

THE PROGNOSIS OF ALBUMINURIA WITH OR WITHOUT CASTS *

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The question as to the significance of albumin and casts in the urine of apparently healthy men is a much-mooted one, the answering of which, from a clinical point of view, has been difficult on account of the scarcity of cases in hospital and private work, and the impossibility of following them through a number of years. During the late nineties several of the large New York insurance companies began to insure men with this condition, and since then records of a large number of such cases have accumulated. It was through the courtesy of one of these companies that we were given an opportunity to investigate the above-mentioned problem under very promising conditions.

The material placed at our disposal consisted of 396 men, residents of New York City, who were insured during 1900-1901. As far as an ordinary physical examination could determine, they were normal at that time except for the presence in the urine of serum albumin with or without casts. Only office specimens of the urine were secured, but albumin was found on at least two occasions in one-half of the cases. This was before the day of blood-pressure observations by examiners for insurance companies.

The preliminary examination of the urine was done by the examining physician, using the ordinary heat and nitric acid test for albumin. His findings were always confirmed by an experienced clinical pathologist, who also made all the microscopical examinations according to the following routine: Fifteen cubic centimeters of the specimen were centrifuged for five minutes and the entire sediment then examined with the aid of a movable stage. All the specimens were examined within eighteen hours of the time they were passed, and many a few hours after passing.

Following their examination during 1900-1901 by the insurance company, these 396 men were divided into three groups. The first, numbering 115, showed albuminuria without tube-casts (no cases of pyuria were included in this group); the second group, numbering 203, showed albuminuria and a few hyaline casts, and the third group included fifty-three men showing albuminuria and a few granular casts.

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The incidence, by decades, of these three groups is of interest and we were able to estimate it fairly accurately with the help of statistics showing the age-distribution of all of the company's entrants during the past ten years. The men showing albuminuria alone were five times more frequent before the twentieth year than after. The albuminuria and hyaline-cast group showed approximately the same incidence in the second, third, fourth, and fifth decades. The men with albuminuria and granular casts showed an increasing incidence in each decade, until,

TABLE 1.—EXAMINATION OF TWENTY MEN, TEN YEARS AFTER ALBUMIN HAD BEEN OBSERVED IN THEIR URINES

Age	Serum Al- bumin on Urinalysis†	1900-1901		1911	
		Examined	Heart	Systolic Blood- Pressure	Urinalysis‡
*17	+	—	—	128	—
19	+++	—	—	120	—
19	+++	—	—	132	—
21	+	—	—	120	—
21	+++	—	—	112	—
22‡	+++	—	—	112	+; no casts
23	+++	—	—	98	No albumin; 1 hyaline cast.
*23	+	—	—	112	—
*24	+	Two,	—	142-132	—
*26	+++	Three,	—	142-132-128	—
27	+++	—	—	128	—
*27	+++	—	—	116	+; few hyaline casts.
*27	+++	—	—	128	—
27	+++	—	—	136	No albumin; 3 hyaline casts; 1 granular cast.
*30‡	+++	Two,	—	140-132	Trace albumin; no casts.
*30	+++	—	—	124	—
*32	+++	—	—	133	+; no casts.
*33	+++	—	—	126	—
*36	+	—	—	122	+; no casts.
39	+++	—	—	124	+; 1 hyaline cast.

*Cases which had shown albumin on two or more examinations.

†In this column, in this and the following charts, + indicates trace of serum albumin; small quantity; the sign — throughout means negative.

‡In these cases traces of albumin have been repeatedly found since 1900.

between 40 and 50 years, they were four times as frequent as between 20 and 30 years. After 50 years of age so few men are insured, as compared with younger entrants, that statistics of later decades are of little value.

The age-incidence in the albumin group and the granular-cast group is quite in accord with general experience. The almost equal decade-

incidence of the hyaline-cast group was, however, unexpected, the usual assumption being an increasing frequency of this condition with advancing age.

TABLE 2.—EXAMINATION OF THIRTY MEN TEN YEARS AFTER ALBUMIN AND A FEW HYALINE CASTS HAD BEEN OBSERVED IN THEIR URINES

Age	1900-1901		1911	
	Uranalysis†	Exam. Heart	Systolic Blood-Pressure	Uranalysis‡
18	++	—	130	+; no casts.
18	++	—	130	—
*22	+	Two exams.	146-132	—
*23	+	—	131	—
*23	+	—	122	—
25	+	—	132	—
*25	+	—	122	—
*25	++	—	130	—
*27	+	—	129	—
28	++	—	134	No albumin; a few hyaline casts.
*30	+	—	128	+; few hyaline casts.
30	+	—	142	—
*32	+	—	130	—
32	+	—	128	+; few hyaline casts.
33	+	—	130	—
34	+	—	134	—
*34‡	++	Two	160-136	+; hyaline casts.
36	+	—	132	No albumin; a few hyaline casts.
36	+	Three	142	+; no casts.
*36	+	—	140-128-136	+; no casts.
*37‡	+	Apex normal position and heaving, otherwise neg. two exams.	140-136	+; few hyaline casts.
37	+	—	143	—
37§	+	Apex 4 in. from midline heaving.	198	+; few hyaline casts.
38	+	—	102	—
*39	+	—	129	1 per cent. glucose.
*39	+	—	128	+; few hyaline casts.
*39	+	—	138	+; few hyaline casts.
*40	+	—	136	—
*43	+	Two	138-130	—
47	+	—	124	—

*Cases which had shown albumin and casts on two or more examinations. The microscopic examination was similar in all these cases, a few hyaline casts being found.

‡Doubtful cases.

§A case of interstitial nephritis.

During the summer of 1911, seventy of the original 396 men were visited and examined, from ten to eleven years thus having elapsed since

their first examination. The history was first discussed, then the heart was examined and the systolic blood-pressure taken. For the latter a Faught instrument with wide cuff was used, the subject being each time in a sitting posture. If the pressure was above normal another reading was made several days or weeks later, and at the same time the heart was reexamined. Also an eight-hour specimen of urine was collected (in most

TABLE 3.—EXAMINATION OF TWENTY MEN TEN YEARS AFTER ALBUMIN AND GRANULAR CASTS HAD BEEN OBSERVED IN THEIR URINES

1900-1901			1911	
Age	Uranalysis†	Exam. Heart	Systolic Blood-Pressure	Uranalysis†
21	+	—	130	No albumin or casts; 6 per cent. glucose.
23	+	—	132	—
26	++	—	136	+; hyaline casts.
*26	++	—	122	—
*26	+	—	132	—
27	++	—	98	—
29‡	+	Apex 4 in. from midline heaving; 2 exams.	137-136	—
*31	+	—	128	—
33§	+	Aortic 2d, accentuated, otherwise neg.	150-144	No albumin; few hyaline casts.
34	+	—	128	—
34	+	—	136	—
*35	+	—	132	+; hyaline casts numerous.
37	+	—	129	+; granular casts.
39§	+	Aortic 2nd accentuated, otherwise neg.	170	+; hyaline casts.
*41‡	+	Apex 5th from midline, heaving.	158	+; many pus-cells.
43	++	—	128	+; hyaline casts.
43§	+	Two —	150-142	+; no casts.
43§	+	—	162	+; no casts; 5 per cent. glucose.
*47	++	—	134	+; granular casts.
47§	++	—	170	+; hyaline casts.

‡Cases of interstitial nephritis.

§Doubtful cases.

The microscopic examination was similar in all these cases, a few granular casts being found.

instances night urine) and examined the next day. Examination of the eyegrounds in these men was not feasible, otherwise we might have had fewer cases in which the diagnosis was doubtful.

Twenty of the men we visited had shown albumin, but no casts, in 1900-1901. Our results in this group are summarized in Table 1.

None of these twenty men now has interstitial nephritis, as far as we can judge from the condition of the heart, the blood-pressure and the examination of the urine. Twelve are, apparently, normal as regards heart and kidneys. In eight we find the same condition of the urine as was found ten years ago, four now showing in addition tube-casts.

The absence of interstitial nephritis in any member of this group after ten years had elapsed was most interesting.

Thirty of the men we visited had shown albumin and a few hyaline casts in 1900-1901. Our results are summarized in Table 2.

One of these thirty men now has interstitial nephritis and two are doubtful cases. Five men show a slightly raised blood-pressure, not marked enough, however, to justify any suspicions of nephritis, considering that ten years has elapsed since the first appearance of trouble. Eighteen men are, apparently, normal as regards heart and kidneys. Nine show the same condition of the urine that they did in 1900.

Twenty of the men we visited had shown albumin and a few granular casts in 1900-1901. Table 3 summarizes our results.

Of these twenty men, two now have interstitial nephritis and in five the diagnosis is doubtful. Eight are apparently normal as regards heart and kidneys.

Considering the entire series of seventy men, at the present time thirty-eight are, apparently, free from cardiac or renal disease. Three have chronic interstitial nephritis and seven possibly have it. Two have diabetes. Twenty-two still show much the same urinary condition as they did ten years ago, but with no circulatory changes.

Of the ten men who now have, or possibly have, nephritis, but one was under 30 years of age at the time trouble was first discovered.

THE MORTALITY IN THE ORIGINAL GROUP OF THREE HUNDRED AND NINETY-SIX MEN

We found that twenty-five of these men had died since their examination in 1900-1901. The causes and dates of death are enumerated below.

ALBUMINURIA GROUP	
Cause of Death	Year of Death
1. Pulmonary tuberculosis; tuberculous meningitis	1902
2. Typhoid fever; perforated ulcer; operation.....	1903
3. Pulmonary tuberculosis	1904
4. Illuminating-gas poisoning	1904
ALBUMINURIA AND HYALINE-CAST GROUP	
1. Appendicitis	1902
2. Fibroid phthisis; gastro-intestinal tuberculosis.....	1903
3. Phenol (carbolic acid) poisoning	1904
4. Pulmonary tuberculosis	1904
5. Rheumatism; malarial fever; heart failure.....	1905
6. Cirrhosis of liver	1907

7. Pulmonary tuberculosis; brain abscess	1910
8. Lobar pneumonia	1910
9. Syphilis; gumma of brain	1909
10. Pulmonary tuberculosis	1910
11. Pulmonary tuberculosis	1909
12. Unknown	1910
13. Heart failure after drinking bout.....	1903

ALBUMINURIA AND GRANULAR-CAST GROUP

1. Appendicitis	1902
2. Cancer of stomach	1907
3. Valvular disease of heart, Bright's disease.....	1909
4. Pulmonary tuberculosis	1907
5. Chronic Bright's disease, cardiac hypertrophy.....	1907
6. Diabetes, coma	1910
7. Chronic Bright's disease, uremia	1910
8. Lobar pneumonia	1907

This mortality is decidedly high. If these 396 men had been standard risks, that is if they had been free from albumin, in addition to being otherwise normal, there would have been *sixteen* deaths, instead of *twenty-five*, at the end of ten years. This excessive mortality represents the usual experience of insurance companies in the general group of albuminurias, with or without casts. A number of years ago the medical director of a large insurance company gave us the following statistics, calculated from the records of at least two companies:

Impairment.	Approximate Yearly Mortality per 10,000 Lives*
1. Small amount of albumin and occasionally hyaline casts, otherwise first-class. (This group is composed chiefly of simple albuminuria cases) . . .	137
2. Small amount of albumin and casts, other than hyaline, otherwise first-class	220

*Average mortality among sound lives being 100.

The mortality is lowest among men showing albuminuria only, but even here it is greater than among healthy subjects.

THE INDIVIDUAL CAUSES OF DEATH AMONG THE THREE HUNDRED AND NINETY-SIX MEN

Assuming that the diagnoses on the death certificates were correct, there were three deaths from nephritis and eight from pulmonary tuberculosis. This is quite surprising, as we had anticipated that the chief cause of death would be renal or arterial disease.

This mortality from nephritis was high, inasmuch as approximately but one death from this cause might have been expected among 396 normal men. It will be noticed that the three deaths occurred in the granular-cast group. Insurance statistics show that the mortality from renal and arterial disease in the general group of albuminurias, with or without casts, is about 250 per cent. greater than among normal people. They

also show that the lowest mortality from these causes occurs in the group of simple albuminurias, but how this mortality compares with that among sound subjects we cannot state. We have no statistics on the mortality in the granular-cast group, but the present condition of the twenty men who showed granular casts in 1900 (seven probably having nephritis), makes it probable that this group has the highest death-rate from renal and arterial disease.

The eight deaths from tuberculosis was a remarkably high mortality, for 396 normal men would have shown approximately but two deaths from this disease. No less interesting was the fact that this mortality exceeds the mortality from nephritis. It seemed as if our figures might have been a coincidence, working with such a small number of cases, but records of some thousands of these subjects showed the death-rate from tuberculosis to be 100 per cent. greater than among normal subjects. So while our figures were unusually high, they indicated correctly the tendency of these people toward tuberculosis.

The next step was to ascertain whether any one particular group of albuminurias showed this tuberculous tendency, or whether it was distributed equally among the three groups. In our small series, two of the four deaths from tuberculosis occurred in the albuminuria group. Statistics based on a study of 1,700 cases of simple albuminuria showed that the mortality from tuberculosis among these people was 275 per cent. greater than among normal subjects, and also that it was much higher than in either the hyaline-cast or the granular-cast group.

The relation between albuminuria and tuberculosis has not heretofore been considered other than a casual one, as far as we can ascertain. Von Noorden, in a recent article,¹ describes various forms of harmless albuminuria, and among them one which he calls a pretuberculous albuminuria. He speaks of this as occurring during any stage of pulmonary tuberculosis and as being caused probably by action on the kidney-cells, of toxins of the tubercle bacillus. He does not speak of it, however, as occurring in a pretuberculous stage, so the reason for the name pretuberculous albuminuria is not clear.

Lawrason Brown² considers albuminuria as rare in incipient tuberculosis; it was found in 5 per cent. of 1,214 cases of pulmonary tuberculosis in all stages, at the Adirondack Cottage Sanitarium. Cornet³ says that the urine is normal in the earliest stages of the disease.

The absence of nephritis, shown in our twenty cases of simple albuminuria, after ten years had elapsed, and the low mortality in this group from renal and arterial disease indicate that it is exceptional for the albuminuria of young adults to be a symptom of incipient nephritis.

1. Von Noorden: Ueber Albuminurie, *Ztschr. f. Urol.*, 1907, i, 1017.

2. Osler's *Modern Medicine*, iii, 323.

3. Cornet: *Die Tuberkulose*, 1907, ii, 634, Nothnagel's *Specielle Pathologie und Therapie*.

On the other hand, the high mortality from tuberculosis in this group leads us to consider albuminuria, in the absence of other symptoms, rather as an evidence of a lowered bodily resistance, which is manifested in later years by the person's increased susceptibility to tuberculous infection.

CONCLUSIONS

1. Renal albuminuria without casts is most frequently found in young adults. It is exceptional for it to be a symptom of incipient nephritis. It is rather to be regarded as an evidence of a generally lowered resistance which predisposes to tuberculous infection. The mortality among these people is higher than among normal subjects.
2. Cases of albuminuria with a few hyaline casts have no particular age-incidence. The mortality in this group is also above normal.
3. People with albuminuria and granular casts show a much higher mortality than normal people and a much greater tendency to renal and arterial disease than either of the preceding groups.
4. Whatever the urinary findings, age is a factor in the prognosis of albuminuria, young people having the most favorable outlook as regards the possibility of an ultimate nephritis.

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