THE CLASSIFICATION OF CASES OF ALBUMINURIA

BY

ALEXANDER LYALL, M.A., M.D., F.R.C.P.

Lecturer in Clinical Chemistry, University of Aberdeen

The careful medical examination of large numbers of entrants to the Services has provided a new opportunity for the study of groups of young adults in whose urine albumin is discovered on routine tests. Analysis of the data collected in the present work has substantiated the figures of previous investigations. In addition, since examination was possible in more complete detail than in earlier observations of this kind, it has been shown that subacute nephritis is relatively common as a sequel of transitory respiratory infections and that early types of chronic nephritis exist in which the condition is unsuspected symptomatically and in which the disease may progress until the later stages become manifest.

Previous Work on Classification

The basis of classification of cases of albuminuria was established during the war period 1914-18. MacLean (1919) investigated 50,000 soldiers in training and observed an incidence of albuminuria of 5.8% ; in 2.8% the amount of albumin passed in the urine was large, and in 1.1% it was accompanied by an abnormal urinary deposit showing hyaline and epithelial casts and occasionally red blood cells. MacLean concluded that 1.1% of soldiers under training showed some degree of renal damage or nephritis. Similar investigations amongst untrained men suggested that these renal changes were not caused by training and that men showing such changes were capable of the strain of vigorous military preparation. From later work on trench nephritis MacLean concluded that the incidence of albuminuria had no influence on the occurrence of that disease ; of 161 cases of trench nephritis among the group of 50,000 men originally examined, only 28 had been albuminurics and only 15 had shown casts in the urinary sediment. This reasoning would be correct only if exposure to the infective agent of trench nephritis were equally distributed.

Although the intervening years of peace added but scanty information to the data, various workers have commented on MacLean's statistics and conclusions. Gulland (1927) analysed data collected for insurance work, and was of the opinion that albumin in the urine accompanied by epithelial casts indicated a desquamative catarrh of the kidneys, which might be trifling or serious, temporary or permanent. He believed that slight degrees of nephritis were more common than was usually thought to be the case. In many instances such mild nephritis was associated with upper respiratory infections. That author was not impressed by the value of renal function tests in cases of mild nephritis ; he felt that to accept the view that only renal efficiency tests gave evidence of defective kidneys might be misleading. Fox (1921) also discussed adolescent albuminuria in relation to life insurance and described 20 such cases which satisfied his criteria for diagnosis and which had been observed for upwards of twenty-five years. Five deaths had occurred in this series, but none from renal diseases. Diehl and McKinlay (1932) examined the urine of 20,000 students who entered the University of Minnesota from 1921 to 1930, and found albumin present in 1,065 samples (5.3%). Persistent albuminuria was observed in 118 students (0.6%), and 65 (0.3%) showed evidence of nephritis. Of 606 students in whom albuminuria was discovered, 404 had no

albumin in the urine at later examinations. This group the authors called transient albuminuria. Ashburn (1928) examined 1,115 Army cadets from two to six times during the years 1924-6. Albumin was found in the urine of 16%, with hyaline casts in 41 instances, granular casts in 14, and red blood cells in 15.

The material investigated in the present work consisted of 110 men who showed albuminuria on more than one occasion when examined for recruitment to the Services. This incidence occurred in the examination of 20,000 men (0.55%). The method of investigation adopted was as follows.

Investigation of Cases of Albuminuria

A sample of oxalated blood and a sample of urine were collected when the patient reported. A set of three bottles with suitable labels and a bottle containing 15 grammes of urea in 100 c.cm. of water were provided, along with the following instructions:

INSTRUCTIONS

Have nothing to eat or drink after 8 o'clock to-night.
Go to bed at 9 p.m. and pass water at 10.30 p.m.
At 7 a.m. pass urine and keep in Bottle 1. Take draught (15 grammes of urea).
At 8 a.m. pass urine and keep in Bottle 2.
At 9 a.m. pass urine and keep in Bottle 3.
Report to laboratory at 9.30 a.m.
Have nothing to eat or drink in the morning.

A further specimen of urine, collected when the patient reported, provided a sample after exercise.

The blood-urea value was determined and the urea-concentration test was performed. All samples of urine were tested for albumin, and microscopical examinations of the centrifuge deposits of the single sample of urine and of the first and last samples of the urea-concentration test were made. From the data thus obtained, from the relevant history, and from the examination of the patient it was possible in practically all instances to decide whether the case was one of orthostatic albuminuria or whether some degree of renal pathology was present.

Classification

Analysis of the data collected in this study showed that patients with albuminuria could be divided into five main groups, as shown in Table I.

TABLE I (110 Cases)

A. Orthostatic albuminuria	31
B. Albuminuria without evidence of nephritis	22
C. Subacute nephritis	14
D. Chronic or subchronic nephritis	31
E. Urinary infections ; haematuria ; various	12

Although statistics are of relatively little value in arriving at a decision in the individual case, these figures show that roughly 30% of cases of incidental albuminuria can be classified as orthostatic in type. On the other hand, 40% are found on investigation to reveal some evidence of renal pathology. In Table II typical instances of Groups A, B, C, and D are collected for comparison. The gradation in abnormality, in ability to concentrate urea, in the amount of albumin, in the character of the urinary deposit, and in blood pressure is demonstrated in this table.

Orthostatic Albuminuria

This term has been chosen for Group A in preference to adolescent albuminuria as the age group (18-35) is beyond the period of adolescence, and also in preference to benign

TABLE II.—*Typical Cases of Groups A, B, C, and D*

Case No.	Age	Blood Urea	Concentration Test				Albumin				Deposit				B.P.	Remarks
			1	2	3	4	1	2	3	4	Casts	R.B.C.	Pus	Crystals		
4	21	29	3.5	3.2	3.8	—	0	trace	trace	trace	0	0	0	0	128/78	Orthostatic
11	24	28	3.3	3.6	3.9	4.0	0	0	0	0	0	0	0	0	124/78	"
27	21	27	2.4	3.2	3.7	3.6	0	0	trace	"	0	0	0	Ca-oxal.	110/70	"
39	24	32	3.2	3.3	3.2	2.9	ft. trace	0	"	"	0	0	0	0	132/104	"
47	28	28	2.7	3.0	3.2	3.8	0	0	"	"	0	0	0	0	136/72	"
77	—	37	2.8	3.2	3.1	3.3	trace	trace	"	"	Occas. hyaline	0	few	0	132/80	No evidence of nephritis
82	18	36	3.4	2.8	2.8	3.3	"	"	"	"	Rare granular	0	"	0	126/76	"
108	32	—	2.9	2.8	2.9	2.6	"	"	+	+	0	0	0	Ca-oxal.	130/80	"
5	—	20	2.7	2.8	3.6	3.4	"	+	++	++	Epithelial ; granular	0	0	0	150/78	Subacute nephritis
23	20	34	3.3	3.1	2.9	3.4	"	+	+	+	Epithelial	+	+	Ca-oxal.	120/72	"
59	20	23	3.2	2.8	3.4	3.1	"	+	+	+	Granular	+	+	0	120/76	"
86	30	30	2.4	2.3	2.6	2.7	++	+	+	+	Epithelial ; granular	+	0	0	150/68	"
97	26	40	3.1	3.3	2.8	3.2	+	+	+	+	"	+	0	0	132/86	"
17	—	29	1.0	1.2	1.4	1.7	++	+	+	++	Hyaline ; granular	+	+	0	138/80	Chronic nephritis
46	24	38	1.5	1.4	1.4	1.7	+	+	+	+	"	+	+	0	154/86	"
55	34	30	1.7	1.6	1.7	2.1	+	trace	+	+	" Granular "	+	0	0	140/90	"
89	40	44	2.3	2.1	2.0	2.4	+	+	+	++	Epithelial ; granular	+	+	0	158/92	"
94	32	52	2.1	2.0	2.3	2.5	+	+	+	+	Granular	+	0	0	164/94	"

albuminuria, a term which would include some cases in Group B. For inclusion in this classification the following criteria are essential:

- Albuminuria is transient and the urine passed during rest is free of albumin.
- The urinary deposit shows no pus cells, red blood cells, or renal casts.
- The urea concentration reaches over 3% and the blood-urea value is normal.
- There is no history of illness, particularly a recent illness, which might result in nephritis.
- The blood pressure is normal and there are no clinical evidences of nephritis or anatomical abnormalities of the urinary tract.

The amount of albumin present in the urine during activity varies from traces to considerable amounts (up to 0.2% Esbach). In 18 out of 32 cases the quantity of albumin seen at the first examination was large. In samples of urine collected next day, only traces of albumin were found, except in one case. There is suggestive evidence that the amount of albumin passed is increased with the temporary rise in blood pressure, which often occurs during medical examinations as one manifestation of adrenal stimulation. In the centrifuge deposit an occasional hyaline or granular cast seen in the first sample of urine may be neglected. This happened in six instances in this group. Calcium oxalate crystals occur frequently, but unless accompanied by red blood cells are not of pathological significance.

The aetiology of the condition is still in doubt. One or more of a number of factors, including constitutional diathesis, lordosis, and pressure on the left renal vein, have been postulated as causative by various workers. In the present group five individuals had had scarlet fever between the ages of 9 and 14 years, two had had diphtheria, and one had had typhoid fever. The influence of previous fevers is still in doubt. Russell (1925) called attention to the fact that orthostatic albuminuria was often a phase of scarlatinal or diphtheritic nephritis and possibly of other forms of the disease, the sequence being: constant albuminuria—orthostatic albuminuria—none. Diehl and McKinlay (1932), on the other hand, could find no statistical significance in the incidence of precursory diseases. With this in mind, it should be emphasized that, although no evidence of renal involvement can be elicited, the diagnosis of orthostatic albuminuria is nevertheless one of personal opinion and not of absolute certainty. But in view of the accumulated evidence regarding the innocuous nature of the condition, men classed as cases of orthostatic albuminuria can be accepted for service in the Forces in the higher grades and frequently in Grade I.

Albuminuria without Evidence of Nephritis

The cases in this group could not be classed as benign albuminuria or orthostatic albuminuria. In each instance some feature was present which raised doubt, although there was not enough evidence to be certain of interference with renal function. The urea concentration was below normal in six instances, with maximum concentration between 2.2 and 2.9% urea. In the rest the urea concentration reached normal figures. Albuminuria was persistent in eight cases even at rest. In the others the resting sample of urine was free of albumin. Occasional polyuria was found in two patients along with reduced figures for urea concentration but without other abnormality in findings. In the urinary centrifuge deposits an occasional granular or hyaline cast was present in five, a few red blood cells in two, and pus cells in six instances. The blood pressure was above normal in five cases, ranging up to 160/80; in this instance the resting blood pressure was 142/80, and in another the pressure was 154/90 during activity and fell to 120/74 during rest. Only three patients in the group had suffered from scarlet fever, in one instance in conjunction with diphtheria and in another with rheumatic fever.

In this group the individual case is difficult to evaluate. Such cases cannot be classified as orthostatic or benign albuminuria, nor, on the other hand, can they be placed among the nephritides, since there is no actual evidence of renal lesion. In all instances the grading suggested was II or III. The following is a description of a typical case.

A painter aged 32, married, with two children, this patient had never had scarlet fever, diphtheria, or other illness, and had never been off work. There had been oedema, dysuria, polyuria, or nocturia. He had had a septic finger in January, 1940, and an injury to the nose and displacement of septum at the age of 20. The pulse rate was 64 and blood pressure 130/80, and the heart sounds were good and pure. No abnormality was found on examination of the chest and abdomen. The kidneys, spleen, and liver were not palpable. The pupils were central and equal, and reacted normally. The reflexes were normal. The blood urea was 28 mg. per 100 c.cm. A urea-concentration test with 15 grammes of urea gave:

1. Fasting urine	2.9% urea	Albumin trace
2. At 1 hour	2.8% "	" +
3. " 2 hours	2.9% "	" +
4. " 3 "	2.6% "	" +

The centrifuge deposits in Sample 1 showed numerous calcium oxalate crystals. No pus cells, red blood cells, or casts were found. The deposit in Sample 4 showed an occasional leucocyte but no casts, red blood cells, or crystals. This case was summed up as persistent albuminuria with urea-concentration values rather below standard, but without evidence of nephritis.

Subacute Nephritis

This group included 14 individuals between the ages of 18 and 37 who showed either clinical or pathological evidences of recent nephritis. Various factors suggested the conclusion that the lesion present was of recent origin and could be classified as acute or subacute nephritis. In all these cases, with two exceptions, there was a history of illness, including sore throats, severe chills, influenza, and cellulitis, within the previous two months. Scarlet fever had not been present in any instance. In two cases oedema of the hands and puffiness of the face were found. The blood-urea value was increased to between 40 and 50 mg. per 100 c.cm. in four instances. The albumin in the urine was considerable in amount (up to 0.3% Esbach), and was constantly present. The urea-concentration tests gave maximum values of over 3% in six cases and of less than 2.5% in one case only. The urinary deposit contained epithelial casts as evidence of acute renal desquamation in all but two instances. Granular casts were also frequently found, and red blood cells were seen in all except two. The blood pressure was raised to between 140 and 150 systolic in five patients; the diastolic blood pressure was never above 88 mm. Hg.

Such men are obviously unsuitable for recruitment. In most instances, if the lesion seemed very recent, a further review of the condition was suggested after an interval of three months. The opportunity occurred to examine two members of this group several months later.

In the first of these two cases the man passed at 6 p.m. a sample of urine which contained much albumin. The centrifuge deposit showed red blood cells and epithelial and granular casts. The blood-urea value was 50 mg. per 100 c.cm. A urea-concentration test next day gave 2.2, 3.0, 3.0, 3.0% urea. All samples of urine contained much albumin, and the deposit showed considerable numbers of red blood cells and epithelial casts. There had been frequent colds and influenza, but the man had not been off work recently. The pulse rate was 68 and the blood pressure 128/70. The heart sounds were good, but a systolic murmur was present at the mitral and pulmonic areas. The throat was congested and the left tonsil infected. Conjunctivitis was present and the face was slightly puffy. The condition was classed as mild subacute nephritis. The case was reviewed three months later, when a urea-concentration test gave 2.4, 2.5, 2.6, and 2.5% urea. All samples of urine contained albumin, and the deposit from several of them showed epithelial casts, blood casts, and red blood cells. The blood urea was now 30 mg. per 100 c.cm. and the blood pressure 128/78. In this instance the condition was progressing to subchronic nephritis.

In the second case, at 4.30 p.m., the man passed urine which contained a large amount of albumin. The deposit showed a few hyaline casts but no pus, blood cells, or crystals. The blood urea was 30 mg. per 100 c.cm. A urea-concentration test next day gave 2.45, 2.3, 2.6, 2.7% urea. All samples of urine contained much albumin, and the centrifuge deposit showed a number of casts, partly epithelial and partly granular, and a few red blood cells. This man had had tonsillitis frequently until four years previously, but had never had scarlet fever. He had been chilled and wet a few nights previously on fire-watching duty and developed a headache and lumbago afterwards. The pulse rate was 100 and blood pressure 150/86; there was a systolic murmur at the pulmonary area and a slight puffiness of the face. The condition was classed as mild subacute nephritis which might resolve. The patient was seen three months later in hospital. His appetite was good and the bowels were regular. He admitted occasional slight frequency of urination, but no blood had been passed. There was no visual trouble, numbness, or anaesthesia, and there had been no giddiness or headaches or vomiting, no cough or dyspnoea. Palpitation on exertion had been noticed, and a tendency to sweat easily. He had had measles as a child, but not scarlet fever or diphtheria. He had had several attacks of tonsillitis, the last three years earlier. He had never had rheumatic fever, but had had lumbago four months previously. His parents and four sisters were alive and

well. He had one child, one month old. Examination showed him to be a well-developed and well-nourished though edentulous man. There was no anaemia. His throat was healthy and his tongue clean. Pulsation was visible in the suprasternal notch. The thyroid gland was not enlarged. The pulse rate was 92 and the blood pressure 140/80 to 150/68. The heart sounds were good, but there was a systolic murmur at the mitral area. The heart was not enlarged. Nothing abnormal was found on examination of the chest, abdomen, reflexes, or cranial nerves.

The urine had a specific gravity of 1008 to 1017, and contained from 0.8 to 0.9 gramme of albumin per litre continually. A urea-concentration test showed: fasting, 2.45% of urea; at one hour, 2.3%; at two hours, 2.6%; and at three hours, 2.7%. The blood urea amounted to 30 mg. and plasma proteins to 6.7 grammes per 100 c.cm. The urine deposit contained numbers of hyaline and some granular and epithelial casts, together with a number of red blood cells. Volhard's water-excretion test gave a specific gravity between 1005 and 1032, and 36 oz. was excreted in three hours. Radiographs failed to reveal any urinary calculus.

Examination of the blood showed 5,120,000 red cells, 7,100 leucocytes, and 90% haemoglobin. The basal metabolic rate was +5%, and the Wassermann reaction was negative.

It is evident from the occurrence of such cases that milder degrees of subacute nephritis may occur in men who otherwise appear healthy and do not seek medical advice or remain off work. The end-result of such attacks is not known, but in the two instances quoted the disease progressed to a subchronic stage.

Chronic or Subchronic Nephritis

This group consisted of 31 individuals, of whom 26 were between the ages of 20 and 35 years, 18 and 47 being the age limits. All were found to have continuous albuminuria, often of considerable degree. The blood urea varied between 20 and 52 mg. per 100 c.cm., with values over 40 mg. in 7 instances. The urea-concentration factor lay below 70 in 11 instances; 7 of these were below 50. The urea-concentration test showed maximum values under 3% in 17; in 13 the maximum values were below 2.1%. In all cases fairly numerous casts, usually hyaline and granular in type, were found repeatedly in the centrifuge deposits of the urine. Red blood cells were present in all except three instances. The blood pressure showed systolic readings of 140 mm. Hg or above in 15 patients, of whom 7 showed readings over 150, the highest being 192. Diastolic pressures were raised to between 90 and 100 mm. Hg in 7 cases. In 10 patients symptoms referable to the presence of chronic renal diseases were elicited on question only. Two men complained of headache, two of occasional frequency of micturition, two of both these symptoms, and two of backache and pain in the renal region. Positive signs referable to renal disease were few. In one instance slight oedema of the face and arms was present, and one patient had dyspnoea on effort; two were much under weight, and one had aortic incompetence. Two were anaemic, and one showed polycythaemia. There was no history of any illness of aetiological significance in eight of these men. Only three men gave a history of having had scarlet fever before the age of 10 years, and one had had scarlet fever two years earlier. In three there was a history of nephritis 2 years, 11 years, and 12 years earlier, and one patient, whose blood urea was 52 mg. per 100 c.cm. and whose blood pressure was 164/94, was known to have had albuminuria 11 years previously. Five men had had recurrent attacks of tonsillitis, and nasopharyngeal infections were actually present in three instances. Other previous illnesses included septic hands (2), erysipelas (1), compound fracture of tibia (1), rheumatic fever (1), and exophthalmic goitre (1). There was very little evidence of urinary infection, and cystitis was

present in only one case. All of these men (except two) were employed, and they comprised labourers (5), millworkers (2), fishermen (2), a blacksmith, a plasterer, a slater, as well as others following less strenuous occupations such as clerk, cinema operator, and collector. Two individuals in this group were examined twice at an interval of a year, and one was observed later in hospital. The records of three of these cases give some indication of prognosis in this group.

A millworker aged 35, married, with nine children, this man had never had scarlet fever, diphtheria, or typhoid fever, although he had been in hospital in 1923 for observation as a doubtful typhoid carrier. Five years earlier he had served in the Territorial Army and had done strenuous training. He had no headaches, polyuria, or oedema; was thirsty occasionally, but only when sweating at work in a hot atmosphere; had occasional indigestion; and was constipated. He did not admit any history of venereal disease. Examination showed a rather thin, pale, undernourished, edentulous man. The pulse rate was 70, regular, and the blood pressure 128/70. The apex beat was in the nipple line. A systolic murmur was present in the mitral area and the second pulmonic sound was accentuated. Examination of the lungs and abdomen revealed no abnormality. The reflexes were normal, the pupils reacted normally, and the throat was clean. The blood-urea value was 46 mg. per 100 c.cm. A urea-concentration test gave 1.8, 2.4, and 2.8% urea, and a urea-concentration factor of 1/40. All samples of urine passed contained from 0.1 to 0.2% of albumin, and the centrifuge deposit showed a number of granular and epithelial casts with numerous red blood cells. This man was seen again 16 months later. He had been well in the interval, but had been unemployed. He noticed that he had to get up to pass water, usually about 4 a.m. He had no headaches or dyspnoea, and took a cheerful view of himself and of his environment. The blood urea was now 40 mg. per 100 c.cm. A urea-concentration test gave figures of 0.8, 1.15, 1.1, and 1.6% urea and a urea-concentration factor of 1/20. All samples of urine contained much albumin (0.3%), and the centrifuge deposit showed numerous granular casts, some epithelial casts, and numerous red blood cells. The pulse rate was 70 and the blood pressure 130/70. The apex beat was outside the nipple line, and systolic murmurs were present over the mitral, pulmonic, and aortic areas, with a suggestion of a diastolic murmur down the left side of the sternum. This evidence shows a progressive case of chronic interstitial nephritis with gradual failure of renal function.

A slater aged 34, married, with one child, had never had any major illness or scarlet fever or sore throats, but had sustained a compound fracture of the right tibia at football thirteen years earlier. This was reduced and plated in hospital, and the patient played football again in later seasons. There had been no headaches, polyuria, or oedema, and his eyesight was good. He looked a healthy well-built man. The pulse rate was 54, the heart sounds were good and pure, and the blood pressure was 120/80. Examination of the chest and abdomen showed no abnormality. The liver, spleen, and kidneys were not palpable. The upper jaw contained three carious molars. The throat was clean. The reflexes were normal and the pupils reacted normally. The blood urea was 32 mg. per 100 c.cm. A urea-concentration test showed 2.3, 2.6, 2.8, and 2.9% urea, with a urea-concentration factor of 1/70. All samples of urine contained albumin, and the urinary deposits showed numerous granular casts, a few epithelial casts, some red blood cells and calcium oxalate crystals. Twelve months later the man felt well, had been working continually, and had no untoward symptoms. The pulse rate was 68 and the blood pressure 142/90. A general examination gave normal findings. A urea-concentration test showed 2.1, 2.4, 2.5, and 2.8% urea. The amount of albumin in the urine was increased and it was found in all samples. The centrifuge deposit contained numerous granular and hyaline casts, a few red blood cells, but no crystals or pus. This case shows chronic nephritis, which has remained almost stationary during one year.

An unemployed storeman aged 24, this patient had never had scarlet fever, sore throats, polyuria, or swelling of face or hands. His appetite was good and his bowels were regular. The pulse rate was 60 and the blood pressure 138/90. The heart sounds

were good and pure, the reflexes were normal, and the pupils reacted normally. The kidneys, liver, and spleen were not enlarged to palpation. The upper teeth were bad and the upper incisors had been extracted, but the throat was clean. A sample of urine passed at 4.30 p.m. on March 6, 1940, contained a large amount of albumin, and the centrifuge deposit showed a number of hyaline, granular, and epithelial casts, some pus cells, and a few red blood cells. The blood-urea value was 29 mg. per 100 c.cm. and the urea-concentration factor 1/34. A urea-concentration test gave 1.0, 1.2, 1.4, and 1.9% urea. All samples of urine contained much albumin, and the centrifuge deposit was similar to that described above. On observation in hospital two months later the blood pressure was found to be 145/95, but it fell to 108/68 after rest in bed for several days. The specific gravity of the urine reached a maximum of 1018 on restricted fluids and urea-concentration tests. Intravenous pyelography with uroselectan showed poor concentration and delayed excretion. The right renal pelvis and ureter were normal, but opacity was not sufficient for an opinion on the left kidney and ureter to be formed. Albuminuria persisted for ten days while he was in bed, and the urinary deposits continued to show granular casts. A diagnosis of chronic interstitial nephritis was made.

The recognition of this group of men with chronic nephritis of varying degree makes it evident that an early type of renal disease exists, often without any defined aetiology and usually without symptoms at this stage of the disease. The further history of such cases is not known, and no information is available on which a prognosis can be based. The disease may progress with rapidity until symptoms of renal failure or cardiovascular insufficiency become obvious to the patient and to the medical attendant, or progress may be delayed for a number of years. It seems reasonably certain that this group forms part of the mosaic in the earlier aetiology of chronic nephritis and constitutes the reservoir from which patients are admitted from time to time to the wards of the general hospitals with the fully developed picture of advanced renal failure, terminating in uraemia. It is doubtful whether at this stage any good purpose can be served by hospital treatment or treatment by any strict dietetic or other regime, and invalidism is to be avoided.

The value of such an investigation as the present one would be greatly enhanced by inclusion of the collected statistics from other areas in the country. This is particularly the case since the patients have been more fully investigated than in MacLean's series during the war of 1914-18 and since the opportunity exists to make follow-up observations on many of these cases at a later date. In local areas with regional hospital administration it should not be impossible to check such admissions in future years.

Urinary Infections; Various

Group E consisted of 12 men who were found to have albumin and whose urine on microscopical examination revealed in addition haematuria or pyuria. In two cases nephrectomy had been previously performed for tuberculosis of the right kidney and tumour of the left kidney. In two cases renal calculi had been passed. One man had had haematuria two years earlier, and the remainder had had urinary infections with much pus in the urinary deposit.

It is of considerable value to review the importance placed on interpretation of the various findings obtained in investigating this group of cases from the renal aspect.

Albuminuria.—If albuminuria is transient, and particularly if the resting sample of urine is free of albumin, the classification is probably albuminuria of the orthostatic type. The amount of albumin present in an isolated sample of urine is no guide to classification, since in men with orthostatic albuminuria such samples may contain much albumin. If albuminuria is persistent the patient belongs to the other groups. In most cases of nephritis albumin continues to be excreted in large amounts.

The Urinary Deposit.—If the centrifuge deposit shows no pus cells, red blood cells, casts, or crystals on several examinations the albuminuria, with few exceptions, is of the orthostatic type if transitory and of the benign type if persistent. An occasional cast of the hyaline or granular type may be neglected. When renal casts are present in considerable numbers—say, several in each low-power field of the microscope, or more—there is undoubtedly a destructive renal lesion present, particularly if accompanied by red blood cells. In recent lesions the casts are mostly of the epithelial type or are partly granular with adherent epithelial cells. In less recent lesions the casts are of the granular and hyaline types.

The Blood Urea.—A normal value of the blood urea does not exclude nephritis. It is only in the more severe degrees of acute nephritis or in the later stages of chronic nephritis that elevation of the blood-urea value occurs. In investigation of material of this type it is rare that other causes of increase of the blood urea are found. A raised blood-urea value is significant of nitrogen retention.

The Urea-concentration Factor.—The ratio of the blood-urea value to the urea content of the fasting sample of urine shows significant variation in the more advanced degrees of renal failure but may show little departure from normal in patients with undoubted destruction of renal parenchyma.

The Urea-concentration Test.—Concentration of urea in the urine after a test dose of urea and under controlled conditions is valuable in assessing the degree of renal insufficiency in renal disease, but may show normal figures in patients with subacute nephritis and with milder degrees of chronic nephritis.

Clinical manifestations of nephritis are more commonly present in acute and subacute nephritis than in the subchronic groups, in which evidence from clinical examination may be scanty or wholly negative.

Each case must be considered on the summation of all data available, but the occurrence of persistent albuminuria and of renal elements and blood in the urinary deposit provides the most valuable diagnostic criteria.

Summary

The classification of 110 cases of albuminuria in adult males is discussed.

Incidental albuminuria occurs in 0.55% of otherwise healthy adult males. Of these 28% can be classed as orthostatic albuminuria, 20% as albuminuria without evidence of nephritis, 13% as subacute nephritis, 28% as subchronic or chronic nephritis, and 11% as due to various infections of the urinary tract.

Subacute nephritis of mild degree is common as a sequel of respiratory infections. Some of these cases progress to chronic nephritis.

The aetiology of chronic nephritis remains obscure.

The occurrence of persistent albuminuria with an abnormal urinary deposit provides the simplest evidence of renal pathology.

I am indebted to Dr. David Rorie, chairman of the Aberdeen Medical Boards, and to Dr. T. D. Kennedy of the Department of Health for Scotland, for assistance in carrying out this work; also to Prof. David Campbell and Prof. R. S. Aitken for permission to publish notes of two cases admitted to their wards in the Aberdeen Royal Infirmary, and to the latter for much helpful criticism.

REFERENCES

- Ashburn, P. M. (1928). *J. Amer. med. Ass.*, **90**, 535.
Diehl, H. S., and McKinlay, C. A. (1932). *Arch. intern. Med.*, **49**, 45.
Fox, R. H. (1921). *Lancet*, **1**, 116.
Gulland, G. L. (1927). *British Medical Journal*, **1**, 363.
MacLean, H. (1919). *Med. Res. Com. Sp. Rep. Ser.*, No. 43, London.
Russell, J. W. (1925). *Lancet*, **2**, 683.

Approximately 40,000 Jews died in Nazi Poland in 1940, according to data published by Jewish communities in Poland. This is a vast increase in Jewish mortality and has no parallel in the history of Polish Jewry. A large proportion of the two million Jews in Nazi Poland are stated to be in poor health. An investigation by a Nazi medical commission to ascertain Jews' medical fitness for hard labour established that 40% of the entire Jewish population were unfit for physical work.

HYPERTHYROIDISM: RELATION OF THE BASAL METABOLISM TO THE CLINICAL SIGNS

BY

A. B. ANDERSON, Ph.D., M.R.C.S., L.R.C.P.

*Clinical Biochemist, Glasgow Royal Infirmary; Lecturer in
Pathological Biochemistry and Carnegie Teaching Fellow
in the University of Glasgow*

A great many data bearing on the basal metabolism in thyroid disease are available, and these have been collected and reviewed by Means and Burgess (1922), Boothby and Sandiford (1924), and Du Bois (1936). In their classifications the diagnoses of exophthalmic goitre, toxic adenoma, clinical thyrotoxicosis, etc., are compared with the basal metabolic rate. In this investigation an attempt has been made to correlate the presence or absence of the clinical signs on which a diagnosis of hyperthyroidism is usually made with the basal metabolism found. A preliminary report on the earlier cases in this series has been made elsewhere (Anderson, 1937).

Methods

The series consisted of 230 patients, of varied ages and both sexes, who had been transferred to the metabolic wards from the medical or surgical wards for determination of the metabolic rate. The presence or absence of the following clinical signs was noted:

1. **Enlargement of the Thyroid.**—Any palpable enlargement, whether generalized or local.
2. **Exophthalmos.**
3. **Tremor** of the fingers of the outstretched hands.
4. **Tachycardia.**—A pulse rate above 90 while at rest in bed.
5. **Sweating.**—Determined by palpation of the skin and from the history.
6. **Loss of Weight.**—Determined from the history given by the patient.

The basal metabolic rate was determined by the open method, using the Douglas bag and Haldane gas analysis. The rate was calculated with the aid of the Du Bois tables for average basal metabolism per square metre as modified by Boothby and Sandiford (Peters and van Slyke, 1932). In order to get satisfactory readings the patient practised breathing through the valves and into an old bag for several days until thoroughly used to the apparatus. Then the actual determinations, usually two or three on successive days, were made. Several days' rest in the ward and familiarity with the apparatus were found to be essential for a proper determination.

Results

For simplicity in tabulating the results three main divisions were made—namely, enlargement of the thyroid with exophthalmos, enlargement of the thyroid without exophthalmos, and tachycardia without enlargement of the thyroid. These were further subdivided according to the number of subsidiary signs present. The basal metabolic results were also divided into three groups: -15% to $+15\%$, $+16\%$ to $+24\%$, and $+25\%$ and over, the divisions corresponding approximately to the normal range, mild or borderline hyperthyroidism, and moderate to severe hyperthyroidism respectively. The results are shown in the table overleaf, which is self-explanatory.

In 3 cases, not classified in the table, exophthalmos but no enlargement of the thyroid was noted. In only one of