cases, (16, 17) and were described as showing severe interstitial nephritis; the glomeruli and blood vessels were described as normal.

During the past five years, we have observed seven patients in whom the clinical featurs of an allergic reaction associated with renal failure developed while they were receiving prolonged large doses of penicillin or methicillin. The renal disease subsided in in each when the antibiotic was discontinued, except for one, who died while administration of penicillin was continued. Pathological material, which was obtained for study in two of the patients who received penicillin and in two who were given methicillin, showed a characteristic type of interstitial nephritis without glomerulitis or arteritis. Immunologic studies were carried out in one patient, and the findings support the hypothesis that the renal lesion is due to hypersensitivity. The clinical features and pathological findings in these seven patients, and the immunologic observations in the one patient who was so investigated form the basis of this report.

MATERIALS AND METHODS

Immunofluorescent studies were carried out on renal tissue from one patient (L.C.). The biopsy specimen was submitted fresh in iced saline solution, and a portion was imbedded in gelatin, frozen and sectioned at 6 μ on a cryostat microtome; the tissue was fixed in Zenker's solution.

PREPARATION AND CONJUGATION OF ANTISERUMS

Rabbit antihuman gamma globulin was obtained by immunization of rabbits with purified gamma globulin. The antiserum was repeatedly absorbed and characterized as previously described. (18) Rabbit antiserum to human fibrinogen was prepared as previously described. Goat antiserum against human beta$_1$A-beta$_1$C components of complement was obtained from Hyland Laboratories. On immunoelectrophoresis it gave a single strong line against normal human serum.

Goat antiserums to IgG, IgM and IgA were obtained from Hyland Laboratories. On immunoelectrophoresis the anti IgC serum showed a single line to cord serum and a single line to normal human serum; the anti IgM showed a weak line to cord serum and a strong line to normal human serum, and the anti IgA showed no line to cord serum and a single line to normal human serum. The IgM antiserum was absorbed with cord serum until no line was seen by the Ouchterlony method against cord blood. The specific antiserum for the benzylpenicilloyl (BPO) haptenic group was prepared by primary immunization of rabbits with 5 mg of BPO-bovine gamma globulin conjugate (BPO_{35}-BGG) in complete Freund's adjuvant injected subcutaneously and three weeks later boosted by the intravenous injection of 5 mg of BPO_{35}-BGG. Bleedings were taken on the seventh, eighth and ninth days after the second injection. The serums from eight animals were pooled. Antidimethoxyphenylpenicillolyl antiserum was prepared by primary immunization of rabbits with 0.5 mg of DPO-bovine fibrinogen (DPO_{65}-BF) in Freund's adjuvant injected into the foot pads. One month later, the animals received boosters of 5 mg of DPO_{65}-BF injected intravenously, and were bled on the seventh, eighth and ninth days after the second injection. Serums from five animals were pooled. Antihapten antibody concentrations were determined by quantitative percipitin assays against multivalent penicilloylpolylysine conjugates. Anti-BPO antibody concentraton was 1.2, and anti-DPO antibody was 1.5 mg per milliliter of protein. The antiserums were fluoresceinated and purified by chromatography as described previously. (18)

PREPARATION OF UNIVALENT HAPTEN

Dimethoxyphenylpenicilloyl amylamine (DPO-amyl) was prepared by reaction of methicillin with 5 molar equivalents of n-amylamine in water at pH 11.5, at 25°C for 60 minutes. DPO-amylamine was precipitated from the reaction mixture at pH 3.7, gathered, washed and dried under vacuum. Reaction with parachloromercuribenzoate (PCMB) caused the expected development of a penamaldate absorption peak at λ max 285 m$\mu\epsilon$=23,500. Further preparative details are reported elsewhere. (19, 21)

RESULTS

CLINICAL AND PATHOLOGICAL OBSERVATIONS

The clinical features in seven pattents in whom signs of nephropathy developed during methicillin or penicillin therapy are summarized in Table 1.