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IgA-containing circulating immune complexes in dermatitis herpetiformis, Henoch–Schönlein purpura, systemic lupus erythematosus and other diseases

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SUMMARY

The sera of patients with dermatitis herpetiformis, Henoch–Schönlein purpura and systemic lupus erythematosus were examined for IgA-containing immune complexes using a newly described radioimmunoassay. The IgG Raji cell radioimmunoassay and the ^{125}I-C1q binding assay were also used to detect IgG- and IgM-containing soluble immune complexes. IgA-containing immune complexes were found in the sera of twelve of forty-nine (24%) patients with dermatitis herpetiformis, four of six (67%) patients with Henoch–Schönlein purpura, and seven of ten (70%) patients with systemic lupus erythematosus. IgG- or IgM-containing immune complexes were also found in six of forty-seven patients with dermatitis herpetiformis, in one of six patients with Henoch–Schönlein purpura, and in nine of ten patients with systemic lupus erythematosus, by either the ^{125}I-C1q binding assay or the IgG Raji cell assay. The finding of soluble IgA immune complexes in a high percentage of patients with systemic lupus erythematosus and Henoch–Schönlein purpura suggests that they may play an important role in the pathogenesis of these diseases. In contrast, their low prevalence in patients with dermatitis herpetiformis suggests that IgA-containing immune complexes may not play a major role in the pathogenesis of dermatitis herpetiformis.

INTRODUCTION

Circulating immune complexes have been implicated in the pathogenesis of a wide variety of diseases. This surge of interest in circulating immune complexes has been due in part to the recent development of a large number of sensitive assays capable of detecting IgG- and IgM-containing immune complexes in biological fluids (Lambert *et al.*, 1978). Recent evidence has suggested that IgA-containing immune complexes may be involved in the pathogenesis of diseases such as dermatitis herpetiformis (DH) and Henoch–Schönlein purpura (HSP); however, assays for the detection of IgA-containing immune complexes have not been available (Katz & Strober, 1978; Baart de la Faille-Kuyper *et al.*, 1973; Tsai, Giangiacomo & Zuckner, 1975; Giangiacomo & Tsai, 1977).

In this study we examined the sera of patients with dermatitis herpetiformis, Henoch–Schönlein purpura and systemic lupus erythematosus (SLE) using a radioimmunoassay for IgA-containing circulating immune complexes (CIC). In addition, the conventional Raji cell radioimmunoassay which detects IgG-containing CIC, and the ^{125}I-C1q binding assay which detects IgG- or IgM-con-

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taining CIC were used to evaluate these patients for IgG- or IgM-containing CIC. Patients with other skin diseases and normal individuals were also studied for CIC.

MATERIALS AND METHODS

Patients. Forty-nine patients with DH (twenty-five female and twenty-four male) as defined by clinical appearance, histology and direct immunofluorescence, showing IgA deposition in uninvolved skin, were studied. The skin of forty-one of forty-nine patients had a granular deposition of IgA; the other eight had a linear pattern of IgA deposition. Five patients were maintained on a gluten-free diet (GFD) alone, two patients on a GFD with sulphones and one on a GFD with sulphapyridine. Seven patients were untreated, one patient was treated with sulphapyridine and thirty-three patients were treated with sulphones.

Six patients with Henoch–Schönlein purpura were studied. These patients had acute purpuric eruptions, which on biopsy showed a leucocytoclastic vasculitis, and had in addition either abdominal pain or renal disease. Six patients with leucocytoclastic vasculitis confined to the skin were also studied.

Ten patients with systemic lupus erythematosus (SLE) were studied. These patients all met the American Rheumatism Association criteria for diagnosis of SLE (Cohen, Reynolds & Franklin, 1971). Forty-two patients with skin diseases of various types were studied (seven pemphigoid, six pemphigus, five ichthyosis, nineteen psoriasis, four Darier's disease, one pityriasis rubra pilaris).

Serum was obtained from twenty-three normal volunteers in the Clinical Center, National Institutes of Health, for determination of normal values.

Raji cell assays. Raji cells were obtained as a gift from Dr Dean Mann (Immunology Branch, National Cancer Institute, Bethesda, Maryland). Characterization of their surface immunoglobulin, Fc IgG receptors and complement receptors was performed as described by Theofilopoulos, Dixon & Bokisch (1974). Surface immunoglobulins were not detected and receptors for complement were present. Raji cells were grown at 37°C in RPMI 1640 (NIH Media Unit) supplemented with 10% heat-inactivated foetal calf serum (Grand Island Biologic Company, Grand Island, New York), 4 mM glutamine (NIH Media Unit), and penicillin-streptomycin–amphotericin antibiotic (Grand Island Biologic Company, Grand Island, New York).

Raji cell assay for IgA-containing immune complexes. Raji cells (2×10^6) in 50 μl of RPMI 1640 were placed in a 1·5-ml microfuge tube (Beckman Instruments Incorporated, Mountainside, New Jersey) along with 25 μl of the test sera diluted 1:4 with pH 7·4 phosphate-buffered saline (PBS) (NIH Media Unit) and incubated in a 37°C water bath for 45 min with gentle agitation every 20 min. All test sera were analysed in duplicate. The cells were then washed three times with RPMI 1640 and resuspended with 18 μg of the IgG fraction of a ^{125}I-goat-anti-human IgA, which was heavy chain-specific (Atlantic Antibodies, Westbrook, Maine), in 50 μl of RPMI 1640 with 1% human serum albumin (Sigma Chemical Company, St Louis, Missouri). The goat-anti-human IgA displayed a single precipitin line by double diffusion in gel against normal human sera and against a purified human IgA myeloma protein (gift of Dr Richard Wistar, Naval Medical Research Institute, Bethesda, Maryland). The goat-anti-human IgA was radiolabelled using Bolton–Hunter reagent (New England Nuclear, Boston, Massachusetts) as described previously (Lawley *et al.*, 1979). The cells were then incubated at 4°C for 30 min with gentle agitation. Finally, the cells were washed three times with cold, RPMI 1640 with 1% HSA, and cell-bound radioactivity counted.

Analysis of Raji cell assay for IgA-containing immune complexes. Statistical analysis was done using a modification of the method of Woodroffe *et al.* (1977), in collaboration with Dr David Alling (Special Assistant for Biometry, National Institute of Allergy and Infectious Diseases). Individual serum samples from thirteen normal subjects were assayed in duplicate on nine different days. Components of variance were calculated from these data to estimate variability among persons (σ_P^2), among days (σ_D^2) and residual variation (σ_R^2). These estimates, expressed as standard deviations were $\sigma_p = 1{,}005$ c.p.m., $\sigma_D = 1{,}020$ c.p.m. and $\sigma_R = 1{,}122$ c.p.m.; the overall mean c.p.m. was 6,595. Four subjects with representative mean values reflecting the range of the total control panel were chosen and daily mean c.p.m. calculated. Differences among these means were taken to

represent day to day variability so that the contribution D^2 could be dropped from the overall estimate of variation. Using the remaining contribution (σ_P^2 and σ_R^2) and the appropriate daily mean (Ci), an upper 95% confidence limit (Ui) was constructed for the mean of duplicate determinations on a test serum assayed on the ith day, namely:

$$Ui = Ci + 1{\cdot}86 \sqrt{5/8\ \sigma_R^2 + 5/4\ \sigma_P^2} = Ci + 2{,}664.$$

The quantity under the square root sign represents the sum of the variances of the mean of the four control sera, and of the mean of the duplicate test serum values, and 1·86 is the upper 0·95 point of the distribution of Student's t with 8 degrees of freedom. The mean of the duplicate values of the test sera (Ti) was then divided by Ui. If this value (Ti/Ui) was greater than 1, the test serum was judged abnormal.

Raji cell assay for IgG-containing immune complexes. The Raji cell assay for IgG-containing immune complexes was performed as described previously by Theofilopoulos, Wilson & Dixon (1976). Raji cells and sera were treated as for the Raji IgA assay (above) except that 18 μg of the IgG fraction of a ^{125}I-goat-anti-human IgG antiserum which was heavy chain specific (Cappel Laboratories, Incorporated, Cochranville, Pennsylvania) was substituted for the anti-IgA.

Analysis of Raji cell assay for IgG-containing immune complexes. Components of variance were calculated as done for the Raji IgA assay. The estimates of variability for the Raji IgG assay, expressed as standard deviations, were $\sigma_P = 3{,}040$ c.p.m., $\sigma_D = 2{,}248$ c.p.m. and $\sigma_R = 2{,}882$ c.p.m.; the overall mean c.p.m. of the control population was 23,962. Ui for the Raji IgG assay was calculated as in the Raji IgA assay, namely:

$$Ui = Ci + 1{\cdot}86 \sqrt{5/8\ \sigma_R^2 + 5/4\ \sigma_P^2} = Ci + 7{,}476.$$

The mean of the duplicate values of the test sera (Ti) was then divided by Ui. If Ti/Ui was greater than 1, the serum was judged abnormal. Ui was found to correspond to 30 μg equivalents of heat-aggregated human gammaglobulin per millilitre of serum.

^{125}I-C1q binding assays. The ^{125}I-C1q binding assay was performed as described previously (Lawley *et al.*, 1979). The upper 95% confidence limit of C1q binding activity (C1q BA) in normal human serum was determined to be 10%.

C3 and IgA determination. Serum C3 and IgA levels were quantitated with commercially available radial immunodiffusion plates (Behring Diagnostics).

RESULTS

Dermatitis herpetiformis

IgA-containing CIC were detected in the sera of ten of forty-one patients with DH who had a granular pattern of cutaneous IgA and in two of eight DH patients with a linear IgA pattern (Fig. 1). Only one patient was markedly positive (Ti/Ui = 6·50) while the remainder had values of less than 2 (mean positive sera Ti/Ui = 1·26). There was no correlation between the level of IgA-containing CIC and disease activity, sulphone treatment or adherence to a gluten-free diet.

Three of forty-six patients with DH had IgG-containing CIC by the Raji cell IgG assay (mean of positive sera Ti/Ui = 1·08). Three of forty-seven patients had evidence of CIC as detected by C1q binding assay. These patients showed only slightly increased C1q BA (< 18%). The three patients who had IgG CIC detected by the Raji IgG assay also had IgA-containing CIC. None of the patients with elevated C1q BA had IgA-containing CIC (Fig. 2).

Henoch–Schönlein purpura

Four of six patients with HSP were found to have circulating IgA-containing immune complexes (mean of positive sera Ti/Ui = 1·3) (Fig. 1). In two patients followed serially no correlation between the level of IgA CIC and disease activity could be detected. Two of six patients with cutaneous leucocytoclastic vasculitis without systemic manifestations also had IgA-containing CIC (Ti/Ui = 1·75; 3·12).

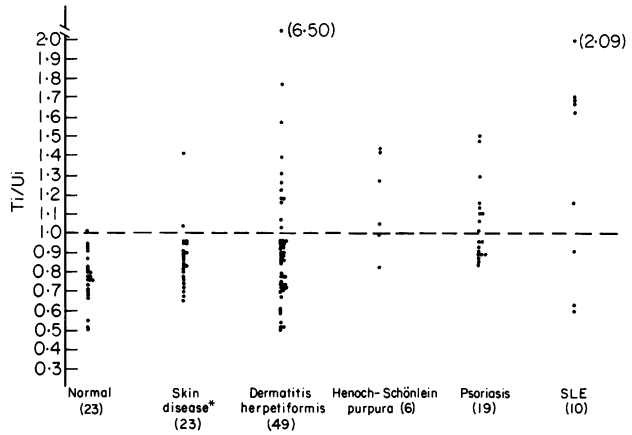

Fig. 1. Levels of IgA immune complexes in patients with dermatitis herpetiformis, Henoch–Schönlein purpura, systemic lupus erythematosus, psoriasis, skin diseases and in normals. Values greater than 1·0 are abnormal. * Skin diseases include pemphigus (6), pemphigoid (7), ichthyosis (5), Darier's disease (4), pityriasis rubra pilaris (1).

One of six patients with HSP had evidence of IgG-containing CIC by the Raji cell assay (Ti/Ui = 1·17). This patient also had increased C1q BA (17%), and evidence for IgA-containing CIC (Ti/Ui = 1·44) (Fig. 2).

Systemic lupus erythematosus

IgA-containing CIC were found in seven of ten patients with SLE (mean of positive sera Ti/Ui = 1·70). Nine of the ten patients with SLE also were found to have IgG-containing CIC by the Raji cell assay (mean of positive sera Ti/Ui = 1·51) (Fig. 2). Abnormal C1q BA was found in seven of

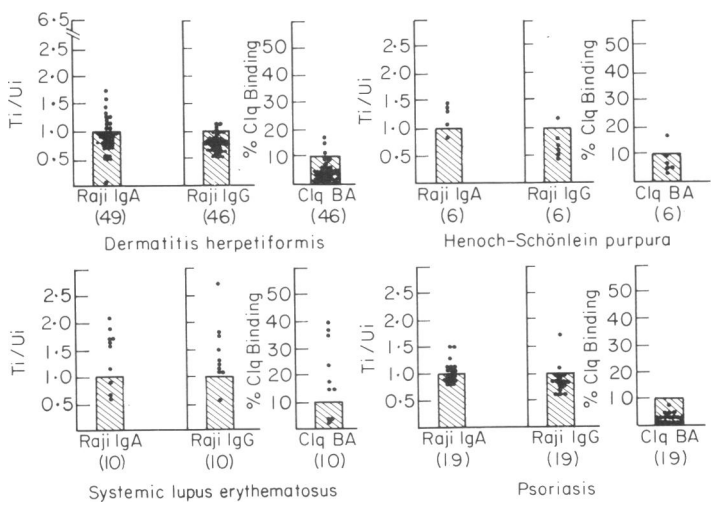

Fig. 2. Comparisons of levels of immune complexes detected using the Raji IgA, the Raji IgG, and the C1q binding radioassays in patients with dermatitis herpetiformis, Henoch–Schönlein purpura, systemic lupus erythematosus and psoriasis. Cross hatched areas represent normal ranges.

the ten patients with a concordance of 80% with the Raji IgG assay. Spearman rank order analysis showed a positive correlation between the Raji IgG assay and the ^{125}I-C1q binding assay ($\rho = 0{\cdot}623$, $P < 0{\cdot}05$). The Raji IgA assay and the Raji IgG assay were concordant in 80% of the patients; however, no positive absolute numerical correlation between these two assays was found by

Spearman rank order analysis. No positive numerical correlation between the ^{125}I-C1q binding assay and the Raji IgA assay in SLE could be demonstrated, although the rate of concordance was 60%.

Other skin diseases

IgA-containing CIC were found in nine of nineteen patients with psoriasis (mean of positive sera Ti/Ui = 1·21), one of seven patients with pemphigoid and one of six patients with pemphigus. None of the ten patients with other skin disease had detectable IgA-containing CIC (Fig. 1).

IgG-containing CIC were detected in two of nineteen patients with psoriasis using the Raji cell IgG assay. None of nineteen patients with psoriasis showed abnormal C1q BA. The psoriasis patients with CIC by the Raji cell IgG assay also had IgA-containing CIC (Fig. 2).

Serum C3 and IgA levels

One of forty-nine patients with DH had a depressed C3 level (50 mg%; normal = 55–120 mg%). This patient had no detectable CIC by all assays used. None of the patients with HSP or psoriasis had low C3 levels; however, six of ten patients with SLE had low C3. Five of these six patients had circulating immune complexes by both the Raji IgG assay and the ^{125}I-C1q binding assay. Four of the six had IgA-containing CIC. No correlation, however, was found in SLE, between the serum level of C3 and the presence or level of immune complexes detected by any of the assays used.

One of the patients with DH had an elevated IgA level (468 mg%; normal = 90–450 mg%). Three patients with psoriasis also had elevated IgA levels. The remaining patients had normal IgA levels.

DISCUSSION

Raji cells are Epstein–Barr virus-infected lymphoblasts which can be maintained in continuous culture. These cells have no surface immunoglobulins, but do have receptors both for complement and for the Fc portion of IgG (Theofilopoulos *et al.*, 1974). The complement receptors are thought either to be present in greater numbers or have higher affinity for their ligands than the Fc IgG receptors. These cells are useful in detecting antigen–antibody complexes because CIC containing the complement fragments C3b or C3d bind firmly to the Raji cell via its complement receptors (Theofilopoulos *et al.*, 1974, 1976). In contrast to the ^{125}I-C1q binding assay, which requires activation of complement by the CIC via the classical pathway, the binding of complement fragments to the Raji cell is independent of the mode of complement activation. When IgA activates complement it is usually via the alternate pathway (Göetze & Müller-Eberhard, 1971) making this method well suited for the detection of IgA-containing CIC. Once bound to the Raji cell the CIC is detected by using an antibody that is specific for the immunoglobulin in the CIC. Previously,

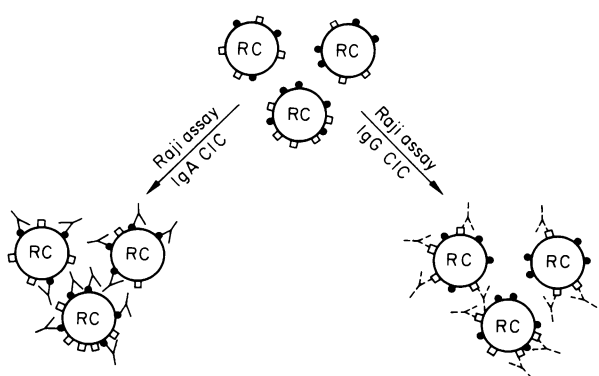

Fig. 3. Schematic representation comparing the Raji IgA and the Raji IgG radioimmunoassays. CIC = circulating immune complex, RC = Raji cell. (•) IgA-containing CIC, (□) IgG-containing CIC, ( ) ^{125}I-goat-anti-human IgA, ( ) ^{125}I-goat-anti-human IgG.

anti-human IgG has been used to detect IgG-containing CIC (Theofilopoulos *et al.*, 1976). We have used an antibody specific for the heavy chain of human IgA to detect CIC containing IgA (Fig. 3), and have used this radioimmunoassay to evaluate patients with DH, HSP and SLE for IgA-containing CIC.

Dermatitis herpetiformis is a blistering skin disease of unknown aetiology. As IgA is regularly detected (Katz & Strober, 1978; Seah *et al.*, 1972) and C3 is frequently detected (Katz *et al.*, 1976; Haffenden, Wojnarowska & Fry, 1979) in the skin of patients with DH, various hypotheses have been advanced to explain the exact role of these immune reactants in the pathogenesis of DH. One which has received increased attention recently is that the cutaneous immunoglobulin and complement represent the deposition of circulating immune complexes (Katz & Strober, 1978; Seah *et al.*, 1972; Mohammed *et al.*, 1976). Circulating immune complexes indeed have been found by one group of investigators in 100% of fifty-nine patients with DH (Mohammed *et al.*, 1976). Their methods, however, were capable of detecting only IgG- or IgM-containing immune complexes, and their findings have not been confirmed in this study, by us previously (Katz & Lawley, 1979), or by others (Zone *et al.*, Jordon *et al.*, personal communications). Since the major immunoglobulin in the skin of patients with DH is IgA it is thought by some that the CIC in these patients may contain IgA. Recently, Zone & Provost (1979) described an immunofluorescence assay using Raji cells to detect IgA CIC and found evidence of IgA CIC in six of eighteen patients with DH. We have used a sensitive radioimmunoassay to examine patients with DH for IgA-containing CIC and have detected IgA CIC in only 24% of patients. The lack of direct correlation to clinical status seems to suggest that IgA immune complexes may not contribute primarily to the pathogenesis of DH. These complexes may be a secondary phenomenon, formed in the skin after the deposition of IgA or formed in the intestine, and then slowly released into the circulation. Alternatively, it may be that we are unable with this assay to detect some IgA CIC due to their inability to fix complement in the fluid phase, or due to a strong avidity for the skin resulting in their rapid clearance from the circulation.

In HSP the finding of IgA in the blood vessels of uninvolved skin, as well as in renal biopsies, has suggested that IgA-containing CIC may be involved in the pathogenesis of this disease (Baart de la Faille-Kuyper *et al.*, 1973; Tsai *et al.*, 1975; Giangiacomo & Tsai, 1977). IgA-containing CIC were found in the sera of four of six patients we examined. The presence or level of CIC did not correlate with cutaneous, renal, or gastro-intestinal disease activity in the two patients studied serially. IgG- and IgM-containing CIC were found in only one patient. Although it is difficult to assign a primary role to IgA CIC in HSP due to the small number of patients studied, the high incdience of IgA CIC in these patients, with little evidence of IgG- or IgM-containing CIC, suggests that soluble IgA-containing immune complexes may play an important role in the pathogenesis of this disease.

As SLE is a prototype disease for the study of antigen–antibody complexes in man, we also examined the sera of these patients for immune complexes by all of our assays. The detection of IgG- and perhaps IgM-containing CIC by the conventional Raji cell assay and by the ^{125}I-C1q binding assay in a high percentage of our patients, as well as the high concordance rate between the two assays, is not surprising. The presence, however, of soluble IgA-containing immune complexes in 70% of our patients with SLE, has not to our knowledge been documented previously. Although IgA deposits have been detected in the glomeruli of some patients with lupus nephritis (Rothfield *et al.*, 1972) and IgA rarely found in cryoglobulins isolated from patients with SLE (Hanaver & Christian, 1967) the role of IgA CIC in SLE is unknown. The high concordance rate between the Raji IgG assay and the Raji IgA assay with a lack of rank order correlation suggests several possible explanations. IgA and IgG may exist in varying amounts within the same lattice structure of the circulating immune complex, or may exist both as separate entities and in combination. Alternatively, it may be that they are totally independent complexes formed in response to common stimuli and displaying similar physico-chemical characteristics.

Braun-Falco, Mannel & Scherer (1977) have reported the finding of CIC in 70% of patients with psoriasis using the C1q deviation test which presumably detects IgG- or IgM-containing CIC. This finding prompted us to examine patients with psoriasis for CIC. We were unable to detect substantial IgG- or IgM-containing CIC; however, IgA CIC were noted in 47% of patients. The significance of these findings at the present time is unknown.

We have detected IgA-containing CIC in a number of patients with DH, SLE, HSP and psoriasis. In SLE IgA-containing immune complexes were found in the presence of high levels of IgG- and IgM-containing CIC. Whether this is due to similar physico-chemical characteristics of the immune complexes or to the presence of multiple immunoglobulin types within a CIC is unknown. In DH, HSP and psoriasis, however, IgA CIC are found despite the relative absence of IgG- or IgM-containing CIC. This suggests a different mode of formation, or different biological behaviour of CIC in these diseases as compared to SLE.

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REFERENCES

BAART DE LA FAILLE-KUYPER, E.H., KATER, L., KOOIKER, L.J. & DORHOUT MEES, E.J. (1973) IgA deposits in cutaneous blood vessel walls and mesangium in Henoch–Schönlein syndrome. *Lancet*, **i**, 892.

BRAUN-FALCO, O., MANNEL, C. & SCHERER, R. (1977) Nachweis von Zirkulierenden löslichen Immunkomplexen im Serum vom psoriasis-patienten mit dem ^{125}I-C1q Ablenkingstest. *Hautarzt*, **28**, 658.

COHEN, A.S., REYNOLDS, W.E., FRANKLIN, E.L., KULKA, J.P., ROPES, M.W., SHULMAN, L.E. & WALLACE, S.L. (1971) Preliminary criteria for the classification of systemic lupus erythematosus. *Bull. Rheum. Dis.* **21**, 643.

GIANGIACOMO, J. & TSAI, C.C. (1977) Dermal and glomerular deposits of IgA in anaphylactoid purpura. *Am. J. Dis. Child.* **131**, 981.

GOETZE, O. & MÜLLER-EBERHARD, H.J. (1971) The C3-activator system. An alternate pathway of complement activation. *J. exp. Med.* **134**, 90S.

HAFFENDEN, G., WOJNAROWSKA, F. & FRY, L. (1979) Comparison of immunoglobulin and complement deposition in multiple biopsies from the uninvolved skin in dermatitis herpetiformis. *Br. J. Dermatol.* **101**, 39.

HANAVER, L.B. & CHRISTIAN, C.L. (1967) Studies of cryoproteins in systemic lupus erythematosus. *J. clin. Invest.* **46**, 400.

KATZ, S.I., HERTZ, K.C., CRAWFORD, P.S., GAZZE, L.A., FRANK, M.M. & LAWLEY, T.J. (1976) Effect of sulfones on complement deposition in dermatitis herpetiformis and on complement-mediated guinea pig reactions. *J. Invest. Dermatol.* **67**, 688.

KATZ, S.I. & LAWLEY, T.J. (1979) Dermatitis herpetiformis: recent advances. In *Immunopathology of the Skin.* (Ed. by E. Beutner). John Wiley and Sons, New York.

KATZ, S.I. & STROBER, W. (1978) The pathogenesis of dermatitis herpetiformis. *J. Invest. Dermatol.* **70**, 63.

LAMBERT, P.H., DIXON, F.J., ZUBLER, R.H., AGNELLO, V., CAMBIASO, C., CASALI, P., CLARKE, J., COWDERY, J.S., MCDUFFIE, F.C., HAY, F.C., MACLENNAN, I.C.M., MASSON, P., MÜLLER-EBERHARD, H.J., PENTTINEN, K., SMITH, M., TAPPEINER, G., THEOFILOPOULOS, A.N. & VERROUST, P. (1978) A WHO collaborative study for the evaluation of eighteen methods for detecting immune complexes in serum. *J. clin. Lab. Immunol.* **1**, 1.

LAWLEY, T.J., MOUTSOPOULOS, H.M., KATZ, S.I., THEOFILOPOULOS, A.N., CHUSED, T.M. & FRANK, M.M. (1979) Demonstration of circulating immune complexes in Sjögren's syndrome. *J. Immunol.* **123**, 1382.

MOHAMMED, I., HOLBOROW, E.J., FRY, L., THOMPSON, B.R., HOFFBRAND, A.V. & STEWART, J.S. (1976) Multiple immune complexes and hypocomplementaemia in dermatitis herpetiformis and coeliac disease. *Lancet*, **ii**, 487.

ROTHFIELD, N., ROSS, H.A., MINTA, J.O. & LEPOW, I.H. (1972) Glomerular and dermal deposition of properdin in systemic lupus erythematosus. *N. Eng. J. Med.* **287**, 681.

SEAH, P.O., FRY, L., STEWART, J.S., CHAPMAN, B.L., HOFFBRAND, A.V. & HOLBOROW, E.J. (1972) Immunoglobulins in the skin in dermatitis herpetiformis and coeliac disease. *Lancet*, **i**, 611.

THEOFILOPOULOS, A.N., DIXON, F.J. & BOKISCH, V.A. (1974) Binding of soluble immune complexes to human lymphoblastoid cells. *J. exp. Med.* **140**, 877.

THEOFILOPOULOS, A.N., WILSON, C.B. & DIXON, F.J. (1976) The Raji cell radioimmune assay for detecting immune complexes in human sera. *J. clin. Invest.* **57**, 169.

TSAI, C.C., GIANGIACOMO, J. & ZUCKNER, J. (1975) Dermal IgA deposits in Henoch–Schönlein purpura and Berger's nephritis. *Lancet*, **i**, 342.

WOODROFFE, A.J., BORDER, W.A., THEOFILOPOULOS, A.N., GÖTZE, O., GLASSCOCK, R.J., DIXON, F.J. & WILSON, C.B. (1977) Detection of circulating immune complexes in patients with glomerulonephritis. *Kidney Int.* **12**, 268.

ZONE, J.J. & PROVOST, T.T. (1979) IgA immune complexes in dermatitis herpetiformis. *Clin. Res.* **27**, 539 (abstract).