Bacteriuria in general practice

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THERE are few data available about the prevalence of bacteriuria in the general population. Kunin *et al* (1960, 1962) examined school-children and students between 5 and 20 years of age. About 1 per cent of 5,132 girls had asymptomatic bacteriuria (defined as more than 100,000 bacteria per ml of urine) against only two boys out of 7,731. Kass (1964) found that 4.4 per cent of women between 15 and 65 years of age had asymptomatic bacteriuria. A study by Sussman *et al* (1969) revealed some details about the natural history of asymptomatic bacteriuria in non-pregnant women between 20 and 65 years of age. The prevalence of bacteriuria in their study was 3.5 per cent (126 of 3,578 women).

Manifest urinary tract infections have, however, been investigated more extensively by other authors. Loudon and Greenhalgh (1962) found a prevalence of 14.6 per thousand per year and Mond *et al* (1965) found 8.3 per thousand in their practice.

The aim of our study, which was made from March to December 1967 in a general practice, was threefold:

1. Collection of data about the prevalence of bacteriuria in women from 15 to 65 years of age in a general practice.
2. Collection of data about diagnostic problems of bacteriuria in general practice.
3. Follow-up of patients with bacteriuria in order to compare the results of the two different methods of treatment.

Methods

A total of 1,001 out of 1,173 (85 per cent) women between 15 and 65 years of age was investigated. After obtaining a brief medical history and recording the blood pressure the women were given instructions to collect a clean-voided urine specimen in a sterile receptacle. Cleaning of the periurethral area was carried out with cottonwool, impregnated in a 1:1,000 chlorhexidine solution.

The urine specimens were investigated within one hour after voiding and stored afterwards in a refrigerator at 4°C.

The following investigations were carried out:

1. Triphenyltetrazolium chloride test (TTC)
2. Unstained smear of centrifuged urine
3. Gram-stained smear of centrifuged urine
4. Methylene blue-stained smear of centrifuged urine
5. Gram-stained smear of uncentrifuged urine.

If the microscopic investigation of a specimen of urine revealed more than five leucocytes or more than five bacteria per high-power field, or if the TTC test was positive, the urine was sent cooled for a culture to the Groningen District Laboratory for Public Health (director Dr R. K. Koopmans). A urine specimen containing more than 100,000 organisms per ml was considered to be positive. Once bacteriuria had been confirmed the patients were divided at random into three groups:

1. 5 days treatment with sulphamethizole
2. 10 days treatment with sulphamethizole
3. 5 days treatment with saccharum lactis.

Follow-up was carried out one week, six weeks and 12 weeks after finishing these treatments.

Interpretation of diagnostic methods

Triphenyltetrazolium chloride test. The test material was supplied by Pfizer & Co. as Uroscreen test. Two ml of urine were added to the Uroscreen tube (which was marked at the 2 ml level). The urine was shaken until the Uroscreen reagent was completely dissolved. Afterwards the urine was incubated at 37°C for four hours. The test was positive when a pink to red precipitate appeared.

Unstained smear of centrifuged urine. 10 ml of urine were spun for five minutes at a rotation velocity of 4,000 rpm (relative centrifugal force=1,610 G). After discarding about 9 ml of supernatant urine the sediment was resuspended in the remaining urine. Subsequently three loopfuls of urine were placed on a slide. After applying a cover glass the specimen was investigated with 400x magnification. Specimens with five or more leucocytes per high-power field were considered to be positive. Women whose urine contained more than one stratified epithelium cell per field were requested to come for a second investigation.

Gram-stained smear of centrifuged and uncentrifuged urine. One loopful of centrifuged urine on a slide and also one loopful of uncentrifuged urine was placed on another slide. These smears were dried and then fixed in a 70 per cent alcohol solution. Afterwards they were stained according to the Gram staining method.

Specimens with five or more bacteria or five or more leucocytes per high-power field were considered to be positive.

Methylene blue-stained smear of centrifuged urine. Finally one loopful of centrifuged urine was dried and fixed as described above and afterwards stained with methylene blue dye. We used the same criteria in studying these specimens as described for the Gram-stained specimens.

Results

In this study we found asymptomatic bacteriuria in 43 (4.3 per cent) of 1,001 women between 15 and 65 years of age and 20 (2 per cent) had symptomatic bacteriuria. The complaints of the women in the latter group were not sufficient to make them seek a medical consultation.

According to their statements women with bacteriuria had more frequently suffered from symptomatic urinary tract infections than the women without bacteriuria.

Conversely women who in their past history had had episodes of cystitis and pyelonephritis were found to have bacteriuria more frequently than the other women investigated. This difference was statistically significant $(X(\frac{2}{3})=17.4, p=0.001)$. We studied 1,001 (85 per cent) women between 15 and 65 years of age out of 1,173 women 'at risk'. As it is possible that the 15 per cent of women who did not reply to our request to participate in this study could have altered our results if they had been included, we analysed the age distribution of the studied and non-studied women, *see* table I, in which are recorded three groups:

(1) 1,173 circularized women
(2) 1,001 studied women, and the percentage of the total amount of women in these two groups
(3) 172 non-studied women and the percentage of these women in each age group.

Especially between 15 and 29 years of age there was a poor attendance. Compared with the age distribution of the population of the Netherlands only the group from 15 to 19 years of age was significantly less represented $(X(\frac{2}{9})=35.4, p=0.005)$. This can possibly be explained by the greater number of working-women in this age group. As

TABLE I

AGE DISTRIBUTION OF THE STUDIED AND NON-STUDIED WOMEN AT RISK

	A		B		C	
Age	Age distribution of the women between 15 to 65 years of age at risk	Percentage	Age distribution studied women	Percentage	Number of non-studied women in each age group	Percentage of non-studied women in each age group
15–19	129	11.0	93	9.3	36	28.7
20–24	142	12.1	112	11.2	30	21.1
25–29	122	10.4	92	9.2	30	24.6
30–34	137	11.7	122	12.2	15	10.9
35–39	110	9.4	95	9.5	15	13.6
40–44	102	8.7	91	9.0	11	10.8
45–49	108	9.2	98	9.8	10	9.3
50–54	98	8.4	92	9.2	6	6.1
55–59	106	9.0	95	9.5	11	10.4
60–64	93	7.9	89	8.9	4	4.3
65	26	2.2	22	2.2	4	10.5
TOTAL ..	1173	100	1001	100	172	—

far as we could check up from our case histories the non-studied women had not suffered more frequently from urinary tract infections than the studied women.

Relation between marriage and bacteriuria

Both in married and unmarried women we found an equal percentage of asymptomatic bacteriuria (table II).

From the numbers in table II, III and IV recorded within brackets, the first column refers to percentages in vertical and the second column to percentages in horizontal direction.

TABLE II

RELATION BETWEEN MARRIAGE AND BACTERIURIA

	Bacteriuria				
	Present		Absent		
	Number	Percent	Number	Percent	Total
Married	52	(83 7)	730	(78 93)	782
Single	11	(17 6)	161	(17 94)	172
Widow	0	(0 0)	47	(5 100)	47
TOTAL	63		938		1001

Relation between age, blood pressure and bacteriuria

As the number of bacteriuric women, separated into age groups of five years, was too small for comparing the prevalence in every group, 10-year groups were made.

The 65-year-old women were excluded from this study. The age seemed not to be a discriminative factor in the occurrence of bacteriuria (table III).

TABLE III

RELATION BETWEEN AGE AND BACTERIURIA

Age	Bacteriuria				
	Present		Absent		
	Number	Percent	Number	Percent	Total
15–24	13	(21 6)	192	(21 94)	205
25–34	8	(13 4)	206	(22 96)	214
35–44	12	(20 6)	174	(19 94)	186
45–54	13	(21 7)	177	(19 93)	190
55–64	15	(25 8)	169	(18 92)	184
TOTAL	61		918		979

As a limit for normal blood pressure we considered a diastolic pressure of 100 mm Hg. Blood pressure was measured after the subjects had been seated for at least five minutes, with a standard mercury sphygmomanometer. We could not find any relation between elevation of blood pressure and bacteriuria (table IV). 13 per cent of the bacteriuric and 14 per cent of the non-bacteriuric women had a raised blood pressure.

TABLE IV

RELATION BETWEEN BLOOD PRESSURE AND BACTERIURIA

Diast blood pressure	Bacteriuria				
	Present		Absent		
	Number	Percent	Number	Percent	Total
Not measured	0	(0 0)	3	(0 100)	3
— 100 mm. Hg	55	(87 6)	803	(86 94)	858
— 100 mm. Hg	8	(13 6)	132	(14 94)	140
TOTAL	63		938		1001

In studying the relation between bacteriuria, blood pressure and age we furthermore matched our bacteriuric women with the non-bacteriurics. Matched for age and diastolic blood pressure, we found no significant difference in systolic blood pressure between the two groups (Student T (62)=0.676); matched for age and systolic blood pressure we also found no difference in diastolic blood pressure (T (62)=— 1.065) and matched for systolic and diastolic blood pressure there was no significant difference (T (62)=1.153) between the two groups.

Furthermore bacteriuria did not occur more frequently in lower socio-economic classes than in middle and upper classes.

In 57 of the 63 bacteriuric women (90 per cent) bacteriuria was caused by *Escherichia coli*. In one patient *Bacillus proteus* was found and in another Achromobacter. In four patients a mixed infection of *E. coli* and *B. proteus* was present.

Diagnostic methods

We compared the diagnostic methods used in our investigation with the results of the quantitative urine-culture of the 63 bacteriuric women. The percentage of false-negative results was used as an indication for the reliability of the various tests (table V). In the same way we collected data about a small group of 22 women between 15 and 65 years of age with an acute symptomatic urinary tract infection (dysuria, pollakisuria and more than 100,000 bacteriuria per ml of urine). These data are recorded in table IV within brackets.

TABLE V

COMPARISON OF FIVE DIAGNOSTIC METHODS WITH THE RESULTS OF THE
QUANTITATIVE URINE-CULTURE IN 63 BACTERIURIC WOMEN

	Percentage false-negative		*Percentage false-positive*	
Triphenyltetrazolium chloride test (TTC)	48	(53)	1	(0)
Unstained smear of centrifuged urine	92	(38)	0	(0)
Gram-stained smear of centrifuged urine	5	(0)	4	(5)
Methylene blue stained smear of centrifuged urine ..	5	(5)	3	(9)
Gram-stained smear of uncentrifuged urine	26	(40)	1	(0)

Table V shows that the results of the Gram-stained and the methylene blue stained smear of centrifuged urine are much more reliable than the other methods investigated.

Only the outcome of the percentage of false-negative results of the unstained smear of centrifuged urine appeared to differ significantly in the two groups of patients $(X(^2_1)=23.3, p=0.001)$.

The other data concerning the epidemiological group and the group of patients with symptomatic urinary infection do not show a significant statistical difference.

Treatment of bacteriuria

Fifty-five of 63 bacteriuric women were divided at random into three groups:

1. Five days treatment with sulphamethizole (19 women)
2. Ten days treatment with sulphamethizole (17 women)
3. Five days treatment with saccharum lactis (19 women)

This treatment consisted of 500 mg of sulphamethizole or saccharum lactis four times daily.

Eight women were excluded from this study for various reasons such as pregnancy, stones, hypersensitivity etc. Follow-up was carried out one week, six weeks and 12 weeks after finishing treatment.

Of the 55 women, we were able to investigate 47 women one week after finishing treatment, 51 after five weeks and all women after 12 weeks. Forty-three women were investigated at all three follow-up controls.

We studied the behaviour of bacteriuria with regard to treatment (tables VI and VII).

First we compared the 55 women all together.

According to the number of women with bacteriuria we could find no difference in results between the women who received a five-days' treatment and those who were

treated for a period of ten days. We found a distinct difference between the women who received sulphamethizole and those who received the placebo.

TABLE VI

NUMBER OF WOMEN WITH BACTERIURIA AT THE TIME OF FOLLOW-UP DIVIDED ACCORDING TO THE THREE DIFFERENT WAYS OF TREATMENT. THE NUMBER OF WOMEN WHO COULD NOT BE INVESTIGATED IS RECORDED BETWEEN BRACKETS

	Before treatment	After treatment		
		1 week	6 weeks	12 weeks
5 days treatment ..	19	0 (2)	3 (3)	4 (0)
10 days treatment ..	17	1 (4)	2 (0)	5 (0)
5 days placebo ..	19	12 (2)	12 (1)	11 (0)

The results were in favour of those having been treated ($X(^2_2)$=6.08, p=0.005).

We also studied the behaviour of bacteriuria in the 43 women who attended all follow-up controls.

There are eight possibilities: bacteriuria may persist in all follow-up studies, bacteriuria may be present in one or in two control studies or it may even be absent in every follow-up study.

In table VII we called patients with bacteriuria + and those without bacteriuria —·

TABLE VII

ARRANGEMENT OF 43 BACTERIURIC WOMEN IN ALL FOLLOW-UP CONTROLS DIVIDED INTO THE THREE WAYS OF TREATMENT

Follow-up studies			Number of patients	5 days treatment	10 days treatment	5 days placebo
1 week	6 weeks	12 weeks				
+	+	+	7	0	1	6
+	+	—	2	0	0	2
+	—	+	1	0	0	1
+	—	—	2	0	0	2
—	+	+	4	1	1	2
—	+	—	3	2	0	1
—	—	+	6	2	3	1
—	—	—	18	9	8	1
TOTAL			43	14	13	16

Table VII shows that in only 17 of 27 women, receiving sulphamethizole treatment, bacteriuria disappeared during a three-month follow-up period. Of seven women who had bacteriuria in all follow-up controls, six received a placebo treatment. In this table we could find no difference between a five days' treatment and a ten days' treatment, at least according to the number of bacteriuric women after treatment. Of 18 women who had no bacteriuria in the follow-up controls, nine received treatment for five days and eight were treated with sulphamethizole for ten days. After five days' treatment with sulphamethizole five of 14 women and, after ten days' treatment, five of 13 women had bacteriuria in one or more follow-up controls.

Discussion

Our finding of 6.3 per cent bacteriuric women between 15 and 65 years is in accordance with the study of Sussman *et al* (1969) who found 7.1 per cent bacteriuria in 3,578 women. If not only one, but two consecutive urine specimens with significant bacteriuria were requested, the above mentioned investigators found a prevalence of 3.5 per cent of bacteriuric women. Kass, Miall and Stuart (1961) found under these circumstances a prevalence of 4.4 per cent bacteriuria in 3,057 women.

In our study we could divide the 6.3 per cent bacteriuric women into 4.3 per cent subjects with asymptomatic and 2 per cent subjects with symptomatic bacteriuria. The latter group had not sought medical help for their complaints. The highly significant difference which we demonstrated in these 1,001 women leaves no doubt that in the population of this study an association existed between the finding of bacteriuria and episodes of symptomatic urinary tract infections in their past history. Sussman *et al* (1969) also found this association. A striking difference between our results and those of Loudon and Greenhalgh (1962) and Fry *et al* (1962) is that we could not establish a relation between age and marriage on one hand and bacteriuria on the other, as they did. They found that the highest infection-rate was noted in women of childbearing age, particularly between 20 and 29 years. After that peak in the third decade they then found a constant level. We found no peak in the 10-year age-groups from 15 to 65 years in the prevalence of bacteriuria.

We noted however a slow increase in the occurrence of bacteriuria, *viz.* from 4 per cent in the group from 25 to 34 years to 8 per cent in the group from 55 to 64 years. The difference between our figures and those found in the literature may be explained by the fact that we carried out an epidemiological study while Loudon and Greenhalgh and Fry *et al* studied selected groups of patients with symptomatic urinary tract infection. Our finding of 90 per cent *E. coli* as the causative organism of urinary infections in general practice approximates to other studies. Kunin *et al* (1960) found 80 per cent, Mond *et al* (1965) 81 per cent, Sussman *et al* (1969) 84 per cent, Brumfitt *et al* (1961) 85 per cent and Turner (1961) also found 90 per cent.

Diagnostic methods

Comparing the results of the unstained smears of centrifuged urine in an epidemiological group of 63 women with bacteriuria and a number of women with acute symptomatic urinary tract infection, with the results of the quantitative urine-culture yielded a statistical difference. The outcome of the unstained smear of centrifuged urine was negative in 92 per cent of the women with bacteriuria in the epidemiological group. This percentage could be 'improved' to 38 per cent if in our study only patients with acute symptomatic urinary infections were involved. However it can be concluded that the unstained sediment cannot be used as a diagnostic test for urinary tract infections. The Gram-stained and the methylene blue-stained smear of centrifuged urine appeared to be reliable tests as only 5 per cent false-negative results were found. We prefer the methylene blue stained smear as a diagnostic test for urinary tract infections in general practice, as Gram staining is more laborious and Gram dye deteriorates more quickly than methylene blue dye. Gram staining has the advantage of differentiating between Gram positive and Gram negative organisms. This knowledge however is of limited value as nearly all urinary-tract infections in general practice are caused by Gram negative rods or Gram positive cocci. The finding of Gram positive rods *e.g.* lactobacilli, may indicate a contamination of urine instead of an urinary-tract infection. This information cannot be obtained by using only a methylene blue staining; in those cases however one will also see squamous epithelium cells between the organisms.

The triphenyltetrazolium chloride test (TTC) was not reliable, as we found false-negative results in 48 per cent. This percentage was higher than most results published

in the literature. An explanation for this discrepancy cannot be given. Even as a screening method this test ought to be considered as unreliable.

Treatment of bacteriuria

In this study no difference between a five days' treatment with sulphamethizole and ten days' treatment was found, but we did note a significant difference between treatment with sulphamethizole and a placebo treatment. Though we found no difference between a five-day period and a ten-day period of treatment it is possible that in a study involving more patients and a longer period of follow-up than ours it might appear that, if there is a relapse or re-infection, this infection will occur later after a ten days' period of treatment than after a period of five days.

On the basis of our results we cannot provide evidence for preferring a five-day period of treatment to a ten days' period. Asscher and his associates (1969) studied 94 bacteriuric non-pregnant women of whom 49 received four times 50 mg of nitrofurantoin daily for one week. The other 45 women received a placebo. This single course of treatment with nitrofurantoin initially cured bacteriuria in 80 per cent, but one year after treatment there was no difference between the treated and the untreated subjects. Further investigation is desired to obtain information about the results of long-term therapy.

For the present we prefer a ten-day period of treatment with sulphamethizole in those cases of bacteriuria which have been caused by rod-shaped bacteria. If bacteriuria in general practice has been caused by cocci, which are mainly enterococci, we prefer nitrofurantoin as the drug of choice, as enterococci are insensitive to sulphonamides. If follow-up studies still reveal an infection, therapy should be given after determining the *in vitro* sensitivity of the organism. Follow-up of patients with a urinary-tract infection is necessary for two reasons:

1. The organism may be insensitive to the drug administered.

2. After initial cure relapse or re-infection may occur.

In connection with the first possibility follow-up control can already be done three days after starting treatment. If the number of leucocytes and bacteria is not considerably decreased, the drug administered has been insufficiently effective. We found in our study that bacteriuria re-occurred after apparent cure, even after 6 to 12 weeks.

Therefore we feel that besides a first follow-up study three days after starting the treatment, a second control 4 to 12 weeks after finishing the treatment is desirable.

Summary

Of 1,001 women between 15 and 65 years of age investigated for the presence of urinary-tract infection, 43 (4.3 per cent) had asymptomatic bacteriuria and 20 (2 per cent) were found to have symptomatic bacteriuria.

There was a correlation between the presence of bacteriuria and acute symptomatic urinary-tract infection in the past history. No relation could be found between age, marriage and blood pressure on one side and bacteriuria on the other. In 90 per cent of the cases of bacteriuria *E. coli* was cultured. The methylene blue stained smear and the Gram-stained smear of centrifuged urine yielded better results than other investigated methods in detecting urinary infection; for practical reasons in general practice methylene blue staining will be sufficient. In this investigation no arguments were found for preferring treatment during a period of five days to that of a period of ten days. Follow-up ought to be considered as a part of the treatment of urinary-tract infections and can be carried out three days after starting and 4 to 12 weeks after finishing the treatment.

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THE COLD BATH

It is of essential importance to know that there is no truth in the vulgar opinion, that it is safer to enter the water when the body is cool, and that persons heated by exercise, and beginning to perspire, should wait till they are perfectly cooled. It is a rule liable to no exception, that moderate exercise ought always to precede cold bathing; for neither previous rest, nor exercise to a violent degree, is proper on this occasion. The duration of cold bathing ought to be short, and must be determined by the constitution and sensations of the individual; for healthy persons may continue in it much longer than valetudinarians. He should, however, not forget that it is safer to continue completely immersed in water during a short time, than to take repeated plunges. The morning is the usual time for using the cold bath, unless it be in a river; in which case the afternoon will be more eligible. While the bather is in the water he should not remain inactive, but apply brisk and general friction. After the bath the body should be immediately dried with a coarse dry cloth.

The beneficial effects of cold bathing may be considered to be ablution or cleansing of the skin, the reduction of excessive heat, and salutary reaction of the system, upon which its tonic power depends.

The cold bath is well calculated to brace the constitution during the middle periods of life, when the powers of the body are firmly established, provided no predisposition to visceral or cutaneous diseases exists.

The cold bath is often resorted to as a tonic with children. Bathing in the open sea is its best form, but the child should not be plunged, as is too often the case, under water in such sudden and quick successions as almost to deprive it of breath. The use of cold bathing with children is to be directed on the same principles as for the adult.

JOHN SAVORY. *A companion to the medicine chest and compendium of domestic medicine.* 1840. London. John Churchill. p. 186.