Varia

Renal Association
(May 13, 1971)


Studies of bladder histology were made in patients with urinary infection or symptoms of cystitis, with a view to establishing a relationship between symptoms, cystoscopic appearances, bacilluria and histological features. Bladder biopsies were taken from the patients and compared with control material obtained at autopsy. Acute inflammatory changes were inconstant and difficult to assess. Chronic inflammatory changes were often marked and were ranked by severity into 4 grades. There was a statistically significant correlation between the more severe grades and the finding of bacilluria, which was not dependent on sex, age or mode of death. The grades in patients with non-bacterial cystitis (‘urethritis’) lay between those of the controls and the infected patients and were statistically different from both. There was no correlation between these grades and either symptoms or the finding of trigonal hyperaemia during cystoscopy. Heavy lymphocytic infiltration, and particularly germinal follicle formation, resulted in macroscopic tubercle-like nodules visible on cystoscopy. Such germinal follicle formation in the bladder may explain the high bacterial antibody titres sometimes found in subjects with lower urinary tract infection, and may contribute to local antibacterial defences.

The significance and type of squamous epithelial change was also assessed. It was a common, apparently non-specific finding in females, unrelated to infection and not productive of symptoms.


The local and general cellular immune response and the sequence of antibody production was studied in experimental retrograde pyelonephritis. The bladders of 75 female Wistar rats were injected per urethram with 1 ml saline containing 10^7/ml live 04 E. coli and observations were made at intervals up to 50 days later. Counts of individual antibody producing cells (APC) were obtained by the haemo-lytic plaque and the immunocytoadherence techniques on cell suspensions from the spleen, lymph glands, renal tissues and bladder.

The rats developed an acute urinary tract infection with high bacterial counts of 04 E. coli in the urine (10^6.8/ml) and renal tissues (10^4.8/g). The kidneys and bladder walls were infiltrated with inflammatory cells. There was an invariable brisk general immunocellular response with direct (IgM) plaque counts rising to 6 × 102 ACP/10^6 spleen cells at 4-6 days, and indirect (IgG) plaques reaching a peak at 15-20 days. The immunocytoadherence assay attained a maximum of 10^4 APC/10^6 spleen cells at 10 days. Similar changes in the number of APC occurred in lymph tissue from the renal hilum and pelvis. There was also an abundant but variable local production of specific 04 antibody (mainly IgG and IgM) by numerous cells in the kidney and the bladder wall. The individual cells producing antibody were identified by the slide plaque and centrifuge slide rosette techniques. Antibody producing cells in the urinary tract were always characteristic
large and small immunocytes and there was no evidence of local antibody production by renal or bladder cells.


Three patients in whom a nephrotic syndrome occurred in association with extra-renal carcinoma are described. The primary tumour sites were bronchus in 2 and breast in 1. Renal vein thrombosis was excluded by venography in 2 patients and at necropsy in the 3rd. Renal biopsies were performed and showed diffuse glomerular abnormalities in all 3 patients. There was no evidence of direct invasion of the kidney by tumour and amyloidosis was excluded.

In 1 of the 3 patients, immunological studies were undertaken. Immunofluorescence of renal biopsy material showed ‘lumpy’ deposits of IgG on the glomerular basement membrane. Elution of these and subsequent immunoelectro-phoresis confirmed the presence of IgG and IgM.

Following death of the patient, further studies were undertaken in an attempt to establish an immunological relationship between the glomerular complexes and membrane antigens of the bronchial tumour cells. Using membrane immunofluorescence staining of the membrane antigens of cells from the bronchial tumour was demonstrated with both the eluate from the glomeruli and the patient’s serum. Immunodiffusion on cellulose acetate membrane was also performed and a line of identity was seen between both the glomerular eluate and the patient’s serum and a crude extract of tumour cells.

It is suggested, therefore, that glomerular damage in patients with malignant disease may result from an immune response to their tumour.


Persistently low levels of the 3rd component of the complement system (C-3) are usually found in patients with membranoproliferative glomerulonephritis. To study the mechanism of hypocomplementaemia turnover studies using radioiodine-labelled purified C-3 have been carried out in 4 patients. The biological half-lives and fractional catabolic rates were normal, suggesting that C-3 synthesis is impaired in this condition. 10 patients were studied for evidence of a circulating factor which will breakdown C-3 in vitro. Evidence for such a factor was found in 7 of these patients. These were patients with very low C-3 levels. The relationship of the C-3 lytic factor to the apparently depressed C-3 synthesis will be discussed.


It has been claimed [Yatzidis et al., 1966; Giovanetti et al., 1968] that methylguanidine is present in uraemic serum in much high concentrations than previously had been supposed. Injection of this substance into dogs in amounts sufficient to produce blood levels similar to those reported in uraemic humans results in many of the complications which occur in uraemia [Giovanetti et al., 1969]. These observations suggested that retention of methylguanidine might be an important factor in the genesis of the ‘uraemic syndrome’.

A new method for the measurement of this substance, based upon cation exchange column chromatography, will be described.

In 10 normal subjects methylguanidine concentration was 0.055 ± 0.019 mg/ 100 ml (mean ± SEM) and in 10 uraemic patients (blood urea 120-430 mg/100 ml,
mean 270 mg/100 ml) it was 0.175 ± 0.033 mg/100 ml (mean ± SEM). This difference is significant (0.01 > p < 0.02). Values observed in uraemic patients are much lower than those found by methods employing charcoal chromatography [Yatzidis et al., 1966; Giovanetti et al., 1968]. Further experiments have shown that methylguanidine is generated from creatinine during these latter methods in amounts sufficient to account for this discrepancy. It, therefore, seems likely that the importance of this compound in the genesis of the complications of uraemia has been overestimated.

References
Swales, J.D.; Tange, J.D., and Evans, D.J.: Uraemic colitis. Inflammatory lesions of the colon associated with diarrhoea have been described as a feature of uraemia, both clinically and experimentally. In both situations, the colitis has been ascribed to bacterial infection, or local vascular lesions. An alternative, long-standing hypothesis is that the colitis is due to the high concentrations of ammonia which are known to be present in the intestinal fluids of uraemic patients, and which exert a pronounced effect upon the local pH. The evidence in favour of this hypothesis is necessarily indirect, and based upon studies with germ-free animals, in which the absence of bacterial urease results in reduced levels of gastrointestinal ammonia. Clearly, such models as these, and those in which the gastro-intestinal tract has been sterilised by antibiotics are insufficiently specific to assess the role of ammonia in uraemic colitis.

We have investigated this problem by using acetohydroxamic acid, a powerful, non-toxic, non-competitive urease inhibitor, which is active in preventing the hydrolysis of urea by both bacterial and human mucosal urease. In vitro, this substance inhibits the formation of ammonia by colonic contents incubated with urea solutions.

Acetohydroxamic acid was administered to bilaterally nephrectomised rats. Ammonia concentration in the colon was reduced to 36% of that in untreated animals. In the caecum, with its very bulky contents there was no reduction in ammonia concentration. Despite these and other biochemical differences between treated and control animals, the incidence of lesions in the caecal and colonic mucosa was not influenced by acetohydroxamic acid. It is concluded that uraemic colitis is not due to high concentrations of ammonia, and that it is a consequence of bacterial infection.

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kidney. Autoradiography has demonstrated that in normal dogs, compartments 1, 2, 3 and 4 (in order of decreasing rates of flow) are related to flow in the cortex, outer medulla, inner medulla and peri-renal fat respectively. It was found that the patients could be divided into 2 approximately equal groups in respect of their renal blood flow characteristics; firstly those in whom the usual 4 compartments were present and secondly those in whom only 3 compartments could be demonstrated. The cardiac output in the patients with 3 compartments only was significantly lower than in those with 4 compartments ($\rho < 0.025$). In the 1st group of patients (4 compartments) there were significant linear correlations between cardiac output and glomerular filtration rate (c.c. = 0.67 $p < 0.05$), and between glomerular filtration rate and intrarenal blood distribution to the 1st compartment (c.c. = 0.68 $p < 0.05$). These correlations were not demonstrated in the 2nd group of patients (3 compartments). In addition, the glomerular filtration rate was often well maintained in this 2nd group, even in the presence of a low cardiac output. It is suggested that as the cardiac output becomes impaired, the renal cortical blood flow cannot be separated from the outer medullary blood flow on the washout curve. However, it is suggested that when the renal blood flow pattern is so changed, renal autoregularity mechanisms may be playing a more important part in maintaining renal function and that this is possibly why the correlations enumerated above that were present in 4 compartment situations were not detectable in the 3 component situations.

**Journées de réanimation de Nancy**

Les Journées de Réanimation médico-chirurgicale de Nancy (7e session) auront lieu les 29 et 30 avril et le 1er mai 1972. Elles seront présidées par le Prof. Derot et le Médecin général Lenoir. Les 3 thèmes retenus sont les suivants: l’in-suffi-sance rénale aiguë; l’organisation des secours sanitaires en cas de grandes catastrophes; les hormones en réanimation. Les titres d’éventuelles communications et les demandes d’inscription sont à adresser au Secrétaire général des Journées, M. le Prof. A. Larcan, Service de Réanimation, CHU F-5 Nancy (France).

**Société autrichienne de Chimie clinique**