THE BACTERIOLOGY OF THE URINE IN FOCAL INFECTIONS; ITS RELATION TO NEPHRITIS *

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In a previous report¹ the bacteriology of the urine in a number of cases of nonsuppurative nephritis was described. In all of the cases examined the urine contained numbers of bacteria, mostly anaerobes. In one case² the bacterial flora of the urine was the same as that of a focus of infection in another part of the body. The bacteria isolated from the urine readily produced experimental nephritis. These facts led us to believe that bacteria multiplying in foci of infection frequently gain entrance to the blood stream and are excreted in viable condition through the kidneys, and that the excretion of bacteria in this way by the kidneys may be a common cause of nephritis.

It seemed desirable to examine a number of patients with evident focal infections to learn how frequently bacteria found in the focus of infection can be isolated from the urine, in what number they occur in the urine, and whether excretion of bacteria occurs to any extent without clinical evidence of injury to the kidneys.

In selecting cases for this study, patients with gonorrhea, other primary infections of the urinary tract, or syphilis were excluded, so far as possible, by means of history, complement deviation tests, evident discharges, pus in the urine, vesical irritation, etc. Infections such as pneumonia, known to be accompanied by septicemia, were also excluded. No patient with evidence of an active tuberculosis was included. Some of the patients studied had evidence, such as arthritis, of migration and lodging of bacteria in other parts of the body. Cases in which the intestine seemed the most likely source of infection were avoided because of the proximity of the urethral and anal orifices, which might lead to the interpretation of correspondence between urinary and fecal flora as due to contamination rather than to transmission by the blood stream.

Eighteen patients were examined. In six of these the bacteria when found in the urine did not correspond to those found in the focus of

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1. Dick, G. F., and G. R.: The Bacteriology of the Urine in Nonsuppurative Nephritis, *Jour. Am. Med. Assn.*, 1915, **65**, 6.

2. Dick, G. F., and G. R.: The Bacteriology of the Urine in Two Cases of Parenchymatous Nephritis, *Jour. Am. Med. Assn.*, 1914, **63**, 1661.

infection from which cultures were made. This may have been due to the bacteria in the urine having come from a source other than the focus of infection studied. In some instances, the negative results may have been due to the time of examination, as it was found that showers of bacteria may occur in the urine just as showers of casts are known to occur. Indeed, the two were observed to appear together in Case 5, to be described. In most cases the bacteria were hard to grow in pure culture and difficulty of technic in isolating and identifying the organisms probably explains some negative results.

In four cases a partial correspondence was found between the bacterial flora of the urine and that of the focus of infection. In eight cases the correspondence was more striking. These eight cases will be described in detail.

Cultures from the focus of infection were made aerobically and anaerobically on human blood agar slants. Shake cultures in plain agar were made with 2 c.c. catheterized urine; 15 c.c. urine were centrifuged and aerobic and anaerobic cultures on human blood agar were made from the sediment.

REPORT OF CASES

CASE 1.—*Chronic tonsillitis, chronic interstitial nephritis, cardiac hypertrophy in a woman, aged 25.* History of frequent attacks of tonsillitis. Blood pressure 150 mm. The catheterized urine showed an occasional hyaline cast and leukocyte; no albumin or erythrocytes.

Cultures from 2 c.c. urine gave colonies too numerous to count of (a) streptococcus, oval, gram-positive aerobic, hemolytic, dextrose acid, mannite negative, lactose faintly acid, milk acid and not coagulated at the end of forty-eight hours; (b) bacillus, small, pleomorphic, gram-negative, anaerobic, no growth on ordinary mediums, no hemolysis, minute transparent colonies on human blood agar.

Cultures from the tonsils gave (a) streptococcus, oval, gram-positive, aerobic, hemolytic, dextrose acid, mannite negative, lactose faintly acid, milk acid, not coagulated at end of forty-eight hours; (b) bacillus, small, pleomorphic, gram-negative, anaerobic, no growth on ordinary mediums, no hemolysis, minute transparent colonies on human blood agar; (c) fusiform bacillus; (d) staphylococcus; (e) coccus, small, gram-negative, anaerobic.

CASE 2.—*Chronic rhinitis, pyelonephritis, post-operative bronchopneumonia, in a girl, aged 12.* History of "cold in head" all of preceding winter, frequent micturition for six months, tonsillectomy two months, and removal of inferior turbinate bones one week before being seen. Blood pressure 114 mm. The urine contained 0.2 to 0.8 gm. albumin to the liter; showed numerous leukocytes and some leukocytic casts, no erythrocytes.

Cultures of 2 c.c. urine gave fifteen colonies of (a) streptothrix, small, true branching, mostly gram-negative, growth in both aerobic and anaerobic cultures, no growth on ordinary mediums, very delicate, transparent growth of minute colonies on human blood agar, no change in the blood; one colony of (b) staphylococcus; one colony of (c) bacillus diphtheroid, gram-positive, aerobic.

Cultures of nasal secretion showed (a) streptothrix, small, true branching, mostly gram-negative, growth in both aerobic and anaerobic cultures, no growth

on ordinary mediums, very delicate, transparent growth on human blood agar, no change in the blood; (b) streptococcus, hemolytic.

CASE 3.—*Recurring bronchitis, chronic arthritis, nephritis, in a woman aged 49.* History of bronchitis every winter. Blood pressure 150 mm. Urine showed trace of albumin, occasional hyaline and finely granular cast, very few leukocytes, no erythrocytes.

Cultures of 2 c.c. urine gave one colony in shake, and several colonies on human blood agar slant, of (a) streptococcus, small spherical, gram-positive growth very scant both aerobically and anaerobically, forming minute, transparent colonies; hemolytic; lactose and dextrose acid, mannite negative, milk acid and coagulated; six small colonies of (b) bacillus, small, pleomorphic, gram-negative, anaerobic, no growth on ordinary media, minute transparent colonies on human blood agar, no change in the blood; one colony of (c) staphylococcus; two colonies of (d) bacillus diphtheroid, gram-positive, aerobic.

Cultures of sputum gave (a) streptococcus, small, spherical, gram-positive, growth very scant both aerobically and anaerobically, minute transparent colonies, hemolytic, lactose and dextrose acid, mannite negative, milk acid and coagulated; (b) bacillus, small, pleomorphic, gram-negative, anaerobic, no growth on ordinary mediums, minute, transparent colonies on human blood agar, no change in the blood; (c) pneumococcus.

CASE 4.—*Chronic tonsillitis, chronic interstitial nephritis, cardiac hypertrophy, in a woman aged 29.* History of tuberculosis at the age of 15; backache, headache, dizziness, dyspnea on exertion noticed during last year. No evidence of active tuberculosis; right tonsil hypertrophied, with tender swelling under angle of right jaw. Blood pressure 230 mm. Urine amounted to 870 c.c. in twenty-four hours; specific gravity 1.020; showed a trace of albumin and hyaline and granular casts.

Cultures of 2 c.c. urine gave colonies too numerous to count of (a) bacillus, small, pleomorphic, gram-negative, anaerobic, no growth on ordinary mediums, pin-point, transparent colonies on human blood agar, no change in the blood; (b) streptococcus, small, gram-positive, grew only in anaerobic blood slant and failed to grow in transfers; (c) leptothrix varying from short bacillary forms to long threads, gram-positive, anaerobic, three colonies obtained from 2 c.c. urine; (d) staphylococcus, one colony grew from 2 c.c. urine.

Cultures of tonsils showed (a) bacillus, small, pleomorphic, gram-negative, anaerobic, no growth on ordinary mediums, pinpoint, transparent colonies on human blood agar, no change in the blood; (b) streptococcus; (c) staphylococcus; (d) coccus, small, gram-negative, anaerobic; (e) bacillus, anaerobic, gram-positive, diphtheroid.

CASE 5.—*Chronic infection about root of an impacted tooth; chronic interstitial nephritis; cardiac hypertrophy.* History of diphtheria, scarlet fever and influenza. Complaint of headache and dizziness for one year. Blood pressure, 170 mm. Urine: 1,500 c.c. in twenty-four hours; sp. gr., 1.008; no erythrocytes or leukocytes, an occasional hyaline cast and no albumin on admission; later, a trace of albumin and a shower of hyaline and granular casts.

Cultures of 2 c.c. urine made on admission to hospital gave one colony of (a) bacillus, small, pleomorphic, not definitely gram-positive or gram-negative, anaerobic, no growth on ordinary mediums, pinpoint transparent colonies on human blood agar, no change in the blood.

Cultures of 2 c.c. urine made at the time the shower of casts appeared showed innumerable colonies of (a) bacillus obtained in first culture; (b) bacillus, fusiform, gram-negative, anaerobic; (c) coccus, very small, spherical, gram-negative, anaerobic, less growth on ordinary mediums than on human blood agar, no change in the blood, delicate growth of pinpoint transparent colonies;

(d) streptococcus, small, oval, gram-positive, anaerobic, hemolytic, small transparent colonies on human blood agar, dextrose and lactose acid, mannite negative, milk acid and not coagulated at end of forty-eight hours; (e) *Staphylococcus aureus*; (f) *Bacillus mucosus*.

Cultures of pus from infection around tooth showed (a) bacillus, small, pleomorphic, not definitely gram-positive or gram-negative, anaerobic, no growth on ordinary mediums, pinpoint transparent colonies on human blood agar, no change in the blood; (b) bacillus, fusiform, gram-negative, anaerobic; (c) coccus, very small, spherical, gram-negative, anaerobic, less growth on ordinary mediums than on human blood agar, no change in the blood, delicate growth of pinpoint transparent colonies; (d) streptococcus, small, oval, gram-positive, anaerobic, hemolytic, small transparent colonies on human blood agar, dextrose and lactose acid, mannite negative, milk acid and not coagulated at the end of forty-eight hours; (e) *Staphylococcus aureus*; (f) bacillus, very small, plump, gram-negative, anaerobic, hemolyzed blood slowly forming black colonies; (g) streptococcus, larger than (d) spherical, long chains, gram-positive, aerobic, heavier growth than (d) milk acid and coagulated at end of forty-eight hours.

TABLE GIVING DATA OF AUTHORS' CASES

Case No.	Clinical Evidence of Kidney Lesion	Organisms Found in Both Urine and Focus of Infection	Number of Bacteria in Urine
1	+	(a) Streptococcus..... (b) Anaerobic bacillus.....	Many
2	+	Streptothrix.....	Few
3	+	(a) Streptococcus..... (b) Anaerobic bacillus.....	Few
4	+	(a) Streptococcus..... (b) Anaerobic bacillus.....	Many
5	+	(a) Streptococcus..... (b) Anaerobic bacillus..... (c) Fusiform bacillus..... (d) Anaerobic coccus.....	Few to Many
6	—	(a) Pneumococcus..... (b) Streptothrix.....	Many
7	?	(a) Streptococcus..... (b) Anaerobic bacillus.....	Many
8	+	Leptothrix.....	Many

CASE 6.—*Bronchiectasis (nontuberculous)*, in a woman aged 44. History of cough and expectoration for three months following an attack of influenza. Blood pressure, 120 mm. Catheterized specimen of urine showed no albumin, casts, leukocytes or erythrocytes.

Cultures of 2 c.c. urine gave numerous colonies of (a) pneumococcus; (b) streptothrix, small, very pleomorphic, forming branched threads at times, at other times appearing as a very irregular, small bacillus, gram-negative, anaerobic, no growth on ordinary mediums, delicate transparent growth on human blood agar, no change in the blood; (c) bacillus, one colony only, of morphology of colon bacillus, gram-negative, aerobic, not motile, thick, moist, yellowish mucoid film on plain agar, no change in blood, lactose, milk acid and slowly coagulated, mannite and dextrose negative.

Cultures of sputum showed (a) pneumococcus; (b) streptothrix, small, very pleomorphic, forming branched threads at times, at other times appearing

as a very irregular small bacillus, gram-negative, anaerobic, no growth on ordinary mediums, delicate transparent growth on human blood agar, no change in the blood; (c) yeast.

CASE 7.—*Exophthalmic goiter, chronic tonsillitis, mitral stenosis and insufficiency, in a woman aged 25.* History of typhoid fever. Nervousness, dizziness, palpitation, diarrhea and one recent attack of nausea during past year. Blood pressure, 150 mm. Urine showed no albumin, casts, leukocytes or erythrocytes.

Cultures of 2 c.c. urine showed numerous colonies of (a) bacillus, small, regular in morphology in direct smears of urinary sediment, pleomorphic in cultures, gram-negative, anaerobic, no growth on ordinary mediums, very delicate growth of pinpoint transparent colonies on human blood agar, no change in the blood; (b) streptococcus, marked tendency to pleomorphism with formation of long oval and bacillary forms, many of which are gram-negative, nonhemolytic.

Cultures of tonsils showed (a) bacillus, small, pleomorphic, gram-negative, anaerobic, no growth on ordinary mediums, very delicate growth of pinpoint transparent colonies on human blood agar, no change in the blood; (b) streptococcus, nonhemolytic, resembling that of urine; (c) streptococcus, hemolytic.

CASE 8.—*Chronic tonsillitis, acute rheumatism, aortic insufficiency, chronic nephritis, in a woman aged 25.* History of measles, whooping cough, tonsillitis, two attacks of rheumatism, dyspnea and palpitation. Blood pressure varied from 165 mm. to 190 mm. Urine showed albumin and coarse and fine granular casts, no leukocytes or erythrocytes.

Cultures of 2 c.c. urine gave about forty colonies of (a) leptothrix, thread-like forms, no branching, gram-positive, anaerobic, growth slow, forming minute, transparent colonies on human blood agar at end of forty-eight hours, which developed into slightly raised, brownish colonies about 1 mm. in diameter at end of five days, blood brownish, growth on dextrose, mannite lactose agar and in milk slight as compared with that on human blood agar.

Cultures of throat showed many colonies of (a) leptothrix of same characteristics as that of urine.

SUMMARY AND CONCLUSIONS

It was pointed out in our previous report³ that staphylococci and gram-positive aerobic diphtheroids are common inhabitants of the urethra. Their occasional presence in small numbers as a contamination in catheterized urine is to be expected. They were found in Cases 2, 3, 4 and 5. It will be noted that aside from these organisms, one or more of the kinds of bacteria found in the urine were isolated from the focus of infection in each of the eight cases. It seems probable that the bacteria found in the urine came from the focus of infection.

It will be seen from the table that two of the eight patients showed no clinical evidence of renal lesion. One of these, however, had persistently high blood pressure (150 mm.). In the remaining patients there were from mild to severe renal lesions present, but there was no very constant relation between the severity of the lesion and the number of bacteria in the urine.

3. Loc. cit., Note 1, p. 15.

The finding of considerable numbers of bacteria in the urine in 66 per cent. of patients with evident foci of infection indicates that in diseases where migration of bacteria from foci of infection takes place, the bacteria are often present in the urine.

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