chronic renal failure who were established on dialysis programmes was 18.1 to 57.3 mEq/hr with a mean rate of 33.6.

The peak acid output of patients with stable chronic renal failure not on dialysis are compared with the preceding groups in the Figure.

Discussion

This study was provoked by three abnormal barium meals undertaken for gastrointestinal symptoms in patients on long-term dialysis. Among the remaining 13 patients on long-term dialysis three more were found to have abnormal barium studies. "Uraemic bleeding" from the gastrointestinal tract is recognized in renal failure. The excessive occurrence of peptic ulceration is not, and where anecdotally acknowledged (Hadjiyannakis *et al.*, 1971) is said to be avoidable by "adequate and prompt haemodialysis." Peptic ulceration is a recognized and documented problem of renal transplantation (Moore and Hume, 1969; Hadjiyannakis *et al.*, 1971) but obviously the immunological aspect clouds the picture. The only opinion which was based on investigatory evidence (Wiener *et al.*, 1969) denied an increased incidence of chronic duodenal ulceration in patients receiving long-term dialysis.

Both direct and indirect peptic secretory studies in renal failure are not without ambiguity, but do not suggest an abnormally increased rate of gastric secretion either under normal circumstances or with histamine (Fillastre *et al.*, 1965; Kiil and Enger, 1968), betazole (Goldstein *et al.*, 1967; Schupak and Ferayorni 1968), or pentagastrin (Gordon *et al.*, 1972) stimulation. However, Goldstein *et al.* (1967) commented that dialysis was associated with an augmented maximum response to betazole hydrochloride stimulation. Contrary to the statement of Gordon *et al.* (1972), who measured the secretion rate of hydrogen ion in their own investigation, the work of Fillastre *et al.* (1965) did not suggest an increase of hydrogen ion secretion rate in azotaemic patients. Fillastre's results indicated an increased hydrogen ion concentration of gastric secretion, but a decreased volume of juice. The appropriate calculations indicate a secretion rate of hydrogen ion in response to histamine stimulation comparable to their normal range.

The final problem is to consider the reality of the appearance of hyperacidity with establishment of dialysis (see Figure). Not only the phenomenon but the mechanism demands investigation. If the raised serum gastrin level as a result of loss of renal metabolism of that peptide is not the source, as doubted by Korman *et al.* (1971, 1972), one must consider the role of calcium. Serum calcium levels seem well related in some cases to gastric activity (Barreras and Donaldson, 1967), but the reliability of this association is questioned by the data of Gordon *et al.* (1972). It is, however, well recognized that there are areas of calcium and bone metabolism which are a complete enigma (Kerr and Hocken, 1971), and this line of investigation is being pursued.

We are grateful to the control subjects for their submission to examination, and to Sisters A. Scurrall and J. Barker for help in the management thereof, as well as to the department of radiology, and Dr. M. J. Imrie in particular, for their interested help and willing co-operation.

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PRELIMINARY COMMUNICATIONS

Rheumatoid Arthritis, Rheumatoid Factor, and Tests for Australia or Hepatitis-associated Antigen

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British Medical Journal, 1972, 4, 23-24

Summary

False-positive results in tests for hepatitis-associated antigen using latex agglutination techniques may be due to rheumatoid factor in the serum. Possibly the use of IgM antibody in preparing the latex particles might

diminish the occurrence of such reactions. No evidence was found for a relation between rheumatoid arthritis and a significant incidence of hepatitis-associated antigen detectable by countercurrent immunoelectro-osmophoresis.

Introduction

The recently described latex agglutination test for the detection of Australia or hepatitis-associated antigen (H.A.A.) (Leach and Ruck, 1971; Fritz and Rivers, 1972) has been claimed to have advantages of speed and sensitivity over many currently used techniques. In this test latex particles coated with guinea-pig anti-H.A.A. whole serum or globulin fraction are agglutinated by H.A.A.-containing sera but not by normal sera. A variable incidence of false-positive results, however, has hindered widespread application of the method (Banatvala *et al.*, 1971; Cossart *et al.*, 1972). Because the H.A.A. latex test is similar in principle to the latex test for rheumatoid factor, in which particles coated with human γ -globulin are agglutinated by sera containing rheumatoid factor (Singer and Plotz, 1956; Valkenburg, 1963), we have examined sera from patients with rheumatoid arthritis in tests with two commercially available H.A.A. latex agglutination kits. Evidence is now presented that false-positive results in this test can be due to the presence of rheuma-

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Reactions of Whole Sera, Serum Fractions with Rheumatoid Factor, and Adsorbed or Inactivated Sera from Five Patients with Rheumatoid Arthritis with Anti-H.A.A. Latex and with Anti-H.A.A. in Countercurrent Immuno-electro-osmophoresis Test (C.I.E.O.P.)

Case No.	Whole Serum		Whole Serum After Adsorption of Rheumatoid Factor		H.A.A. Latex Titre in Whole Serum Treated with Mercaptoethanol and Heat	Fraction with Rheumatoid Factor		Whole Serum C.I.E.O.P.
	R.F.* Titre	H.A.A.† Latex Titre	R.F. Titre	H.A.A. Latex Titre		R.F. Titre	H.A.A. Latex Titre	
1	163,480	16	2,560	2	0	5,120	4	0
2	163,480	4	1,280	4	0	160	2	0
3	10,240	2	160	0	0	2,560	4	0
4	20,480	8	320	0	2	320	2	0
5	10,240	4	320	0	2	1,280	2	0

*Titre of rheumatoid factor determined by method of Valkenburg (1963).

†Titre of antigen in slide agglutination with H.A.A.

toid factor; the latter is shown not to affect the widely used countercurrent immunoelectro-osmophoresis technique for detecting H.A.A.

Methods and Results

The H.A.A. latex agglutination tests were performed following the procedure recommended by the respective manufacturers (Pfizer Ltd., Sandwich, Kent; Hoechst Pharmaceuticals, Hounslow, Middlesex). The reagents were mixed together on a glass slide, and a test was regarded as positive when strong or moderate macroscopic agglutination occurred within the prescribed time. Routine countercurrent immunoelectro-osmophoresis was performed by a technique resembling that of Prince and Burke (1970). Titres of rheumatoid factor in sera were determined by a tube latex test at the Northern General Hospital by the method of Singer and Plotz (1956) as modified by Valkenburg (1963). Purified rheumatoid factor was prepared by passing sera over polymethylmethacrylate beads coated with denatured human globulin (Cohn Fraction II) and with subsequent elution of the absorbed rheumatoid factor (McCormick, 1972). In addition, rheumatoid factor was inactivated in some samples of serum by heating to 56°C for 30 minutes and subsequently treating them overnight at 4°C with 0.04 M 2-mercaptoethanol (Ziegenfuss *et al.*, 1972).

Five sera examined all gave positive results with both commercial H.A.A. latex reagents. The results obtained with the Hoechst kit are shown in the Table. The agglutination titre was much lower with the latex H.A.A. reagent than in the tube latex test for rheumatoid factor; probably differences in the species and degree of denaturation of the globulins, and in sensitivities of tube and slide tests, account for this. Partial adsorption of rheumatoid factor from the sera or heating to 56°C and subsequent mercaptoethanol treatment greatly reduced agglutination of the anti-H.A.A.-coated latex particles; also activity was shown in the fractions containing purified rheumatoid factor. Sera from persons without rheumatoid arthritis were negative when examined for latex agglutination, and all sera were negative in the countercurrent immuno-electro-osmophoresis test for H.A.A. (see Table).

Rheumatoid factor has been claimed to mask the detection of H.A.A. by countercurrent immunoelectro-osmophoresis (Ziegenfuss *et al.*, 1972). Accordingly the sera were tested by this method after heat and mercaptoethanol treatment, and also after mixing untreated rheumatoid sera with an equal volume of H.A.A.-positive serum. No masked H.A.A. was detected in the rheumatoid sera and no diminution in detectable H.A.A. occurred due to rheumatoid factor.

Discussion

We have shown that rheumatoid factor may cause a false-positive result when testing sera for H.A.A. with the currently available H.A.A. latex reagents. A similar explanation for false-positive reactions was proposed by Bennett and Bailey (1971) in the detection of *Cryptococcus neoformans* using latex particles coated with rabbit globulin. Possibly the use of IgM antibody in the preparation of anti-H.A.A.-coated

latex particles for the detection of H.A.A. might diminish the frequency of false-positive reactions; at least a control reagent of latex particles coated with normal guinea-pig serum should be used to check all ostensible positives. Rheumatoid factor may be found in at least 5% of the general population and in conditions other than rheumatoid arthritis, including chronic liver disease.

On the broader matter of a possible role of serum hepatitis virus in rheumatoid arthritis Ziegenfuss *et al.* (1972) found H.A.A. in the serum of nine out of 19 patients with systemic lupus erythematosus by countercurrent immunoelectro-osmophoresis, a reaction detectable only after heat and mercaptoethanol treatment, and they suggested that rheumatoid factor may be responsible for interfering with the detection of H.A.A. In addition Alarcon-Segovia and Fishbein (1971) detected H.A.A. in 19 out of 76 patients with systemic lupus erythematosus by complement fixation, although no specimens were positive for H.A.A. by immunodiffusion. As in some cases of systemic lupus erythematosus there is some clinical overlap with rheumatoid arthritis it was obviously of interest to test a larger series. Thirty-four patients were tested—29 with rheumatoid arthritis (19 of whom were positive for the rheumatoid factor) and 5 with other types of arthritis. None showed H.A.A. by countercurrent immunoelectro-osmophoresis before or after treatment of sera with mercaptoethanol and heat. Further work is in progress to exclude a relation between rheumatoid arthritis and the presence of H.A.A. using synovial membrane tissue cultures and radioimmunoassay of H.A.A. Results have been negative so far.

We are grateful to Mr. J. M. Leach, of Pfizer Ltd., and Mr. Denzil Evans, of Hoechst Pharmaceuticals, for their generous supply of H.A.A. latex agglutination kits, and to Mr. R. Hopkins and Dr. P. C. Das, of the Blood Transfusion Service, Edinburgh, for helpful discussions. This work was supported by grants from the Nuffield Foundation and the Arthritis and Rheumatism Council.

Addendum

Tests using recent Pfizer preparations of latex coated with normal guinea-pig globulin and with guinea-pig anti-H.A.A. globulin have shown considerably less agglutinability with rheumatoid sera than earlier preparations.

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