaria and purpura may be present, but clinically urticarial vasculitis, chronic urticaria, and urticaria associated with systemic lupus erythematosus may be impossible to distinguish. Other manifestations of systemic lupus erythematosus may be present, including facial erythema, discoid plaques, livedo reticularis, and lesions of the nail folds. Cerebral, retinal, and renal lesions may also occur. Serological changes of systemic lupus erythematosus are usually present, and direct immunofluorescence is likely to show granular deposits in clinically normal as well as lesional skin. Considerable overlap between systemic lupus erythematosus and urticarial vasculitis seems the most likely explanation of these findings.

Perhaps the most interesting aspect of urticarial vasculitis lies in its relation to ordinary chronic urticaria. In a series of patients with chronic urticaria fully investigated some 5-10% have been shown to have leucocytoclastic vasculitis (this includes the 1-2% with systemic lupus erythematosus), and less than half have shown complement abnormalities.

Patients with severe urticarial vasculitis show more obvious clinical manifestations of the condition, and are more likely to have serological and histopathological changes than those with milder disease. The important question is, therefore, at what point does urticarial vasculitis merge with ordinary chronic urticaria?

Phanuphak *et al*[7] investigated 42 consecutive patients with chronic urticaria. Although their criteria for the histological diagnosis of vasculitis differed from those of other workers, they recorded 22 with vasculitis and a further eight with minor histological changes of oedema in the vessel wall and perivascular infiltrates suggesting a minor degree of the same condition. Monroe *et al*[8] investigated 45 patients with chronic urticaria, whom they divided into three groups. The first nine showed leucocytoclastic vasculitis with fibrinoid deposits, the second group of 15 a dense perivascular infiltrate of lymphocytes and eosinophils, and the third group of 21 showed sparse lymphocytic perivascular infiltrate. Direct immunofluorescence showed deposition in blood vessels of immunoglobulins and complement or fibrin, or both, in 33% of the first group, 13% of the second group, and 9% of the third. Similarly serological investigations showed an increased incidence of circulating immune complexes in the first two groups, and in these groups

10% had hypocomplementaemia compared with 5% in the remainder.

Russell Jones and colleagues[9 10] have made some important contributions to this aspect of vasculitis, and their study of 24 patients with chronic urticaria showed a complete gradation between obvious vasculitis and ordinary chronic urticaria with regard to the severity of the histopathological features, appearances on direct immunofluorescence, immune complex determination, and serological changes. The detailed investigations by Callen and Kalbfleisch in nine patients with urticarial vasculitis showed the same merging with chronic urticaria.[11]

If, then, we accept that 5-10% of patients with ordinary chronic urticaria have leucocytoclastic vasculitis and that there is a continuum of overlapping changes, what are the possible mechanisms underlying ordinary chronic urticaria? It may well be that in many patients urticaria is due to immune complexes deposited in skin venules which then give rise to a varying degree of liberation of inflammatory mediators depending on many factors (including, rarely, complement abnormalities). These inflammatory mediators then give rise to reactions which can be modified by various drugs and chemicals. Thus, although the weals may be initiated by immune complexes, their development will be influenced by all the other factors known to effect the production of weals in urticaria.

The most effective treatment for urticarial vasculitis is with parenteral steroids, usually required in a full dose, and continued for months. Nevertheless, many patients with urticarial vasculitis eventually settle down spontaneously, and even in the face of a clear cut diagnosis steroid treatment is required in only a few patients who have not been helped sufficiently by conventional measures including adequate antihistamine treatment. A few of these patients respond to dapsone, particularly those with a picture similar to systemic lupus erythematosus.[12] In one report indomethacin was said to be effective in nine out of 10 patients with urticarial vasculitis[13]; this has not been the experience of other workers—and indomethacin may have an aspirin like exacerbating effect on urticaria.

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Regular Review

Venous ulceration

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Venous ulcers do not occur in any other animal, but they have probably afflicted man since he achieved an upright posture. Because they are an uncommon complication of simple varicose veins but a common sequel of deep vein thrombosis they may have been rare until the advent of "civilised" living. They must have been known to Hippocrates and the ancients, but the first to recognise the relation between venous thrombosis and ulceration is usually said to have been John Gay.[1] The connection was revived in 1917 by John Homans,[2] who also drew attention to the fact that legs with venous ulcers often had few visible varicose veins—thus banishing the commonly used but misleading term "varicose ulcer."

Once cause and effect—calf pump deficiency and ulceration—were established, little thought was given to the actual mechanisms. Yet even on close inspection it is difficult to see how an inefficient calf pump can cause necrosis of the skin on the lower medial aspect of the leg. The common explanations were venous stasis,[2] venous hypertension,[3] and tissue ischaemia secondary to microscopic arteriovenous fistulas,[4] but none of these theories fitted all the facts.

The extent to which the calf pump may be damaged by thrombosis became apparent as phlebography and measurements of intravascular pressure became easy and accurate during the 1940s and '50s. Phlebography showed that thrombosis often destroyed all the deep veins, leaving either narrow irregular valveless channels—if the veins recanalised—or tortuous dilated collaterals with incompetent valves if they did not. Measurements of pressure in the foot veins during exercise showed that this damage obstructed or reversed the