

Reference Laboratory who provided us with the specimens of human and rabbit sera.

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#### Serum gamma-glutamyltransferase and alkaline phosphatase in rheumatoid arthritis

The paper by Spooner and colleagues<sup>1</sup> in the June issue prompts us to record our own observations on patients with rheumatoid arthritis. In a consecutive series of 46 patients (34 females, 12 males), all with positive serology, serum gamma-glutamyltransferase (GGT) activity was increased in eight patients (17%) and alkaline phosphatase (AP) in six (13%). This incidence of raised GGT is slightly lower than that found by Spooner *et al*, whereas the incidence of raised AP is much less.

On all patients showing raised serum enzyme activity we carried out isoenzyme examination by electrophoresis.<sup>2,3</sup> GGT-2 was the principal GGT isoenzyme in six of the eight patients showing raised GGT activity, GGT-3 was present in all, and markedly increased in three. This pattern is typical of, but not exclusive to, patients with liver disease,<sup>4</sup> and is especially found with intrahepatic cholestasis. In all six patients with increased total AP activity there was increased activity of the liver AP isoenzyme. In four of these, this was accompanied by increased "biliary" isoenzyme, and in one by additional increase of the bone isoenzyme.

Our studies indicate that in patients with rheumatoid arthritis showing raised activities of GGT or AP, this is likely to be of hepatic origin.

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#### Standardisation in the laboratory control of oral anticoagulant therapy

In collaboration with the International Committee for Standardisation in Haematology (ICSH), the European Community Bureau of Reference (BCR) has produced three certified reference materials for the standardisation of commercial or laboratory-made human, bovine and rabbit thromboplastins, respectively. These reference materials have been calibrated against the WHO international reference preparation (IRP 67/40). By using the appropriate BCR reference material (human, bovine or rabbit) a sensitivity index can be assigned to any thromboplastin working preparation which will thus be directly related to the WHO primary reference preparation.

In clinical practice a prothrombin ratio obtained by means of thromboplastin reagent with an assigned sensitivity index can then be converted to an international normalised ratio (INR) by a simple equation:  $INR = \text{antilog of } (\log \text{ prothrombin} \times \text{sensitivity index})$ .

Manufacturers are being encouraged to establish the sensitivity indices of their thromboplastin reagents and to provide an appropriate Table of INRs. A therapeutic range for INR of 2.0-4.0 has been recommended.

Details of the scheme have recently been described.<sup>1</sup> Information of the availability of BCR Certified Reference Materials, a report of the certification protocol and recommended methodology for calibration of working preparations are available from

the European Community Bureau of Reference, Rue de la Loi 2000, Brussels B-1049, Belgium.

SM LEWIS

Chairman, International Committee  
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#### Direct evidence of localised immunological damage in vulvar lichen sclerosus et atrophicus

Lichen sclerosus et atrophicus (LSA) is known to be associated with an increased incidence of organ-specific autoantibodies<sup>1</sup> and autoimmune diseases<sup>2</sup>. In addition a raised incidence of HLA-B40 in this disease has recently been reported and has led to the suggestion that this antigen may be in linkage disequilibrium with immune response genes controlling the susceptibility to both LSA and their autoimmune diseases<sup>3</sup>.

The present study has been designed to determine whether LSA is associated with immunological phenomena. A search has been undertaken for immunohistochemical evidence of deposition of immunoglobulin, complement (C3) and fibrin in the vulvar lesion and using adjacent normal skin as a control. In addition, sera from these patients have been screened for autoantibodies.

#### PATIENTS AND METHODS

Biopsies from 16 caucasian women (age range 36-78 yr, mean 64.6 yr) with vulvar LSA were collected over a period of six years. The histopathological diagnosis was confirmed by two independent observers and was based on the presence of hyperkeratosis, epidermal atrophy, homogenisation of the collagen of the upper dermis and an underlying chronic inflammatory cell infiltrate. Wedge biopsies of the affected and non-affected skin were snap-frozen and then examined by a standard direct immunofluorescence technique for the presence of immunoglobulin (IgG, IgA, IgM and IgE), complement (C3) and fibrin with commercially prepared fluorescein-labelled antisera (Wellcome Foundation and Hoechst Pharmaceuticals). Serum samples from 14 patients were obtained and screened routinely in the immunopathology laboratory for the presence of organ-specific and non-organ-specific antibodies