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ON THE PERMANENCE OF RECOVERY IN ACUTE GLOMERULONEPHRITIS

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Although there is common agreement and occasional mention of the fact that nephritis once healed does not recur, there has been little evidence presented in the literature to substantiate this impression. Longcope (1) reports 4 cases out of a series of 24 with healed acute nephritis in whom *beta* hemolytic streptococci were found subsequently. Two of these, in a single throat culture each, revealed *beta* hemolytic streptococci, and, in a third patient, *beta* hemolytic streptococci were cultured repeatedly from chronically infected tonsils. Active invasion of tissue by the streptococcus, as measured by the antistreptolysin titer, was not reported. The fourth patient suffered a severe bronchitis caused by the *beta* hemolytic streptococcus. In none of these patients was there evidence of an exacerbation or recurrence of nephritis. Boyle *et al.* (2) mention the cases of 2 boys, each of whom they state had two distinct attacks of nephritis, each followed by complete recovery. Detailed data on the courses and urinary findings in these 2 patients were not given.

In the present study, a group of patients was observed during an attack of acute glomerulonephritis, after recovery, and during a subsequent infection. The infection at the onset of the acute glomerulonephritis and the subsequent infection were proved bacteriologically and immunologically to be caused by the hemolytic streptococcus. It was hoped that such a study might throw light on the alleged permanence of recovery in this disease. The present paper offers bacteriological, immunological, and clinical data on two groups of patients.

The case histories have been divided into 2 groups which are described in the following protocols and are presented in Tables I and II respectively. The 8 cases of Group I include all those observed over an approximately four-year period, from 1933 to 1937. The two individuals in Group

II are selected on the basis of their unique manifestations.

GROUP I

Case 1. C. B. (Hospital Number 80805)

A girl of 5 was admitted with otitis media, recurrent mastoiditis, a postauricular abscess and acute nephritis. Blood pressure was 135/85 and nonprotein nitrogen 34 mgm. per 100 cc. There was no edema. The urine showed albumin ++++, many red blood cells, and casts. Hemolytic streptococci were cultured from the postauricular abscess and the antistreptolysin titer reached 833 units 3 days after onset of the nephritis.

Course. The urine cleared gradually and, in 6 weeks, showed albumin ++ and no red blood cells. In 2½ months, the urine was completely normal and remained so throughout the next 9 months, during which time 5 urine examinations revealed normal findings. The antistreptolysin titer declined progressively, reaching 250 units at the time of the first normal urine. Nine months from the date of the healing of her nephritis, the patient was readmitted with bilateral otitis media and pharyngitis. Hemolytic streptococci were cultured from the mastoid. Three weeks after admission, the patient developed erysipelas of the right cheek, and hemolytic streptococci were cultured from a bleb in this area. The antistreptolysin titer rose to 1250 units. The urine on admission showed minimal amounts of albumin and a normal sediment over a 6-weeks' febrile period. There were no clinical features suggestive of nephritis. The urine was found to be normal on 8 occasions in the next five months.

Case 2. R. B. (Hospital Number 257472)

A boy of 4 was admitted with a history of cervical adenitis and bilateral otitis media occurring 2 weeks before the onset of acute glomerulonephritis with gross hematuria. Blood pressure 116/70. There was no edema. Blood nonprotein nitrogen was 63 mgm. per 100 cc. The urine, in addition to gross hematuria, showed albumin ++++ and casts. Hemolytic streptococci were cultured from the throat and the antistreptolysin titer reached 333 units 1 month after the onset of nephritis.

Course. The urine cleared progressively, showing albumin + and many red blood cells and casts at the end of a month. It was completely normal in 3 months and remained so over a period of 17 months during

TABLE I
Group I

Case, hospital number, sex, and age	Infection preceding nephritis	Onset of nephritis	Urinary findings	Hemolytic streptococcus recovered	Maximum anti-streptolysin titer	Date of healing	Subsequent bases of anti-streptolysin titer	Duration of nephritis	Interval between healing and next hemolytic streptococcal infection	Subsequent hemolytic streptococcal invasion	Hemolytic streptococcus recovered	Maximum anti-streptolysin titer	Urinary findings associated with subsequent hemolytic streptococcal invasion
1. C.B. 80605 ♀ Age 5	Otitis media, mastoiditis, postauricular abscess	Apr. 30, 1934	Alb. + + + + + Many RBC and casts	From post-auricular abscess May 1, 1934	833 May 4, 1934	July 11, 1934	71 Dec. 6, 1934	2½ mos.	9 mos., with 5 neg. urine exams.	Apr. 4, 1935, bilateral otitis media, pharyngitis, postauricular abscess, erysipelas	From post-auricular abscess Apr. 10, 1935	1260 Apr. 9, 1935	Alb. +, sediment neg. throughout 6 wks. 8 neg. urine exams. over next 5 mos.
2. R.B. 257472 ♂ Age 4	Bilateral otitis media, cervical adenitis	Feb. 10, 1934	Alb. + + + + + Gross hematuria, many casts	From throat Mar. 8, 1934	333 Mar. 14, 1934	May 23, 1934	11 June 13, 1934	3 mos.	17 mos., with 17 neg. urine exams.	Oct. 30, 1935, common cold, pharyngitis	From throat Nov. 1, 1935	500 Nov. 13, 1935	Alb. +, sediment neg. for 2 days, 6 neg. urine exams. over next 6 mos.
3. T.B. 403728 ♂ Age 6	Pharyngitis, otitis media	Jan. 1, 1934	Alb. + + + + + Many RBC and casts	From mastoid Jan. 6, 1934	333 Jan. 10, 1934	Aug. 15, 1934	16 Sept. 26, 1934	7 mos.	9 mos., with 5 neg. urine exams.	May 20, 1935, cervical adenitis	From throat June 8, 1935; none June 11, 1935; none June 16, 1935; none	500 June 11, 1935	Alb. + with sediment neg. for 12 days, 5 neg. urine exams. in next 2 mos.
4. B.G. 379237 ♂ Age 6	Head cold with fever	June 19, 1933	Alb. + + + + + Gross hematuria, many casts	From throat June 22, 1933	500 July 3, 1933	Mar. 7, 1934	83 June 13, 1934	9 mos.	9 mos., with 2 neg. urine exams.	Dec. 28, 1934, "common cold," "common cold,"	From throat Jan. 3, 1935	830 Jan. 23, 1935	Alb. + in 1 spec. sediment neg. 1 wk. later and over next 3 mos. 3 neg. urine exams.
5. N.S. 410777 ♂ Age 5	Pharyngitis, otitis media, mastoiditis	Apr. 1, 1934	Alb. + + + + + Many RBC and casts	From ear Mar. 21, 1934; from mastoid Apr. 2, 1934	1000 Apr. 10, 1934	Apr. 22, 1934	166 Jan. 3, 1935	3 wks.	3 yrs., with 10 neg. urine exams. and 1 showing orthostatic albuminuria (see protocol)	Mar. 21, 1937, head cold, cough, T. 101°	From throat Apr. 7, 1937; Apr. 14, 1937	333 Apr. 7, 1937	Urine neg. except 1 occasion of probable orthostatic albuminuria (see protocol) 3 urine exams. over next mo. revealed only orthostatic albuminuria
6. J.L. 410752 ♂ Age 4	Pharyngitis, otitis media	Mar. 24, 1934	Alb. + + + + + Gross hematuria, many casts	From throat and draining mastoid Mar. 26, 1934	1000 Apr. 12, 1934	June 6, 1934	71 Feb. 27, 1935	2½ mos.	10 mos., with 6 neg. urine exams.	Apr. 17, 1935, acute mastoiditis	From throat, draining ear, and post-auricular abscess Apr. 17, 1935	333 May 16, 1935	Alb. + for 4 days in hospital, 1 mo. later urine neg. (pt. lost to follow-up)
7. A.V. 379219 ♂ Age 7	Pharyngitis, cervical adenitis, peritonsillar abscess	June 13, 1933	Alb. + + + + + Gross hematuria, many casts	From peritonsillar abscess June 15, 1933	250 July 20, 1933	Nov. 22, 1933	83 Nov. 22, 1933	5 mos.	18 mos., with 2 neg. urine exams. (1st and 18th mo.)	Cervical adenitis "all winter," May 15, 1935, acute cervical adenitis	No culture made	833 May 22, 1935	1 urine exam. 1 wk. after acute infection neg. (pt. lost to follow-up)
8. R.M. 419533 ♀ Age 21	Pharyngitis, cervical adenitis	June 15, 1934	Alb. + + + + + Few RBC and casts	From throat May 27, 1934; from cervical abscess June 15, 1934	555 June 20, 1934	Aug. 1, 1934	50 Apr. 27, 1935	1½ mos.	8 mos., with 15 neg. urine exams.	Apr. 28, 1935, pharyngitis, cervical adenitis; May 1, 1935, erythema nodosum; May 3, 1935, bronchopneumonia	From throat Apr. 28, 1935; from sputum nodosum; May 3, 1935	333 May 14, 1935	Neg. on 15 occasions over 1 mo.

TABLE II
Group II

Case, hospital number, sex, and age	Infection preceding nephritis	Onset of nephritis	Urinary findings	Hemolytic streptococcus recovered	Maximum anti-streptolysin titer	Date of healing	Subsequent base of anti-streptolysin titer	Duration of nephritis	Interval between healing and next hemolytic streptococcal infection	Subsequent hemolytic streptococcal invasion	Hemolytic streptococcus recovered	Maximum anti-streptolysin titer	Urinary findings associated with subsequent hemolytic streptococcal invasion
9. F. K. 336043 ♂ Age 14	Pharyngitis, peritonsillar abscess, T. 104.9°	Apr. 16, 1933	Alb. +++++ Gross hematuria, many casts	From pus of peritonsillar abscess	555 Apr. 25, 1933	May 14, 1932	33 Jan. 10, 1935	1 mo.	10 mos., 35 neg. urines, 32 in 1st 6 wks., 3 on subsequent examinations	Cold with cervical adenitis for 1 wk., Mar. 27, 1933	None recovered from throat 2 wks. after onset of infection	Not determined	Gross hematuria noted by pt. 1 wk. before visiting clinic and progressively clearing over the following month. Subsequently over 3 yr. period 15 urine specimens showed no abnormalities
10. J. L. 242332 ♂ Age 16	Lobar pneumonia Type 1	Aug. 2, 1924	Alb. +++++ Smoky urine, many casts	None	Not done	Nov. 18, 1925	Not done	16 mos.	10 yrs. with 8 neg. urines	Pharyngitis, cervical adenitis, T. 101 May 6, 1935	None recovered on throat culture	333 May 16, 1935	Alb. ± gross hematuria, 1 wk. later, no hematuria. 1 yr. later alb. ± sediment neg.

which time urine specimens revealing normal findings were observed on 17 occasions. The antistreptolysin titer had declined to 50 at the time of examination of the first normal urine. Seventeen months after the healing of his nephritis, the boy was readmitted with a head cold and pharyngitis. Hemolytic streptococci were cultured from the throat, and the antistreptolysin titer reached 500 units. The urine showed minimal amounts of albumin and a normal sediment over the 2 days during which fever was present. There were no clinical signs of nephritis. The urine then became negative and remained so over a 6-month period of observation in the clinic, during which time there were monthly urine examinations.

Case 3. T. B. (Hospital Number 403728)

A boy of 6 with a month's preceding history of pharyngitis and otitis media, was admitted with acute nephritis. There was no edema or hypertension. Blood nonprotein nitrogen was 39 mgm. per 100 cc. The urine showed albumin +++++, many red blood cells, and casts. Hemolytic streptococci were cultured from the mastoid at operation, and the antistreptolysin titer reached 333 units.

Course. The urine cleared progressively, showing only albumin ++ and 1 to 2 red blood cells at the end of 2 weeks, which minor findings persisted until they completely disappeared at the end of 7 months. At this time, the antistreptolysin titer had declined to 16 units. During the next 9 months there were 5 urine examinations all revealing normal findings. At the end of this time, the patient was readmitted with a history of cervical adenitis for 9 days, fever having reached 104° F. Throat cultures on 3 occasions failed to show hemolytic streptococci, but the antistreptolysin titer was 500 units. The urine showed minimal amounts of albumin over a 12-day febrile period. There were no clinical features of nephritis. Five urine examinations over the next 2 months were normal.

Case 4. B. G. (Hospital Number 379237)

A boy of 6 with a history of head cold and fever for 2 weeks was admitted with acute nephritis, gross hematuria having been noted 3 days before admission. There was no edema, blood pressure was 104/60, and blood nonprotein nitrogen was 59 mgm. per 100 cc. The urine showed albumin +++++ and casts in addition to the gross hematuria. Hemolytic streptococci were cultured from the throat. The antistreptolysin titer reached 500 units.

Course. The urine improved progressively, showing albumin ++ and 3 to 4 red blood cells per high power field at the end of 6 weeks when he was discharged. After 2 months, he was readmitted with an otitis media, his urine still showing albumin + and 1 to 3 red blood cells per high power field. The otitis media subsided in a week and the urine cleared progressively, becoming normal 9 months from his first admission. During the following 9 months, a urine examination upon 2 occa-

sions revealed normal findings and the antistreptolysin titer was 111 units. At this time, the boy was seen in the clinic with a cold. Temperature was 103° F. Hemolytic streptococci were cultured from the throat and the antistreptolysin titer reached 830 units. There was no clinical evidence of nephritis. The urine showed minimal amounts of albumin and a negative sediment on admission. One week later, and on 3 occasions over the next 3 months, the urine was negative.

Case 5. N. S. (Hospital Number 410777)

A boy of 5 with a 2 weeks' preceding history of pharyngitis and otitis media was admitted with acute mastoiditis and acute nephritis. There was no edema, blood nonprotein nitrogen was 31 mgm. per 100 cc., and blood pressure was 118/65. The urine showed albumin ++, many red blood cells, and many casts. Hemolytic streptococci were cultured from the mastoid at operation and had been cultured from a draining ear 10 days before, during a clinic visit. The antistreptolysin titer reached 1000 units.

Course. The urinary findings cleared progressively over the next 3 weeks and were normal at the end of this time. Subsequently, in the clinic, over a period of 12 months, 8 urine examinations revealed normal findings, and the antistreptolysin titer had declined to 144 units. At the next visit, 3 months later, the boy reported fever for 2 days following swimming. He complained of general muscle stiffness. There had been some dysuria but no frequency or hematuria. Physical examination revealed no signs of nephritis. No throat culture was taken. The urine showed albumin ++++ and a normal sediment. The antistreptolysin titer was 200. Ten days later, a urine specimen was normal. The boy was next seen in the clinic approximately 1½ years later, reporting a severe head cold and cough, fever having reached 101° F. over the preceding week. Hemolytic streptococci were cultured from the throat on two occasions and the antistreptolysin titer was 333 units. The urine showed only heavy albuminuria proven to be an orthostatic albuminuria on 5 examinations during the subsequent month. There were no clinical signs of nephritis.

Case 6. J. L. (Hospital Number 410752)

A boy of 4 with a 2½ weeks' history of pharyngitis, otitis media, and fever 102° F., was admitted with acute nephritis. There was no edema, blood nonprotein nitrogen was 36 mgm. per 100 cc., and blood pressure was 95/55. The urine showed gross hematuria, albumin ++++, and many casts. Hemolytic streptococci were cultured from the throat, draining ears, and from the mastoid area at operation. The antistreptolysin titer rose to 1000 units.

Course. The urine cleared progressively, becoming completely normal in 2½ months. Ten months later, during which period urine examinations upon 6 occasions revealed no abnormality, the patient was read-

mitted with acute mastoiditis. Temperature was 101° F. There was no clinical evidence of nephritis. Hemolytic streptococci were cultured from the throat, ear, and from a postauricular abscess. The antistreptolysin titer reached 333 units. The urine showed a minimal albuminuria and a normal sediment daily during the 4 days that the patient was hospitalized. The urine 1 month later was normal. The patient was then lost to follow-up.

Case 7. A. V. (Hospital Number 379219)

A boy of 7 with a history of pharyngitis and cervical adenitis for 2 weeks was admitted with a peritonsillar abscess and acute nephritis with gross hematuria. There was slight edema of the extremities, blood pressure was 116/68, blood nonprotein nitrogen 31 mgm. per 100 cc., serum albumin 3.9 per cent, and serum globulin 3.4 per cent. In addition to gross hematuria, the urine showed albumin ++++, and casts. Hemolytic streptococci were cultured from the peritonsillar abscess, and the antistreptolysin titer reached 250 units.

Course. The urinary abnormalities subsided gradually, showing albumin + and occasional red blood cells at the end of 6 weeks. At the end of 5 months the urine was completely normal and the antistreptolysin titer revealed 83 units. Eighteen months after the date of healing, during which time urine examinations in the 1st and 18th months revealed normal findings, the child was seen in the clinic with the complaint of cervical adenitis "off and on all winter," a recent exacerbation with fever having occurred one week previously. No clinical signs of nephritis were present. No throat culture was made, but the antistreptolysin titer was found to be 833 units. The urine at this time, one week after exacerbation of an infection with fever, revealed no changes. Unfortunately, the patient could not be followed.

Case 8. R. M. (History Number 419533)

A girl of 21 was admitted with pharyngitis and cervical adenitis. The urine was normal on admission and remained so during a period of 10 days of exacerbation and remission of the adenitis. Throat cultures revealed hemolytic streptococci and the antistreptolysin titer reached 555 units. Ten days later, the urine began to show ++++ albumin, a few casts, and red blood cells. There was no edema and no hypertension, but the blood urea rose to 0.79 gram per liter. The adenitis persisted and surgical drainage of a cervical abscess revealed, on culture, the presence of hemolytic streptococci. Blood cultures showed no growth. The urinary abnormalities gradually diminished and at the end of 6 weeks the urine was normal. Eight months after healing had occurred, during which period there had been 15 urine examinations, all normal, and the antistreptolysin titer had declined to 50 units, the patient was readmitted with pharyngitis and cervical adenitis of 12 hours' duration. Temperature was 101° F. Throat culture showed a pure growth of hemolytic streptococci. The antistreptolysin

titer rose to 333 units. Six days after admission, the patient developed mild erythema nodosum of the left foot and leg and right forearm. Eight days after admission, she developed a bronchopneumonia with sputum showing hemolytic streptococci and no pneumococci. Throughout this second admission, over a period of 1 month, there were 15 urine examinations all of which were normal. Fever was high, 101° to 104° F. over the first week of illness. There were no clinical signs of nephritis.

GROUP II

Case 9. F. K. (Hospital Number 336058)

A boy of 14 with a 2 weeks' history of pharyngitis was admitted with a peritonsillar abscess and acute nephritis with gross hematuria. Temperature was 104.6° F., and blood pressure 134/64. There was no edema. The urine, in addition to gross hematuria, showed albumin ++++ and many casts. Hemolytic streptococci were cultured from the incised peritonsillar abscess and the antistreptolysin titer reached 555 units. The patient left against advice after 3 weeks in the hospital, at which time the urine showed albumin ++ and rare red blood cells. Five days later, when seen in the clinic, the urine showed albumin ++ and 10 red blood cells per high power field. There was no history of intercurrent infection. When readmitted 1 week later, the urine was normal and remained so throughout his stay of 2 months. During this time, the antistreptolysin titer had declined to .200. Throughout the next 6 months, 3 more urine examinations revealed normal findings. Ten months from the date of healing, the patient returned to the clinic, reporting a cold and cervical adenitis for 1 week, gross hematuria having appeared on the 2d day. A urine examination in the clinic revealed albumin +, many red blood cells and no casts. There was no edema, and blood pressure was 130/95. A throat culture at this time failed to show hemolytic streptococci. No determination of the antistreptolysin titer was made. Over the next 4 weeks, numerous red blood cells with albumin + and without casts were found in his urine on 3 examinations. One month later an examination revealed normal urine. During the next 3 years, there were 15 urine examinations revealing normal findings.

Case 10. J. L. (Hospital Number 242232)

A boy of 16 was admitted with Pneumococcus Type I lobar pneumonia of 3 days' duration. Urine on admission showed albumin +, occasional casts, and rare red blood cells. Blood pressure was 100/65. Three days later, his eyes became puffy, blood pressure 130/65, and the urine became smoky. Albumin ++++ was present. Blood urea rose to 1.6 grams per liter, and the phthalein excretion fell to 25 per cent. He was discharged 3 months later with urine still showing albumin ++ and many red blood cells. Subsequent follow-up in the clinic 1 month later showed albumin + and a few red blood cells per high power field and 1 year later

albumin ± with a normal sediment. During the next 10 years, he was followed in the clinic, the urine being negative on 8 occasions. At the end of this 10-year period the patient returned to the clinic with sore throat, dysphagia, cervical adenitis, and temperature 101° F.; blood pressure was 115/80, and there was no edema. Urine showed albumin ± and 35 red blood cells per high power field. A throat culture revealed no hemolytic streptococci but the antistreptolysin titer was found to be 333 units. During the next week, the patient's symptoms disappeared. The urine 1 year later, showed albumin ±, sediment negative. The antistreptolysin titer was 333 units.

SUMMARY

The case histories of two groups of patients with healed acute nephritis are presented. The first group, offered in Table I, consists of 7 children and 1 adult. All of them had typical acute glomerulonephritis, associated at onset with an infection, bacteriologically and immunologically proved to be due to the hemolytic streptococcus. The duration of the nephritis in these patients varied from 3 to 9 months. There was a period of observation during the healed state ranging from 9 months to 3 years. All of the patients suffered subsequent infection, again bacteriologically or immunologically proved to be due to the hemolytic streptococcus. The antistreptolysin titers ranged from 333 to 1250 units. There were no clinical symptoms of nephritis associated with the second hemolytic streptococcal invasions in this group of patients. The urine showed no red blood cells and only an initial minimal and transient albuminuria associated with the febrile episodes. Thereafter, throughout periods of observation varying from 1 to 6 months in 7 of these patients, the urine showed no changes distinguishable from the normal.¹ Unfortunately, in the remaining patient (Case 7, A. V.), only 1 urine was available for examination, 1 week after an attack of acute cervical adenitis. The findings at this time, however, were entirely normal.

One of the patients in this group (Case 5, N. S.) was of particular interest. During his healed period, he developed fever with mild dysuria, without hematuria or frequency. A urine speci-

¹ It should be said that one of us, J. D. L., has been able to find from time to time, with special technique, minimal amounts of albumin, occasional casts, and red blood cells in the urine of these patients, as he does with the same technique in the urine of normal children.

men revealed albumin ++++ and occasional red blood cells. Ten days later, the urine was normal. One and a half years later, an examination, following a hemolytic streptococcal infection, showed that the boy had developed orthostatic albuminuria and was without evidence of nephritis. In the light of this, one is unable to state whether the single specimen showing heavy albuminuria 1½ years previously, associated with fever and dysuria, and followed later by one urine revealing normal findings, was of the orthostatic type or whether it represented nephritis. However, the second proved hemolytic streptococcal infection did not induce recurrence of the nephritis and 5 urine specimens observed over the next month continued to show only albuminuria of the orthostatic type.

The second group of patients consists of 2 adolescents presented in Table II. This group differs from Group I inasmuch as it consists of individuals healed of acute glomerulonephritis, who, on being subjected to subsequent infection, developed marked hematuria. In Case 9, F. K., aged 14, the original bout of nephritis followed an infection proved to be due to the hemolytic streptococcus; in the other, Case 10, J. L., aged 16, the nephritis followed Type I lobar pneumonia, and a concomitant infection with the hemolytic streptococcus was not known to be present. The nephritis lasted only 1 month in Case 9 but abnormal urinary findings persisted 15 months in Case 10. Each suffered subsequent infection. This was proved to be due to the hemolytic streptococcus in Case 10 and occurred 10 years after the healing of his nephritis. The ensuing infection in the other patient, Case 9, F. K., occurred 10 months after the healing of his nephritis and was presumably due to the hemolytic streptococcus but was not proved so. As has been stated above, the feature distinguishing these two patients from the individuals in Group I was the development of marked hematuria concomitant with subsequent hemolytic streptococcal infection and following a period in which they had been amply observed, as will be seen by the tables, to have been healed of their nephritis. The hematuria, although marked, was unaccompanied by significant albuminuria; it lasted 4 weeks in Case 9 and 1 week in Case 10. Subsequently, in Case 9, 15 urine examinations over the next 3 years revealed no

abnormalities. Only 1 examination has been obtained in Case 10 and that 1 year after the disappearance of his hematuria. At this time, no urinary abnormalities were present.

In connection with these 2 patients exhibiting hematuria without significant albuminuria, it is of interest to point out that about 15 per cent of the patients with rheumatic fever at the Presbyterian Hospital show varying degrees of hematuria and slight albuminuria during their acute episodes whereas, at autopsy, only 3 of about 100 patients in Coburn's series (5) dying of active rheumatism showed any evidence of glomerulonephritis. It seems possible that the hematuria associated with the subsequent hemolytic streptococcal infection occurring in the two individuals in the second group of patients and unassociated with other signs, symptoms, or laboratory evidence of nephritis may be analogous to the renal manifestations occurring in many cases of rheumatic fever. However, it must be stated that the mechanism of the hematuria is unknown.

It is of interest immunologically that in acute nephritis, a disease the typical onset of which follows an infection with the hemolytic streptococcus, a second similar infection in these patients has not led to the chronic form of the disease. In the rheumatic state, however, a disease of proved association with the hemolytic streptococcus, recurrence of the disease, with or without apparent progressive damage, is common.

If the 10 cases presented may be assumed to be representative of the disease in general and if acute glomerulonephritis be a disease initiated by the hemolytic streptococcus, the permanence of recovery maintained in the face of subsequent hemolytic streptococcal invasion, as evidenced by the 10 patients under discussion, presents one aspect of immunity in hemolytic streptococcal disease.

The nature of this immunity is not known. Whether the defense mechanism results from the actual presence of immune bodies or whether it may result from histological and physiological changes within the kidney such as MacNider (3, 4) described occurring in his dogs with uranium nitrate nephritis, who were resistant to further damage by uranium nitrate, can only be a matter for conjecture at present. The important fact to be emphasized again in connection with this series

of patients with healed acute nephritis is that, in spite of recurrent hemolytic streptococcal infection, and, in two instances, despite an accompanying recurrent hematuria, no one of these individuals has gone on to develop chronic progressive kidney disease.

The observations reported in this study receive amplification and support in the experience of Atchley and Loeb in the nephritic clinic at the Presbyterian Hospital over a period of 14 years and in the experience of one of us (J. D. L.) at the Babies Hospital over a 10-year period. No case of healed acute glomerulonephritis has subsequently been observed to develop the chronic form of the disease. These cases, for the most part, were not studied from the bacteriological and immunological standpoint, but were presumably, in the majority of instances, secondary to infection with the hemolytic streptococcus.

CONCLUSIONS

1. A clinical, bacteriological, and immunological study with reference to hemolytic streptococcal infection has been made in 10 patients. These individuals were observed (1) during their acute glomerulonephritis, (2) throughout a subsequent healed period, and (3) during and following a subsequent infection with the hemolytic streptococcus.

2. Eight of the patients whose nephritis at onset was preceded by hemolytic streptococcal infection were observed through healed periods

varying from 8 months to 3 years. Thereafter, in each instance, an intercurrent hemolytic streptococcal infection produced no recurrence of their nephritis.

3. Two of the patients with acute glomerulonephritis, preceded by hemolytic streptococcal infection in one and by Type I lobar pneumonia in the other, were observed through subsequent healed periods of 10 months and 10 years respectively. Each then underwent an infection proved to be caused by the hemolytic streptococcus in one instance and presumably caused by that organism in the other. Both developed transient gross hematuria without significant albuminuria.

4. No one of the 10 patients studied has developed the chronic form of glomerulonephritis.

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