Increased Plasma IgA, slgA, and C3- and IgA-Containing Immune Complexes
With Renal Glomerular Deposits in Diabetic Rats

LEON L. MILLER, MARY JANE IZZO, DRUSILLA WEMETT, BERNARD J. PANNER,
AND ERIC A. SCHENK

Male Sprague-Dawley rats were fasted 18 h and given streptozocin (STZ; 60 mg/kg body wt i.p.). The resultant diabetes mellitus, not treated with insulin, was associated with persistent manifoldly increased plasma IgA levels, as measured by single-radial immunodiffusion after reduction with dithiothreitol and alkylation with iodoacetamide. Also observed were concurrent increases in plasma levels of secretory IgA (slgA) and of C3- and IgA-containing immune complexes (C3-IgA-CIC). After 104 days without insulin treatment, six of the diabetic rats were given daily injections of 2 U of insulin for 11 days. Insulin treatment was associated with a precipitous decrease in plasma levels of IgA, slgA, and C3-IgA-CIC.

Cessation of insulin treatment resulted in restoration of greatly increased levels of all three IgA-containing species. Histoimmunofluorescence studies of kidneys from untreated rats with diabetes of 192-324 days revealed glomerular capillary wall and mesangial deposits reacting strongly with anti-lgA (α-chain–specific) antiserum. Kidneys from two of the diabetic rats (324 days) were tested with anti-rat C3 and anti-rat secretory component (SC) antisera, and they reacted positively. Control kidneys from normal rats examined simultaneously were negative. The concurrent changes in plasma levels of three IgA-containing species in the untreated STZ-induced diabetic rat and the demonstration of abnormal immunoreactive IgA-containing renal glomerular deposits make this experiment an attractive model for studying the possible role of disturbed IgA metabolism in the pathogenesis of diabetic nephropathy. Diabetes 37: 185–93, 1988

In a separate article (p. 177–184) we describe the occurrence of persistent, greatly increased plasma levels of immunoglobulin A (IgA) in the untreated streptozocin-induced diabetic rat (STZ-D). In the diabetic rat maintained with daily insulin, plasma IgA levels also increased, but to a lesser degree.

Along with increased plasma IgA levels in the untreated diabetic rat, we describe concurrent increased levels of plasma secretory IgA (slgA) and increased levels of circulating immune complexes containing C3-complement and IgA (C3-IgA-CIC), the striking reversal of these increased levels after insulin treatment, and their restoration after withdrawal of insulin treatment. We also describe evidence from histoimmunofluorescence studies of renal glomerular deposits showing that IgA, slgA, and/or C3-IgA-CIC accumulate in the kidneys of long-term untreated diabetic rats.

There is considerable literature, briefly reviewed by Sorger (1), Fuchs et al. (2), and Michael et al. (3), on the occurrence of increased deposits of IgG and IgM in the glomeruli of human and rat diabetic kidneys. However, little has been written about the occurrence of deposits of IgA in the kidneys of diabetic humans (1,4), and we know of no report associating diabetes mellitus with renal glomerular deposits of IgA in the rat.

In a retrospective clinical study of human diabetes, Triolo and co-workers (5,6) describe the occurrence of increased levels of IgA and of C3-IgA-CIC associated with clinical evidence of retinal and renal complications.

MATERIALS AND METHODS

Induction of STZ-D. Eighteen adult male Sprague-Dawley rats (Holtzman, Madison, WI) weighing 275–300 g were housed and fed as described previously (p. 177–184). Although not certified as “pathogen-free,” the rats appeared healthy, with clean well-groomed fur. They were maintained without isolation precautions in a temperature-controlled (22 ± 2°C) air-conditioned room. After an 18-h fast, 12 rats.
were lightly anesthetized and given 60 mg/kg body wt i.p. streptozocin (STZ; Sigma, St. Louis, MO) in 30 mg/ml ice-cold isotonie citrate buffer (pH 4.5) to induce diabetes mellitus. The other 6 rats served as controls and received only ice-cold citrate buffer. Typically, the diabetic rats manifested gross polyuria, glycosuria (Tes-Tape, 3–4 +), and ketonuria (Acetest, 0–2 +) within 24–48 h. On day 10, the plasma glucose of diabetic rats was between 400 and 800 mg/dl, and that of controls was between 80 and 150 mg/dl (Chemstrip, Boehringer Mannheim, Indianapolis, IN). Fed and watered ad libitum, the diabetic rats consumed larger quantities (grossly estimated) of food and water and appeared less well groomed than the normal controls; 97 days after the onset of diabetes, their weight gain of 95 ± 30 g was substantially less than the 242 ± 45 g of the controls. Individual 24-h urine volumes of 3 of the diabetic rats before and after receiving 2 U s.c. of protamine zinc insulin for 3 days decreased from 140–225 (2–3+ glucose) to 10–40 ml (1–2+ glucose), respectively.

Six more STZ-D rats were not treated for diabetes and were fed rodent chow and water. After 192, 225, and 324 days, a pair of rats was exsanguinated and killed by cardiac puncture under light ether anesthesia along with a similarly maintained normal control of the same age. Samples of kidney were immediately frozen on dry ice and then stored at −70°C for subsequent immunofluorescence studies; other kidney samples were taken in buffered formalin for routine staining with hematoxylin and eosin.

BLOOD SAMPLES
With the rats held in a restraining cage (7), blood samples were obtained without anesthesia by resecting the terminal 1–2 mm of the rats’ tails; a total of 0.5–0.6 ml of blood was drawn into heparinized microhematocrit tubes (Clay-Adams, New York) from which plasma was obtained and stored at −30°C. Blood samples were taken between 0900 h and
TABLE 1
Plasma glucose levels of diabetic rats treated with insulin on days 104–115

<table>
<thead>
<tr>
<th>Days after streptozocin administration</th>
<th>Plasma glucose (mean ± SD)</th>
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<tr>
<td>n</td>
<td></td>
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<tr>
<td>10</td>
<td>10</td>
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<tr>
<td>10</td>
<td>98</td>
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<tr>
<td>10</td>
<td>108</td>
</tr>
<tr>
<td>5</td>
<td>115</td>
</tr>
<tr>
<td>10</td>
<td>121</td>
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midnight from diabetic and control rats, initially the day before STZ was administered and at about weekly intervals until day 104. On that day, six of the diabetic rats were arbitrarily selected for their higher IgA levels to allow the maximum amplitude for a response to insulin, and between 1600 and 1700 h, they were given the first of 11 daily doses of insulin (2 U protamine zinc insulin, Lilly, Indianapolis, IN). The remaining diabetic rats served as untreated controls. Blood samples were taken on days 108 and 115, after which insulin treatment was discontinued; blood sampling continued for an additional 3 wk.

Measurement of plasma IgA levels. Plasma IgA levels were measured by single-radial immunodiffusion analysis after reduction with dithiothreitol and alkylation with iodoacetamide.

Measurement of plasma levels of C3- and IgA-containing immune complexes. We measured C3-IgA-CIC in triplicate by essentially following the procedure used by Pereira et al. (8) on human plasma. Rabbit antiserum to rat C3 was prepared as before (p. 177–184) and used to prepare the F(ab')2 fraction by the method of Nisonoff et al. (9). In step 1 of the four-step assay, 0.10 ml of a solution of 4.4 μg anti-C3 F(ab')2 in 0.05 M bicarbonate buffer (pH 9.1) was added to each well of a Costar Serocluuster V vinyl plate (Cambridge, MA), which was allowed to stand at 4°C for 18–20 h. The excess F(ab')2 was removed by suction and washed three times with phosphate-buffered saline (PBS; 0.04 M in 0.15 M NaCl, pH 7.2, containing 0.05% Tween 20). In step 2 we added to each well 0.2 ml of 1% bovine serum albumin (BSA) in PBS. The plates stood for 1 h at room temperature, and the unabsorbed BSA was removed by suction, followed by three washes with PBS-Tween 20. In step 3, 0.1 ml of a 1:10 dilution in BSA-PBS of each plasma or serum sample was pipetted in triplicate into separate wells, and the plates were incubated 2 h at 37°C; the residual samples were removed by suction and followed by three washes with PBS-Tween 20. In step 4, to each well was added 0.1 ml of 125I-anti-IgA (α-chain specific), prepared and iodinated as described (p. 177–184), containing 1.5 μg of protein with 1.5 × 10⁴ dpm. After 2 h at 37°C the excess antiserum was removed by suction, each well was washed five times with PBS-Tween 20, and the plates were inverted to drain dry on absorbent tissue. Then we cut each well from the plates and placed the wells in polyethylene tubes to be counted for 10 min in a γ-scintillation spectrometer. Because there is no satisfactory practical primary standard for rat C3-IgA-CIC, the mean value obtained from samples of all of the rats before STZ administration and of the controls throughout the experiment was arbitrarily assigned a normal value of 100%, and values of the STZ-D rats were expressed as a percentage of normal.

Measurement of plasma sigA levels. Using the direct-competition radioimmunoassay of Delacroix and Vaerman (10),
TABLE 2
Association of plasma IgA levels and slgA levels in untreated streptozocin-induced diabetic rats

<table>
<thead>
<tr>
<th>Rat</th>
<th>Immunoelectrophoretic reaction vs. anti-SC*</th>
<th>Plasma slgA (µg SC/dl)</th>
<th>Plasma IgA (mg/dl)</th>
</tr>
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<tbody>
<tr>
<td>240</td>
<td>+++</td>
<td>540</td>
<td>1190</td>
</tr>
<tr>
<td>241</td>
<td>+++</td>
<td>460</td>
<td>700</td>
</tr>
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<td>242</td>
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<td>246</td>
<td>-</td>
<td>360</td>
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<td>251</td>
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*Plasma samples taken from each of the diabetic rats (on day 60) and samples taken from the same rats on the day before administration of streptozocin were subjected to immunoelectrophoresis on the same slide by standard techniques, and their reactions to the rabbit anti-rat secretory component (SC) reagent were compared. Positive-reaction arcs observed only for slgA were rated from + to +++ as a gross estimate of precipitin intensity; all of the prediabetic samples and several of the diabetic samples reacted negatively (−).

We measured plasma slgA levels; we modified the procedure somewhat by using rat secretory component (SC) purified from rat bile and iodinated by the oxidative ICI method of Helmkamp et al. (11). Our assay thus depends on competition between a standard amount of 125I-labeled SC and the SC bound in slgA of plasma samples. The results of the slgA assay are expressed in terms of SC equivalents as estimated from a standard curve based on known purified SC (Fig. 1). Such values may readily be converted to an estimate of slgA content by assuming the slgA is multimeric, with an average molecular weight of 540,000 M, and that 1 molecule of SC (70,000 M) is covalently bound per multimeric slgA; on that basis the content of slgA in normal and diabetic rat plasma is ~0.1 and 0.6% of total IgA, respectively.

The substitution of 125I-labeled SC for the 125I-labeled slgA (10) was possible because free SC was not demonstrable in any of the diabetic plasma samples when both free SC and plasma samples were compared on immunoelectrophoresis in their reaction with the specific rabbit anti-rat SC reagent; this antisera did not react with a specimen of authentic monoclonal rat IgA but reacted strongly with known rat SC and with rat slgA.

Measurements of plasma IgG levels. We measured plasma IgG levels of all samples of diabetic and normal rat plasma by single-radial immunodiffusion analysis with a rabbit anti-rat IgG antiserum as reagent and isolating rat IgG as previously described.

2-D GELS OF UNDENATURED PLASMA PROTEINS
Samples of plasma taken from four of the diabetic rats before (day 104) and after (day 115) insulin treatment were subjected to isoelectric focusing and gradient acrylamide gel electrophoresis followed by silver staining according to our previously described methods (p. 177–184).

HISTOLOGICAL METHODS
All immunofluorescence studies were done on 6-µm cryostat sections, which were air dried, washed in PBS for 10 min, fixed in cold acetone for 1 min, and again washed in PBS for 10 min before incubation with antisera.

Sections of kidney were stained for rat IgA, secretory component, and C3 complement by a two-step procedure. Sections were first incubated with the specific rabbit anti-rat antisera (diluted 1:10) for 30 min, rinsed and washed for 10 min, then stained with fluoresceinated goat anti-rabbit IgG
FIG. 5. Time course of total plasma IgG levels in 4 untreated (•) and 4 insulin-treated (○) diabetic rats compared with 6 normal controls (△). Points represent means; bars = 1SD.

(diluted 1:100). Second, slides were rinsed and washed for 10 min, counterstained with 1% methyl green, and mounted in 10% glycerol in PBS. We examined and photographed coded sections using an Olympus fluorescence photomicroscope equipped with a mercury lamp and appropriate filters.

RESULTS

Effects of insulin treatment on the hyperimmunoglobulinemia A of STZ-D rat. After the development and persistence of grossly increased IgA levels for 104 days in untreated diabetic rats, six rats were given daily injections of 2 U protamine zinc insulin for the next 11 days, and four rats were maintained as untreated controls. Insulin treatment was associated with a precipitous decline in IgA levels to almost normal values. Cessation of the insulin treatment from day 115 was followed by an equally sharp rise in IgA levels, which reached pre-insulin-treatment values within 16 days (Fig. 2, top). The absence of insulin treatment, abnormally high IgA levels in the untreated diabetic rats persisted when the levels in the insulin-treated diabetic rats were dramatically decreased (Fig. 2, bottom).

Plasma glucose levels of the insulin-treated rats for days 10, 98, 108, 115, and 121 after STZ administration were estimated on the same samples obtained between 0900 h and midnight for analysis of IgA species. (Samples were taken 17–20 h after the insulin was administered and probably do not reflect the major hypoglycemic effect most likely manifest in the hours immediately after insulin.) Effects of insulin treatment on plasma glucose levels are summarized in Table 1. Because the plasma samples for days 108 and 115 were obtained 17–20 h after insulin treatment, only moderate hypoglycemic effects were seen.

Effects of insulin treatment on levels of circulating C3-IgA-CIC in STZ-D rats. Figure 3 shows the increase and persistence of C3-IgA-CIC circulating in six diabetic rats. Because it was not practical to use an absolute standard for the measurement of circulating C3-IgA-CIC, measurements are expressed in terms of the apparent content of these immune complexes based on the measured mean content in the plasma of normal controls, taken as 100 ± SD of 50%. It is clear that insulin treatment of the diabetic rats between days 104 and 115 after STZ administration was associated, particularly in those rats with high levels, with a precipitous decline in the content of C3-IgA-CIC, which roughly parallels the changes in higher IgA levels shown in Fig. 2 (top). Cessation of insulin treatment was shortly followed by a return toward the higher levels prevailing before insulin treatment. Not all untreated diabetic rats with elevated IgA levels had abnormally increased levels of C3-IgA-CIC, nor did the rats with the highest IgA levels have the highest levels of C3-IgA-CIC.

Appearance of slgA in plasma of untreated STZ-D rats. Immunoelectrophoresis revealed that the appearance of slgA in the plasma of STZ-D rats varies (Table 2). Plasma slgA levels of ≤380 µg/dl SC were negative to the anti-SC reagent on immunoelectrophoresis. Plasma slgA estimated by either immunoelectrophoresis or radiimmunoassay correlates only grossly with total IgA levels (Table 2). With initial prediabetes control values for plasma slgA ranging from 30 to 60 µg/dl, the observed increased slgA values in Table 2 correspond to about a 4- to 10-fold increase; total plasma IgA levels for the same rats ranged from 6 to as much as 100 times control values.

Effects of insulin treatment on levels of circulating slgA in STZ-D rats. Plasma levels of slgA roughly parallel the levels of IgA and of C3-IgA-CIC (Fig. 4, top). Though relatively small in absolute terms, the circulating levels of slgA are persistently elevated in the untreated diabetic rat, decrease sharply in response to insulin treatment, and after insulin withdrawal, increase rapidly to preinsulin treatment values. Elevated slgA levels in three untreated diabetic rats persisted (Fig. 4, bottom). As explained in MATERIALS AND METHODS, slgA values were calculated and are depicted in Fig. 4 as SC equivalents; thus the levels of circulating slgA before STZ was administered was ~0.1% of total IgA, and after the development of diabetes, they did not exceed 0.6% of total IgA.

Plasma IgG levels of rats during the development of STZ-D and treatment with insulin. We measured IgG levels in the same plasma samples as total IgA for comparison; the results are presented in Fig. 5, which shows that the circulating levels of total IgG appear to be slightly higher in the diabetic rats, but in insulin-treated and untreated rats, IgG levels did not change significantly, whereas total IgA levels were undergoing major changes with the development of diabetes and insulin treatment.

2-D gels of undenatured plasma proteins of four untreated STZ-D rats before (day 104) and after (day 115) insulin treatment. Protein spots 5, 6, and 7, presumptively identified in a separate study (p. 177–184) as IgA multimers and found to be characteristic of untreated diabetes in the rat (Fig. 6, top), virtually disappeared after insulin treatment (Fig. 6, bottom), when the levels of total IgA had decreased to 1/40 of that present in this diabetic rat before insulin treatment; this may be regarded as additional presumptive evidence for identification of protein spots 5, 6, and 7 as IgA multimers.

Histoimmunofluorescence studies of kidneys from six long-term untreated diabetic rats. There were widespread glomerular capillary basement membrane and mesangial deposits of IgA (α-chain–specific) immunoreactive material in the kidneys of long-term diabetic rats who had high levels of IgA in their circulations (Fig. 7, top). Corresponding glomerular areas of normal control kidneys were negative (Fig. 7, bottom). Kidneys from two additional untreated long-term (324 days) diabetic rats with high circulating levels of IgA, slgA, and IgA-C3-CIC were examined by specific immu-
IgA, slgA, AND IgA IMMUNE COMPLEXES IN DIABETES

FIG. 6. Top: typical silver-stained 2-D gel of plasma proteins, prepared from 0.1 μl of plasma obtained from untreated diabetic rat (242) on day 104; note prominent spots 5, 6, and 7 presumptively identified as IgA multimers. Protein bands at right are Pharmacia high-molecular-weight standards run only in second dimension (4–20% linear acrylamide gel gradient). Bottom: silver-stained 2-D gel prepared under identical conditions from 0.1 μl plasma taken from same rat after 11 days of insulin treatment. Note gross decrease in intensity of staining of spots 5, 6, and 7 corresponding to marked decrease in total plasma IgA (Fig. 2, top; day 115).

no fluorescence for abnormal glomerular deposits, and both revealed reactive deposits for IgA (similar to those seen in Fig. 7, top), SC (Fig. 8), and C3 (Fig. 9). Simultaneously examined secretions from normal control kidneys were negative for glomerular deposits and looked like Fig. 7, bottom.

In contrast to the striking glomerular deposits revealed by histoimmunofluorescence, the hematoxylin-eosin–stained kidney sections (from rat diabetic for 9 mo) showed only focal glomerular mesangial hypercellularity consisting of infrequent scattered glomeruli with more than two or three nuclei visible in the mesangial areas and a minor degree of focal glomerular hyalinization.

DISCUSSION

The studies described here not only confirm and extend our previous observations on the occurrence of persistent hyperimmunoglobulinemia A in untreated STZ-D rats but also indicate that the increased levels of IgA are associated with simultaneously increased levels of C3-IgA-CIC and with relatively small but significant increases in slgA levels. Equally noteworthy is the fact that the plasma levels of all three IgA-containing entities are sensitive to treatment with insulin and drop to almost normal values after 11 days of insulin treatment, only to regain higher values within 5 or 6 days of insulin deprivation.
We are without an explanation for the wide variance in IgA levels of individual untreated diabetic rats, and in particular the spontaneous partial decline in IgA levels of some of the diabetic rats between 50 and 90 days after STZ was administered. On the basis of plasma glucose levels of individual diabetic rats on days 10, 98, 108, 115, and 121 after STZ was given (data not presented), there was no correlation or even a discernible trend between individual plasma IgA and glucose levels.

The above observations are of special interest because of our finding of immunoreactive deposits of IgA-, SC-, and C3-material in renal glomeruli of long-term diabetic rats, which suggests that deposits of IgA and IgA-CIC may have more than a merely coincidental role in the development of the microvascular complications of diabetes.

Triolo and co-workers (5,6) have briefly reviewed literature describing the occurrence of circulating immune complexes in human diabetes mellitus and the postulated relationship to late diabetic complications. They have also described a retrospective clinical study in which they found a significant correlation between clinical evidence of renal and retinal vascular complications and the occurrence of increased levels of circulating IgA and C3-IgA-CIC.

Andreani et al. (12) have reported a retrospective clinical study in which C1q-binding and conglutinin-binding assays were used to measure circulating immune complexes in diabetic humans and to correlate them with clinical evidence of nephropathy and/or retinopathy; they found an increased incidence of elevated immune complex levels by both assay methods; however, microangiopathy was always associated with increased complex levels by the C1q assay, and increased levels by the conglutinin assay were more commonly present in diabetic subjects but were not correlated with microangiopathy. Both assay methods used by Andreani et al. depended on quantitation of protein A–binding and therefore measured primarily IgG-CIC; possible involvement of other immunoglobulin types such as IgA was not considered.
IgA, slgA, AND IgA IMMUNE COMPLEXES IN DIABETES

The observation that insulin treatment reduced the abnormal levels of IgA, slgA, and C3-IgA-CIC of diabetic rats to normal values suggests that insulin has an important, but as yet undefined, role in the metabolism of IgA; it also suggests that the levels of these IgA species in most of the diabetic humans studied by Triolo and co-workers (5,6) may have been kept at relatively low levels because the patients were treated with insulin or sulfonylureas. Hoddinott et al. (13) have examined a group of insulin-treated type I (insulin-dependent) diabetic patients and found that serum IgA and IgM levels were not different from those of a normal control group; no mention was made of the occurrence of circulating immune complexes or of complications of diabetes.

The many references to renal deposition of immunoglobulins and complement components in diabetic humans have been reviewed by Sorger (1), Fuchs et al. (2), and Mauer et al. (14). The mention of renal IgA deposits in diabetic humans is much less frequent than that of IgG and IgM (1,4). To our knowledge, our studies are the first to describe IgA deposits in experimental diabetes in the rat. In 1972, Mauer et al. (15)...
described the detection by immunofluorescence methods of IgG and C3 in the renal glomeruli of long-term alloxan-diabetic rats. Later, Mauer et al. (16) presented evidence for the reversibility of such deposits when the kidneys from diabetic rats were transplanted to normal syngeneic recipients and thereby provided evidence that diabetes per se was implicated in the genesis and persistence of the abnormal glomerular deposits. However, as Fuchs et al. (2) and Mauer et al. (15) have emphasized, the extent to which such abnormal glomerular deposits are related to disturbed immune mechanisms or to other pathogenetic factors, including damage to vascular cell membranes, is not clearly established.

Because of the known association of increased levels of plasma IgA, sIgA, and immune complexes containing them in human noninsulin dependent diabetes (17,18), the possibility of impaired hepatic function in the STZ-D rat deserves consideration; however, we have no evidence for impaired hepatic synthesis and biliary secretion of SC or of sIgA. The possibility that increased plasma IgA levels are the result of impaired phagocytic clearance of foreign antigens and their IgA-containing immune complexes remains to be evaluated, because impairment of phagocytic function is known to occur in diabetic animals (19). Our measurements of the apparent half-life of IgA from diabetic rats do not support the theory that increased nonenzymatic glycosylation of IgA could prolong its half-life in plasma.

The occurrence of IgA- and C3-reactive renal mesangial glomerular deposits in rats (20) and mice (21) subjected to cholestasis from total bile duct ligation suggests that otherwise normal murine species are especially prone to developing such deposits in response to normal blood levels of IgA and C3-IgA-CIC. The latter, taken together with the observations of Mauer et al. (22) on the impaired processing of macromolecules by the altered renal mesangium of diabetic rats, suggests that persistent abnormally increased blood levels of multimeric IgA, sIgA, and C3-IgA-CIC in the untreated diabetic rat would promote enhanced mesangial uptake; however, slowed mesangial clearance of these IgA species would be expected to result in their abnormal accumulation.

The occurrence of nephropathy with renal glomerular deposits of IgA or IgA-CIC in nondiabetic disease states (17,18) has raised the question of why IgA-CIC is more likely to accumulate in the kidney than is IgG-CIC. Waxman et al. (23) have compared the relative binding by erythrocytes of IgA- and IgG-CIC in primates and found IgA-CIC to be much less firmly bound and therefore much more likely to be cleared from the circulation by lung and kidney rather than by liver or spleen. They propose a hypothesis based on these observations that would help explain the occurrence of abnormal renal IgA deposits in human disease states such as idiopathic IgA nephropathy. Observations similar to those made by Waxman et al. in the baboon have not been reported for rodents; accordingly, the possibility that such a mechanism may operate in the diabetic rat to help explain the occurrence of IgA deposits in the glomeruli has not been proved.

The demonstrated concurrence in the untreated diabetic rat of persistent hyperimmunoglobulinemia A, increased levels of C3-IgA-CIC, and renal glomerular mesangial and capillary deposits of IgA make the STZ-D rat an attractive model for evaluating the possible role of IgA in the genesis of renal complications of diabetes mellitus.

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