The Association of Clinical Pathologists: 95th general meeting

The 95th general meeting was held at Imperial College, London from 24 to 26 September 1975. Abstracts of most of the scientific communications and of some of the papers read at symposia on 'Thyrototoxicosis' (Chairman: Professor E. D. Williams), 'Immune complex diseases' (Chairman: Dr L. E. Glynn), and 'Preleukaemic states' (Chairman: Dr J. E. MacIver) follow.

A case of Paraquat poisoning

G. J. LAWS (*Department of Pathology, General Hospital, Hexham, Northumberland*) A case, originally diagnosed as pneumonia, was considered as Paraquat poisoning because of failure to respond to treatment. The patient at first made no mention of having consumed Paraquat, then denied it, but later admitted the possibility. Traces of the compound were detected in urine sampled 10 days after the presumed date of ingestion, and death occurred on the 23rd day from respiratory failure.

At necropsy, lung changes typical of the condition—haemorrhage and oedema, degeneration of the alveolar lining cells, hyaline membrane formation, interstitial fibrosis, bronchiolar proliferation, and dilated air spaces—were present.

The missed diagnosis of amoebiasis

W. P. STAMM (*Amoebiasis Diagnostic and Research Unit, St Giles' Hospital, London*) Amoebiasis is a cosmopolitan disease which can mimic most other abdominal or hepatic disorders. It is easily treatable and should for that reason have a high place in any list of differential diagnoses.

The advent of good serological tests and specific immunofluorescent staining of amoebae in tissues and pus have made diagnosis much easier when the proper facilities are available. Serum from all patients thought to have diseases such as ulcerative colitis, Crohn's disease, or abdominal or hepatic neoplasm should be tested for amoebiasis before surgical intervention or the giving of steroids.

Upwards of 200 patients are diagnosed annually in England and Wales as suffering from amoebiasis. An analysis of the hospital records of 30 patients who died of amoebiasis between 1963 and 1973 showed that on 12 of them the diagnosis was made

only at necropsy. An abdominal laparotomy was performed on six of the patients; on five of them the correct diagnosis was still not reached as a result of the operation, and on three of them the diagnosis was made *post mortem*. These figures suggest that the diagnosis of amoebiasis is missed in about 40% of patients with a lethal amoebic infection; the probability is that the proportion of missed diagnosis is even greater in patients with a milder type of infection.

In the hope of improving this sad situation the DHSS has supported the establishment of an amoebiasis diagnostic and research unit at St Giles' Hospital where advice and technical assistance are available.

Immune complex disease in vinyl chloride workers

A. MILFORD WARD (*Department of Immunology, Hallamshire Hospital Medical School, Sheffield*) The occurrence of Raynaud's phenomenon and loss of bone density in association with dermal thickening, the syndrome of acro-osteolysis (AOL), has been recognized in the vinyl chloride industry since the mid 1950s. Recent investigation has indicated that there is multisystem involvement in a widespread disease process. Immunological and immunochemical investigation of 52 workers from a single factory has revealed evidence of a chronic soluble complex disorder in 28 individuals. The features of the disorder include hyperimmunoglobulinaemia, cryoglobulinaemia, and cryofibrinogenaemia, and *in vivo* complement activation via the classical pathway with C4 and C3 conversion. There is, in addition, evidence of a reduced T-cell population and B-cell proliferation. Some patients also show low levels of various non-organ-specific anti-tissue antibodies.

Immunofluorescent examination of biopsy material from selected patients shows the presence of circulating immune complexes with deposition on vascular endothelium and incorporation into a subintimal proliferation which eventually constricts the vascular lumen.

The data available from immunological investigations permit the construction of a provisional model of the disease process. The circulating immune complexes together with complement activation and cryoprecipitation cause the observed vascular abnormalities, and thence the clinically observed abnormalities. The initiating sequence is still speculative but experimental metabolic data suggest that vinyl chloride metabolites may be incorporated into protein synthesis. The presence of structurally modified or antigenically foreign protein would be sufficient stimulus to initiate the observed reaction sequence.

The therapeutic use of plasmapheresis in an immune complex disease

T. J. HAMBLIN AND J. VERRIER JONES (*Royal Victoria Hospital, Bournemouth and Southmead Hospital, Bristol*) A 30-year-old man with active systemic lupus erythematosus characterized by circulating immune complexes was treated by intensive plasmapheresis. There was clinical improvement, and the circulating complexes became undetectable. Preliminary experience with this and other cases suggests that plasmapheresis is a useful procedure in active SLE when circulating immune complexes can be detected.

Laboratory diagnosis of hyperthyroidism

P. J. N. HOWORTH AND P. MARSDEN (*Departments of Chemical Pathology and Medicine, King's College Hospital Medical School, London SE5*) At present the most

useful tests on the basis of general availability and diagnostic discrimination are serum T3, T4, TSH, and technetium thyroid scanning. In a prospective study on 55 patients with suspected hyperthyroidism serum T3 was raised in all 46 toxic patients, T4 was raised in 83%, T3:uptake ratio raised in 78%, and two-stage (uptake $\times$ T4) FTI raised in 76%. A variety of kits measure T4 followed by a single stage or 'sequential FTI' which correlates well with free T4 concentration. However, in a trial on 100 patients the two-stage FTI was slightly superior to both the Ames Thyrolute sequential FTI or T4 alone (Howorth *et al*, 1975). Eight of 17 patients with solitary autonomous 'hot' nodules, as defined by scanning, were toxic with raised T3; five had a normal T4. Nine were euthyroid with normal T3 and T4. Patients receiving carbimazole for hyperthyroidism had normal or slightly low T4 and elevated T3 and TSH when euthyroid and very low T4, normal T3, and markedly elevated TSH when clinically hypothyroid. Euthyroid patients after therapy usually had normal T4 and TSH with minimally raised T3. Relapse occurred in 13 of 22 patients followed up for one year after carbimazole therapy. T3 measurements gave the earliest warning of relapse but T4 was adequate for routine follow-up since relapse was preceded by an elevated T4 (8 cases) or accompanied by it (3 cases). Biochemical hyperthyroidism preceded clinically apparent relapse for 12 weeks on average.

Red cell zinc and the zinc-metalloenzymes are promising tests of the peripheral metabolic effect of thyroid hormone. Red cell zinc and carbonic anhydrase B level fall in hyperthyroidism but a marked elevation in glyceraldehyde - 3 - phosphate dehydrogenase activity, which catalyzes the formation of 1:3 diphosphoglycerate, has been reported (Pangaro *et al*, 1974). 2:3 Diphosphoglycerate, an important regulator of oxygen delivery to the tissues, is formed from 1:3 diphosphoglycerate and is elevated in hyperthyroidism (Miller *et al*, 1970).

References

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- Models of immune complex diseases and the role of antibody affinity**
- M. W. STEWARD (*Immunology Division, The Mathilda and Terence Kennedy Institute of Rheumatology, London*) Several experimental models of human immune complex disease are currently being studied and can be classified into three main types: (a) those in which non-replicating antigens, such as serum proteins, are injected into animals to induce either an acute or chronic disease; (b) those in which the injection of replicating antigens, ie, viruses, are used to induce immune complex disease in susceptible hosts; and (c) spontaneously occurring immune complex diseases of animals. The extent to which the study of these models has contributed to the understanding of the immunopathology of immune complex disease will be discussed. Discussion will also focus on the factors which affect the formation and clearance or deposition of immune complexes with particular reference to the role of antibody affinity in these processes.
- Systemic lupus erythematosus and rheumatoid arthritis**
- G. R. V. HUGHES (*Department of Rheumatology, Royal Postgraduate Medical School, Hammersmith*) In both RA and SLE evidence for immune complex mechanisms is abundant. In RA, they are principally detectable within the synovial space and adjacent cartilage (measurement of synovial fluid complement levels is one of the few useful early diagnostic tests in RA), while in SLE circulating complexes as well as tissue-bound deposits are more frequent.
- However, despite the strong evidence obtained from immunofluorescence and elution studies, a number of questions remain unanswered. In RA, the factors concerned — genetic, antibody, affinity, chemical mediators, and rheumatoid factor—which result in the marked localization of complexes are not clearly defined.
- In SLE, despite the strong evidence for DNA—anti-DNA complex involvement, the relative roles of other complexes such as denatured DNA—anti-d-DNA, lymphocytotoxins—'shed' lymphocyte antigen, RNA—anti-RNA virus-antivirus etc, as well as the reasons for varying disease
- patterns (eg, CNS or renal lupus) are unclear.
- Recently, detailed serial studies were carried out over a four-year period in this unit on 38 patients with SLE. As well as the usual markers of disease activity including DNA-binding and haemolytic complement CH_{50} determinations, evidence for circulating complexes was regularly sought by electron microscopy, Clq precipitation, anticomplementary activity, and DNAase digestion of serum.
- Clq precipitins were detectable in 21 out of 56 SLE patients and correlated poorly with disease activity. Anticomplementary activity was detected in 44 of 150 sera from 19 patients. Positive results correlated well with disease activity but were not confined to patients with renal disease.
- DNAase digestion, suggested as a method for the detection of DNA—antibody DNA complexes, was significantly positive in only one patient, a child with aggressive renal lupus, in whom low MW complexes were detected. This technique may depend on antibody affinity and has major drawbacks.
- The factors currently known to affect disease pattern and activity in SLE and RA are discussed.
- Hepatitis B, immune complexes, and pathogenesis of polyarteritis nodosa**
- A. J. ZUCKERMAN (*Department of Virology, School of Hygiene and Tropical Medicine, London*) Early studies have suggested that hepatitis B antigen immune complexes may play an aetiological role in the pathogenesis of some cases of polyarteritis nodosa. In collaboration with Trepo, Prince, and Bird (Trepo *et al*, 1977; Zuckerman, 1975) sera from 55 patients with histologically confirmed polyarteritis nodosa were tested for hepatitis B surface antigen and surface antibody by sensitive techniques. The surface antigen was detected by radioimmunoassay in 54.5% of the patients and there was an approximately equal distribution of subtypes av and ay . Surface antibody was found by passive haemagglutination in 28% of the patients. Overall, 69% of the patients had either antigen or antibody in their serum and 11% had had both.
- Circulating immune complexes were found by electron microscopy in eight out of 27 patients, but no correlation was found between clinical and laboratory indicators of activity of polyarteritis and detection of circulating immune complexes.
- Seroconversion or the presence of anti-