The serum was collected from student volunteers fully immunized for the first time and from volunteers from factories in Leeds who had been previously fully immunized in the Forces.

The titres of antitoxin in the serum of those volunteers given a booster dose of toxoid after previous immunization were on average much higher than the titres in those newly immunized. It is suggested that the high titres obtained in these donors 10 to 15 years after the previous immunization show that latent immunity persists for much longer than previously estimated.

The results of treatment with antitoxin from horse serum and human serum in 57 cases showed that the crude death rate in 25 cases treated by human serum was found to be half that in 31 cases treated by horse serum. In one very severe case given both human and

horse serum recovery occurred. In the last four years 36 patients were treated without a death, 22 of them having been given human serum. Increased skill in the management of the patient under total paralysis is thought to be the chief cause of this successful run. Human serum was not found to cut short the course of the disease except in one case.

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ACUTE OLIGURIC RENAL FAILURE ASSOCIATED WITH MULTIPLE MYELOMA

REPORT OF THREE CASES

BY

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Renal insufficiency is responsible for 43% of deaths in multiple myeloma (Allen, 1951). This commonly takes the form of chronic renal failure, often without significant hypertension (Osserman, 1959). Acute oliguric renal failure developing in a few days has been described in only eight cases (Holman, 1939; Addis, 1948; Bartels *et al.*, 1954; Myhre *et al.* 1956 (2 cases); Killmann *et al.*, 1957; Perillie and Conn, 1958; Macalister and Addison, 1961). This paper presents three new cases of acute oliguric renal failure occurring in multiple myeloma and briefly examines their clinical and pathological data along with those of the eight other cases. The new cases are referred to as Cases 9, 10, and 11.

Case 9

A woman aged 64 was admitted to the renal unit of Sydney Hospital on August 26, 1961. She had suffered pain over the left lower ribs and back for two years. X-ray films of her spine had shown moderate decalcification. Osteoporosis had been diagnosed and female hormones given. Over 12 months prior to admission she had become increasingly tired, and had lost 1 stone (6.4 kg.) in weight. In July, 1961, she developed cough, sputum, and a sore throat. Her ankles became swollen and she vomited occasionally. Weakness became marked. On August 19 she was admitted to another hospital with thrombophlebitis of the left leg. There she was found to be oliguric and basal crepitations were noted. Heparin was given in view of the thrombosis and several epistaxes developed on August 21. Her blood urea at that time was 200 mg./100 ml. and haemoglobin 9.4 g./100 ml. Anuria developed over the following week, and she was transferred to the renal unit on August 26. She was not noted to be hypotensive at any stage.

Physical examination revealed a pale and slightly confused patient. The liver edge was felt 3 cm. below the costal margin. Her blood-pressure was 160/85 mm. Hg. There were no other abnormal findings.

Investigations at Sydney Hospital revealed: blood-urea nitrogen, 250 mg./100 ml.; haematocrit, 25%; erythrocyte sedimentation rate, 86 mm. per hour (Westergren); white-cell count, 8,900/c.mm.; the blood film showed a normo-

cytic normochromic anaemia with a few myelocytes and a number of rouleaux. Platelets were plentiful. Serum electrolytes: potassium, 7.4 mEq/l.; chloride, 86 mEq/l.; otherwise normal. Microscopy of urine—5–10 red cells per high-power field with leucocytes covering 50% of the field. Culture grew *Proteus vulgaris*. Serum albumin, 4.0 g./100 ml.; serum globulin, 3.3 g. Electrophoretogram of plasma showed elevated alpha-2 and beta-1 bands and also an abnormal gamma-globulin. X-ray examination showed several pathological fractures of ribs, several rounded areas of bone erosion in the skull, and generalized decalcification of the thoracic and lumbar spine with collapse of several vertebrae. Marrow aspiration showed 27% plasma cells and 10% lymphocytes. Serum calcium, 8.6 mg./100 ml., serum phosphorus, 17.1 mg./100 ml., serum magnesium, 3.0 mg./100 ml., serum alkaline phosphatase, 21 King-Armstrong units.

The patient was given a high-carbohydrate low-protein diet and a basal water requirement of 400 ml. per day plus replacement of obvious fluid losses. Vitamin supplements and anabolic hormones were given. Chloramphenicol was given for the urinary-tract infection. Dialysis with the artificial kidney was not performed. She remained anuric and died 14 days after admission.

Necropsy showed congestion of lower lobes of both lungs. The kidneys weighed 170 and 190 g. Their capsules stripped easily to reveal a pale finely granular surface. The cortex was pale and 0.4 cm. in average width. The medulla was congested. Melaena stool was present in the small and large bowels. The histology of the kidneys is dealt with later.

Case 10

A diabetic woman aged 64 was admitted to the renal unit of Sydney Hospital on August 6, 1961. Diabetes had been diagnosed in 1955 and had recently been controlled by diet alone.

In February, 1961, she complained of intermittent back pains and progressive weakness and tiredness. Pallor, ankle oedema, and effort dyspnoea developed and the weakness became such that she spent much of her time in bed. She was admitted to another hospital on July 13 because of pallor and oedema. The electrocardiogram showed left bundle-branch block. Her haemoglobin value was 8.4 g./100

ml, with a normocytic and normochromic anaemia. A number of myelocytes and normoblasts were present in the peripheral blood film. Her blood urea was 16 mg./100 ml. She was treated with bed rest, low salt-intake, digoxin, mersalyl, chlorothiazide, and acetazolamide without much improvement of symptoms.

On August 3 her urine output fell to 345 ml. and on the 4th to 60 ml. On the 5th she developed mild fever, chest pain, and thrombophlebitis in the left leg. A small pulmonary infarction was suspected and heparin therapy was started. She was not at any stage noted to be hypotensive. The oliguria persisted and she was transferred to Sydney Hospital on August 6 with a blood urea of 94 mg./100 ml.

Physical examination revealed an obese and orthopnoeic woman. Her blood-pressure was 180/60 mm. Hg, pulse rate 96 per minute and regular, jugular venous pressure raised 6 cm., and she had slight ankle oedema. A few bruises were present on the arms. There were no significant signs in her chest and no other positive findings.

Investigations at Sydney Hospital revealed: Blood-urea nitrogen, 118 mg./100 ml.; haematocrit, 22%; E.S.R., 145 mm. per hour (Westergren); white-cell count, 4,100/c.mm. (59% neutrophils, 38% lymphocytes, 3% monocytes, and a few metamyelocytes, myelocytes, and normoblasts). The blood film showed a normocytic normochromic picture with numerous rouleaux. Platelets were plentiful. Serum electrolytes were within normal limits. Microscopy of urine showed packed fields of red cells and 0-3 white cells per high-power field. There was no growth on culture. Serum albumin 4.8 g./100ml., globulin 9.8 g. Electrophoretogram of plasma showed a very sharp band in the gamma-globulin area. X-ray examination of the chest, abdomen, and skull showed no bony abnormalities. Cardiomegaly and pulmonary congestion were seen in the chest x-ray film. Marrow aspiration was unsuccessful. Random blood-sugar level (10 a.m.), 135 mg./100 ml. Thymol turbidity, 1 unit; zinc sulphate turbidity, 48 units. Serum uric acid level, 27 mg./100 ml. Cryoglobulins were not detected. Electrocardiogram showed ischaemic changes and left bundle-branch block.

The patient remained oliguric until death a week after admission. She was treated with a similar dietary and fluid regime to that in Case 9. Heparin was discontinued because of haematuria. On August 9, in view of continuing haematuria, bilateral ureteric catheterization was performed. No obstruction was found and retrograde films were normal with normal kidney sizes. She continued to deteriorate, and died in uraemia on August 14. Dialysis with the artificial kidney was not performed.

Necropsy showed congested lungs with fibrinous pleurisy and blood-stained sputum. Fibrinous pericarditis was present with 60 ml. of blood-stained fluid and several areas of petechial haemorrhages at the base of the heart. The liver was large (2,030 g.) and mottled dark brown and yellow. The spleen was large (310 g.). The kidneys weighed 240 and 260 g. and had smooth surfaces and a pale cortex but a dark medulla. Blood-vessels were normal. Three neoplastic haemorrhagic masses were found in the stomach measuring 6 cm., 1 cm., and 5 cm., in diameter. A haemorrhagic infiltrating mass was present in the caecum. The histology of the kidneys is dealt with later. Histology of the gastrointestinal masses revealed them to be plasmacytomas.

Case 11

A man aged 54 was admitted to the renal unit of Sydney Hospital on May 15, 1959. In April he had noticed faint jaundice, which passed off after a few days. He had lost 1 stone (6.4 kg.) in weight over the previous 12 months. On May 6 he developed fever, malaise, and muscular aches, and was treated for two days with sulphonamides and codeine tablets. On May 8 he started vomiting, and this continued for two days. On May 9 he was admitted to another hospital and found to be oliguric. The vomiting ceased, but from May 10 to 13 he became more confused and

jaundice was again detected. On May 14 he had an epileptic fit, and next day he was transferred to the renal unit of Sydney Hospital. He had passed only 450 ml. of urine in the four days prior to admission.

Physical examination revealed a jaundiced, confused patient. His blood-pressure was 150/100 mm. Hg. Scattered rales were audible in the chest, but there were no other abnormal physical findings.

Investigations at Sydney Hospital revealed: blood-urea nitrogen, 211 mg./100 ml.; haematocrit, 42.5%; the blood film showed normal red cells and plentiful platelets; a neutrophilia with a shift to the left was present. Many rouleaux were seen. Serum electrolytes were normal. Microscopy of urine showed red cells almost covering the high-power fields; 3-6 white cells per high-power field; and numerous granular casts. No organisms were seen and no growth was obtained on culture. Serum albumin, 2.2 g./100 ml.; serum globulin, 5.2 g. These rose later to serum albumin 2.9 g. and globulin 8.4 g. Electrophoretogram showed a marked increase in the gamma-globulins in a fairly sharp band. Chest x-ray films showed densities consistent with bronchopneumonia in the right mid-zone and left base. X-ray picture of the abdomen was normal. Marrow aspiration showed a hypercellular marrow with cells predominantly of the lymphocyte and plasma-cell type and a few very large blast cells. This finding was thought to be compatible with multiple myeloma. Cryoglobulins were not present. Bence Jones protein was present in the urine; zinc sulphate turbidity, 3 units; thymol turbidity, 3 units. Serum bilirubin, 8.6 mg./100 ml. Electrocardiogram normal.

Retrograde pyelography and bilateral ureteric catheterization were normal when done on May 16 to exclude sulphonamide crystalluria. He remained oliguric for two days after admission, then passed normal volumes of urine until June 12, during which time investigations as above were done and the diagnosis of multiple myeloma was made. He was treated conservatively with protein restriction and symptomatic therapy, his blood-urea nitrogen never falling below 150 mg./100 ml. during that month. Urine volumes gradually fell again, reaching levels below 400 ml. per day on June 24, after which he remained severely oliguric until his death on July 1, 1959. Before his death he developed bone pain and increasing cachexia.

Necropsy showed lobar pneumonia in the right middle lobe and left lower lobe. The liver weighed 2,970 g. and had a coarse nutmeg appearance on section. The kidneys weighed 180 and 165 g. and had a smooth surface. The cortex was pale and the medulla congested. The renal histology is dealt with later.

Discussion

Incidence.—Acute oliguric renal failure has now been described in 11 cases of multiple myeloma. The diagnosis of myelomatosis was not previously suspected in nine of these (Table I). The three cases reported above were among approximately 200 consecutive cases of acute oliguric renal failure admitted to the renal unit of Sydney Hospital over three years. This is a higher incidence than has been reported in other series of cases of acute renal failure. Myeloma therefore deserves a place in discussions on anuria, although most authors have omitted it (Smith, 1951; Merrill, 1955; Harrison *et al.*, 1958; De Wardener, 1961). However, Cecil and Loeb (1959) mention myeloma as a cause of oliguria, and Kolff (1955) states that patients with myeloma may, for reasons unknown, suddenly develop acute anuria.

Aetiology

There is no adequate explanation in the literature for the development of acute renal failure in these cases. Obstruction to flow in the tubules by the sudden

deposition of Bence Jones protein as casts has been held responsible (Addis, 1948; Perillie and Conn, 1958; Cecil and Loeb, 1959). However, Killmann *et al.* (1957) pointed out that, in their case of acute renal failure in multiple myeloma, cast formation was negligible and could not have caused significant obstruction (Case 6, Tables I and II). In two of the cases reported here (Cases 9 and 10) typical Bence Jones protein casts were infrequent. The fact that 3 of the 10 cases with histology available show so few casts of this nature suggests that they may be coincidental and not the basic cause of the anuria. It is possible that where Bence Jones protein casts are numerous they may add an obstructive element as a secondary phenomenon and that this may aggravate the anuria.

It is possible for Bence Jones protein to damage the kidneys in ways other than by producing obstruction. A syndrome of the Fanconi type due to proximal tubular damage from absorption of the abnormal protein has been described (Engle and Wallis, 1957; Milne, 1962). Vassar and Culling (1962) suggest that glomerular basement membrane thickening may result from Bence Jones protein, and this feature was noted in three cases (Table II). It is conceivable that some such toxic effect could produce acute anuria; but two cases (Nos. 1 and 6) did not have Bence Jones proteinuria. As further evidence against this, Smith (1951) pointed out that the severity of renal impairment in myeloma does not correlate with the amount or duration of Bence Jones proteinuria, and Osserman (1959) found a similar lack of correlation of this feature with either functional or histological impairment. It therefore seems unlikely that anuria in multiple myeloma is due to a direct toxic effect of Bence Jones protein alone.

Armstrong (1949) showed that tests of glomerular function in myeloma patients with chronic renal failure were often impaired while tubular function tests remained normal, suggesting a primary glomerular defect. Whether some such defect is the cause of acute renal failure in these cases is not known. Goldman *et al.* (1952) were unable to reproduce Armstrong's results, however. It does seem that factors which lower the glomerular filtration rate may contribute to the aetiology of anuria in myeloma, notably dehydration and

intravenous pyelography. Dehydration was present in 8 of the 11 cases, either from gastro-intestinal loss or in preparation for pyelography; but it was never severe enough to cause hypotension. The three remaining cases (Nos. 1, 9, and 10) were either normally hydrated or overhydrated.

Anuria followed intravenous pyelography in 5 of the 11 cases, and this procedure has been incriminated because of its tendency to lower glomerular filtration rate by dehydration and abdominal compression (Bradley and Bradley, 1947; Bartels *et al.*, 1954; Myhre *et al.*, 1956; Perillie and Conn, 1958). Renal vasoconstriction may also occur as a reaction to the dye and further lower the filtration rate. Anuria is a rare complication of intravenous pyelography in other conditions (Berlyne and Berlyne, 1962), and this association with multiple myeloma is too frequent to be coincidental. One may conclude that factors which lower the glomerular filtration rate are often but not invariably present in patients with multiple myeloma who develop acute oliguric renal failure.

Pathology

Table II shows that the glomerular change is usually minimal, proximal tubular damage is mild to moderate, distal tubule damage is often severe, and cast formation is severe. Infiltration of the interstitial tissues is frequent but mild; extensive plasma-cell infiltration does not occur. Blood-vessels were involved in mild to moderate degrees, probably compatible with the ages of the patients. Nephrocalcinosis and amyloid tissue are minimal.

The most obvious feature in the kidneys of cases of multiple myeloma associated with chronic renal failure is cast formation, usually of the homogeneous type ascribed to Bence Jones protein. Renal damage in these cases has been said to be principally due to intrarenal obstruction. A number of authors have applied the same theory to the renal damage in acute renal failure in multiple myeloma (see under "Aetiology"); but Bartels *et al.* (1954), Killmann *et al.* (1957), and Macalister and Addison (1961) are unwilling to accept obstruction as the whole explanation. The casts may be, in fact, the result of the acute renal failure and not

TABLE I.—Summary of Clinical Data

Case No.	Author	Sex and Age	Diagnosis Previously Known	Days till Death	Dehydration	Pyelography	Good Function on I.V.P.	Other Recent Evidence of Previous Renal Function	Bence Jones Protein	Abnormal E.P.G.	Bone Changes
1	Holman (1939)	F 43	No	21	Unlikely	1 month prior to anuria ? R.G.P.	—	N.P.N. 29 mg./100 ml.	No (x4)	Probable A/G = 3.3/4.7 g./100 ml.	Yes
2	Addis (1948)	M ?	"	—	Yes (castor oil)	No	—	—	—	—	—
3	Bartels <i>et al.</i> (1954)	M 69	"	40	Yes (I.V.P.)	Yes (I.V.P.)	No	Blood urea 81 mg. Albuminuria	—	—	Yes
4	Myhre <i>et al.</i> (1956)	M 70	Suspected	11	Yes (I.V.P.)	Yes (I.V.P.)	Yes	Blood urea 30 mg.	Yes	No	"
5	" "	M 42	No	Recovered	Yes (I.V.P.)	Yes (I.V.P.)	"	Blood urea 36 mg. Urea clearance 86%	"	—	"
6	Killmann <i>et al.</i> (1957)	M 36	"	9	Yes (I.V.P.)	Yes (I.V.P.)	"	Urea clearance 80%. Max. conc. 1.027	No (x1)	Yes	"
7	Perillie and Conn (1958)	M 34	Suspected	90	Yes (I.V.P.)	Yes (I.V.P.)	"	Blood urea Nit. 11 mg. Creat. 1.3 mg.	Yes	"	"
8	Macalister and Addison (1961)	M 56	No	12	Yes (vomiting)	No—until after onset of anuria, R.G.P.	—	Evidence of slowly deteriorating function (years)	"	"	Yes (rib only)
9	Healy (1962)	F 64	"	14	No	No—until after onset of anuria, R.G.P.	—	No	—	"	Yes
10	" "	F 64	"	11	"	No—until after onset of anuria, R.G.P.	—	Blood urea 16 mg.	—	"	No
11	" "	M 54	"	53	Yes (vomiting)	No—until after onset of anuria, R.G.P.	—	Hb normal after rehydration. Otherwise no	Yes	"	"

I.V.P. = Intravenous pyelography. R.G.P. = Retrograde pyelography. E.P.G. = Electrophoretogram.

the cause of it, since a fall in glomerular filtration rate could increase the precipitation of protein and facilitate the deposition of cellular debris.

One could therefore consider acute renal failure in multiple myeloma as secondary to a tendency for the glomerular filtration rate to fall. This could be due to either vascular insufficiency or glomerular damage. There is no convincing evidence of the former in the pathology of these cases. It is of interest, however, that there is thickening of the basement membrane in three of the nine cases with histological reports on glomeruli, and minor changes in three others. Slight changes in glomeruli can produce profound changes in renal function—for example, the nephrotic syndrome—and these histological features should be taken seriously. Allen (1951) commented on low-grade capillary thickening in the glomeruli in multiple myeloma kidneys, but he did not think these were specific changes. Kobernick and Whiteside (1957) drew attention to basement-membrane thickening in 14 out of 16 cases studied in myeloma with chronic renal involvement and stressed the importance of this. Vassar and Culling (1962) also drew attention to these changes. Armstrong's (1949) comments regarding impaired glomerular function in myeloma and the frequent presence of albuminuria as well as Bence Jones proteinuria is further evidence of glomerular damage. Any event (such as dehydration) which further lowers the filtration rate may possibly precipitate anuria in these patients.

All the comments on renal pathology in the three cases reported here were made by Dr. A. A. Palmer without any knowledge of the patients, the diagnosis, or the purpose of the investigation. He also commented in this way on sections of kidneys from three patients with multiple myeloma who died with mild degrees of chronic renal involvement but not directly from renal disease. The most noticeable difference in these sections was that giant-cell reactions around casts were more prominent than in the cases with acute renal failure. Broadly, the features of the histology with either clinical picture are similar and no pathological feature enabled the diagnosis of acute renal failure to be made in any case. Amyloid, nephrocalcinosis, and interstitial tissue infiltration are not usually prominent enough to regard them as responsible for functional change, although in Case 9 of the acute renal failure group secondary pyelonephritis was significant.

Management

One of the outstanding features of these 11 cases of acute renal failure in multiple myeloma is that the previous renal function in five cases (Nos. 4, 5, 6, 7, and 10) within a few days or weeks prior to the onset of anuria was normal or only slightly impaired. This information is derived from the results of intravenous pyelography, urea-clearance studies, and blood-urea levels. This finding is in accordance with that of Kolff (1955), who commented that the degree of renal

TABLE II.—Summary of Pathological Data

No.	Glomeruli	Proximal Tubules	Distal Tubules	Interstitial Tissue	Blood Vessels	Cast Formation	Amyloid	Macroscopic Appearance
1	Mild. Sl. dilatation of caps. spaces; sl. thickening of capsular basement membrane	Moderate. Dilated and lining flattened	Severe. Casts and foreign body giant cells	Mild. Some oedema. Groups of mononuclear cells	Nil	Severe. Filled distal convol. tubules and loops of Henle	—	Normal size. Pale. Smooth. Cortex 0.6 cm.
2	Not known	Not known	Severe. Cast formation mainly	Not known	Not known	Severe. "Throughout reaches of collecting system"	—	Not known
3	Mild. Occasionally atrophic. Slight dilatation of capsular spaces	Mild. Slightly dilated	Moderate. Many casts. Dilated. Sl. atrophic epithelium	Mild. Oedema infiltration by lymphocytes	Mild. Arterioles slightly hyperplastic	Moderate. Homogeneous acidophilic casts. Occas. granular and brownish	—	Small kidneys. 6 cm. long
4	—	—	—	(No necropsy)	—	—	—	—
5	Moderate. Varying degrees of atrophy	Mild. ? dilated. ? casts	Moderate. ? dilated. Homogeneous casts	Moderate. Infiltr. with lymphocytes, plasma cells, etc.	No comment	Moderate. Eosinophilic structureless casts	Nil	Not known
6	Nil	Nil. (Some epithelial cells desquam. ? P.M. change)	Mild. A few leucocytes. Occas. faintly staining casts	Mild. Infiltr. with lymphocytes	Nil	Mild. Felt not enough to cause obstruction	—	Large kidneys. Pale and smooth. Cortex normal size
7	"	Moderate. Cast formation prominent	Moderate. Casts again. Some crystals noted. Some giant cells	Mild. Very slight cellular infiltration	"	Severe. Proximal and distal tubules	—	Large kidneys
8	Mild. Occasionally atrophic. Slight capsular thickening	Moderate. Cloudy swelling. Narrow lumens	Moderate. Dense acidoph. granular casts. Epithelial cell reaction	Mild. Patchy in filtration with lymphocytes and plasma cells	Mild. Recent small venous thrombi	Moderate. Flecks of calcium in some casts	—	Large pale kidneys
9	Mild. Doubtful slight increase in digitation	Moderate. Some hydropic degeneration	Severe. Dilated. Epithelium ragged. Slight regeneration	Severe. Diffuse fibrosis. Infiltr. with lymphocytes, plasma cells and granulocytes	Moderate. Intimal fibrosis. Reduplication of Int. El. Lamina	Severe. Hyaline, red cell, granular, and pus casts. Crystals in some casts	(Nil) (Doubtful metachromasia of some casts)	Normal size but finely granular surface dark medulla
10	Nil	Autolysis prevented comment	Severe. Epithelium disintegrated. Some crystals	Moderate. Infiltr. with eosinophils, neutrophils, lymphocytes and plasma cells (oedema)	Moderate. Intimal fibrosis	Moderate. Granular ? artifacts. Some pigmented	Nil (methyl violet)	Large, smooth kidneys. Pale cortex. Dark medulla
11	Moderate. Bas. membrane thick in patches. A few fibrosed glomeruli	Mild. Slight hydropic degeneration	Severe. Dilatation ++. Casts ++. Some atrophied	Moderate. Infiltr. with plasma cells, lymphocytes and polymorphs	Mild. Occasional fibrosis of smaller arteries	Severe. Mostly hyaline. Occas. pigmented	"	Normal-sized kidneys. Pale cortex. Infarct in cortex and haem. in medulla

functional impairment prior to the onset of anuria need only be slight. This encourages one to use more vigorous therapy—for example, dialysis with the artificial kidney—than has been the custom in these cases, in the hope that the anuria may be a reversible state. A further indication for vigorous therapy may be obtained by renal biopsy. If casts are infrequent the secondary obstructive element will be absent and a successful outcome might be more reasonably expected. However, as it is not possible to assess either the importance of the obstructive factor or the reversibility of cast formation, all cases should at present be given every chance for survival, provided that other disabilities from the multiple myeloma are not great.

The usual precautions with renal biopsy should of course be taken, bearing in mind the frequency of a bleeding tendency in multiple myeloma.

Summary and Conclusions

Three cases of acute oliguric renal failure developing suddenly in the course of multiple myeloma are described and compared clinically and pathologically with eight other cases previously reported in the literature.

The cause of this clinical picture is as yet unknown. Obstruction of the tubules by Bence Jones protein casts may play a large part, but the small numbers of these casts in three cases suggests some other cause. There is some evidence for glomerular damage, and this could precede the development of casts and play a greater part in the renal damage of myelomatosis than has previously been thought.

Events likely to lower the filtration rate, such as dehydration and intravenous pyelography, are especially likely to produce acute oliguric renal failure in patients with multiple myeloma and should be avoided. Previous tests of renal function have often shown very little, if any, impairment before the sudden onset of anuria.

There is no specific pathological finding to account for the acute oliguria in these cases, and their renal pathology resembles that found in cases of chronic renal involvement with multiple myeloma.

Because of the previous good renal function in many cases, and because the anuria may be reversible, cases of acute renal failure with multiple myeloma should be treated vigorously, provided other symptoms of the disease are not disabling.

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ADDENDUM.—Since this paper was submitted for publication another example of acute oliguric renal failure arising suddenly in a previously undiagnosed case of multiple myeloma has been admitted to this unit. He was a man aged 56, and one week prior to the event was thought to be well and was doing heavy work. Anuria developed in two days in association with pneumonia, and the patient died in uraemia a week later, just before a dialysis was about to be performed. Extensive marrow replacement with plasma cells was found, together with secondary amyloid of a number of organs, including the kidneys.

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ACUTE RENAL FAILURE COMPLICATING A RETICULOSIS REMISSION FOLLOWING HAEMODIALYSIS

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Acute renal failure is a well-recognized complication of leukaemia, the lymphomas, polycythaemia vera, and myelofibrosis (Merrill, 1940; Merrill and Jackson, 1943; Lear and Oppenheimer, 1950; Kravitz et al., 1951; Weisberger and Persky, 1953; Kritzer, 1958; Greenbaum and Hope Stone, 1959). Cellular infiltration and amyloidosis are important contributory causes in some cases, but the usual cause of the renal failure is hyperuricaemia secondary to excessive cellular breakdown. It is therefore most commonly seen after successful treatment with cytotoxic drugs or irradiation, but can occur spontaneously, when it presumably coincides with a sudden increase in the output of uric acid. These peaks of uricosuria are often seen in the course of untreated leukaemia (Sandberg et al., 1956).

Quite large amounts of uric acid are removed when patients with renal failure are treated with the artificial kidney (Goldberg et al., 1960; Kennedy et al., 1961), and haemodialysis has been used in treating the hyper-