Pyuria and Bacteriuria

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Urinary tract infection in childhood has long been recognized as a far from benign condition, yet the criteria for diagnosing such a condition are by no means uniform. While the final diagnosis rests on bacteriological evidence, the interpretation of significant bacteriuria in paediatric practice is particularly difficult. Various screening tests have been designed of which urine microscopy in search of pus cells remains the simplest. The accepted standard of significant pyuria varies from five or more pus cells per high power field in centrifuged urine (Kass, 1956), to ten or more pus cells per c.mm. in uncentrifuged urine (Dukes, 1928a, b; Stansfeld and Webb, 1953; Masters, 1953; Houston, 1963). Much controversy also arises about the correlation between pyuria and bacteriuria. While Stansfeld (1962) and Houston (1963) found close correlation between the two, Pryles and Eliot (1965) found only 61% of those with significant bacteriuria had 10 or more white cells/c.mm. of uncentrifuged urine. Doubts have been cast on the reliability of pyuria as a screening test for urinary tract infection (Kass, 1956; Randolph and Greenfield, 1964; Pryles and Eliot, 1965).

It was the purpose of this study to reinvestigate the limit of urine white cell counts found in infants and children, their correlation with colony counts, and their reliability as a screening test for urinary tract infection.

Material and Methods

Studies were carried out on 168 babies and children aged from 1 day to 13 years old in the medical wards of the Royal Hospital for Sick Children, Glasgow, and the paediatric department of the adjacent Queen Mother's Maternity Hospital. An attempt was made to exclude all cases of urinary tract infection and renal disease, and all cases that might give a high white cell count in the urine because of their primary illness (Pryles, 1960). Correlation of the urine white cell count and colony count was made in 180 specimens, and colony count alone was done in 213 specimens.

The perineum of these children was cleansed with 1% cetrimide and washed with 0.9% saline by student nurses or staff nurses with minimal disruption of ward routine. Mid-stream urine was collected in children over 3 years old and female newborn infants; sterile and non-sterile plastic urine bags (Down Brothers) were used in infants under 3 years of age, and sterile glass test-tubes were used in male newborns. After collection the urine was transferred into two sterile universal glass containers, one for cell count and the other for culture. If delay for culture was inevitable, the urine specimen was immediately refrigerated at 4° C. In any event, both culture and cell count were done within 4 hours of collection.

Urine white cell counts were done in centrifuged urine as described by McGeachie and Kennedy (1963). 10 ml. urine was centrifuged at 3000 r.p.m. for 3 minutes; the upper 9.5 ml. were removed with a Pasteur pipette, and the deposit was resuspended in the remaining 0.5 ml. urine. A drop of the suspension was used to fill a Neubauer counting chamber. The quantity of urine counted was equivalent to 1.2 c.mm. of uncentrifuged urine. In newborn infants whose collections were less than 10 ml., 5 ml. urine was used for centrifuging, and the quantity of uncentrifuged urine counted was equivalent to 0.6 c.mm. These latter results were multiplied by two to give the number of cells/1.2 c.mm.

Bacterial counts were performed by the stroke-plate method and Gram-stained films were made of a measured loopful of uncentrifuged urine, as described by the same authors (McGeachie and Kennedy, 1963).

Results

Urine white cell counts were done on 63 newborn infants, 65 infants under 3 years, and 52 older children (Table I). There was no obvious difference between male and female newborns, but in other age-groups there was a larger number of females with higher urine white cell counts. 78-94% of infants and children, depending on age, had urine white cell counts of 15 or less/1.2 c.mm.

Bacteriologically negative urine (sterile or less than 10,000 organisms per ml.) was found in 46% of female newborns, 53% of male newborns, 60-63% of infants under 3 years old, and 92% of older children (Table II). The results from urine

TABLE I
Urine White Cell Count

No. of Cells/1.2 c.mm.	Newborn Infants			Infants (under 3)			Older Children		
	Male	Female	%	Male	Female	%	Male	Female	%
10 or less	33	21	86	29	19	74	26	20	88
11-15	2	0	3	1	2	5	2	1	6
16-25	0	1	1.5	1	9	15	0	2	4
26-50	2	3	8	0	2	3	0	1	2
51-75	1	0	1.5	0	2	3	0	0	
Total	38	25	100	31	34	100	28	24	100

TABLE II
Bacterial Count

Colony Count	Male Newborns (sterile test-tubes)		Female Newborns (mid-stream urine)		Infants Under 3 (non-sterile plastic bags)			Infants Under 3 (sterile plastic bags)			Older Children (mid-stream urine)		
	No.	%	No.	%	No. of Male	No. of Female	%	No. of Male	No. of Female	%	No. of Male	No. of Female	%
Sterile	12	31	4	15	8	12	34	2	6	32	25	23	74
< 10,000	9	23	8	31	7	10	29	0	7	28	5	6	17
10-100,000	13	33	12	46	7	6	23	6	1	28	1	1	3
> 100,000	5	13	2	8	5	3	14	2	1	12	1	3	6
Total	39	100	26	100	27	31	100	10	15	100	32	33	100

collected in sterile plastic bags were not better than those collected in clean, but non-sterile plastic bags.

It was intended to perform repeat culture immediately on all those with significant colony counts ($> 100,000$ organisms/ml.), but three of these children with significant counts were discharged before their initial culture results were known. Since all three were admitted with diseases outside the renal tract and all had normal urine white cell counts, it was decided not to pursue further study on them. All older children and two-thirds of infants with significant growth in their urine initially had negative cultures on repeat examinations. In newborns, there seemed to be little change in results of the second culture from those of the first (Table III). The correlation of bacterial counts and quantitative white cell counts is shown in Table IV. It is noted that in those urine specimens with bacterial counts less than 100,000 organisms/ml., over 85% had urine white cell counts of 15 or less per 1.2 c.mm. In the bacteriologically negative urines (sterile or less than 10,000 organisms/ml.), 92% (109 out of 119 specimens) had 15 or less cells per 1.2 c.mm. In those specimens with significant growth (100,000 organisms/ml.), the lack of correlation between urine white cell counts and bacterial counts might give an erroneous impression, because most of these children with initial high bacterial counts had negative bacterial counts on repeat urine culture.

Findings on Gram-stained films closely correlated with colony count. Only one specimen with a colony count of less than 10,000 organisms/ml. had a positive Gram-stained film, while Gram-stained films of all specimens with colony counts of more than 100,000 organisms/ml. showed organisms (Table V).

Discussion

Pyuria. Based on the observations of 1000 urines in adult men and women, Dukes (1928a, b) concluded that under 10 cells/c.mm. of uncentrifuged urine was normal, and over 100 cells was pathological. Masters (1953) and Stansfeld and Webb (1953) found that urine obtained by catheter in either sex, or naturally voided in boys, contained less than 10 cells/c.mm. in over 92% of normal children. Stansfeld (1962) defined significant pyuria as 10 or more leucocytes/c.mm. in uncentrifuged samples of clean or catheter urine.

Using centrifuged urine in adults, McGeachie and Kennedy (1963) found that in bacteriologically negative urine, 76 contained 10 or fewer cells per measured area (equivalent to 1.2 c.mm. of uncentrifuged urine) and only 13% with positive cultures had less than 10 cells. In this series, 92% of the bacteriologically negative urines (sterile or less than 10,000 organisms/ml.) contained 15 or less cells/1.2 c.mm. and 87% contained less than 10 cells/

TABLE III

Repeat Urine Culture and Cell Count in Those with Significant Growth Initially

Specimens	Case No.	Sex	First Specimen		Second Specimen	
			Bacterial Count/ml.	Cell Count /1·2 c.mm.	Bacterial Count/ml.	Cell Count /1·2 c.mm.
Mid-stream urine (older children) ..	1	F	> 100,000	10	13,110	8
	2	M	> 100,000	14	Sterile	2
	3	F	> 100,000	2	10,000	—
	4	F	> 100,000	20	Sterile	—
Non-sterile plastic bags (infants)	5	F	> 100,000	0	Not done	
	6	F	> 100,000	0	10,000	9
	7	F	> 100,000	50	36,965	—
	8	M	96,600	0	> 100,000	8
	9	M	> 100,000	6	> 100,000	3
	10	M	> 100,000	0	Sterile	—
	11	M	> 100,000	—	< 10,000	0
	12	M	82,800	18	> 10,000	—
Sterile plastic bags (infants)	13	F	> 100,000	16	< 10,000	2
	14	M	> 100,000	0	72,450	—
	15	M	> 100,000	0	Not done	
Sterile test-tubes (male newborns) ..	16	M	> 100,000	30	> 100,000	60
	17	M	34,320	12	> 100,000	43
	18	M	> 100,000	1	Not done	
	19	M	> 100,000	0	96,096	10
Mid-stream urine (female newborns) ..	20	F	> 100,000	49	> 100,000	27

— not counted.

TABLE IV

Correlation Between Bacterial Count and Urine WBC Count

Cells/1·2 c.mm.	Colony Count							
	Sterile		< 10,000		10-100,000		> 100,000	
	No.	%	No.	%	No.	%	No.	%
10 or less	69	89	34	83	33	82·5	12	57
11-15	4	5	2	5	1	2·5	1	5
16-25	5	6	2	5	4	10	2	9
26-50	0	0	2	5	1	2·5	5	24
51-75	0	0	1	2	1	2·5	1	5
Total	78	100	41	100	40	100	21	100

TABLE V

Correlation Between Gram Film of Uncentrifuged Urine and Colony Count

Gram Film	Colony Count							
	Sterile		< 10,000		10-100,000		> 100,000	
	No.	%	No.	%	No.	%	No.	%
Positive	0	0	1	2	12	26	22	100
Negative	92	100	51	98	35	74	0	0
Total	92	100	52	100	47	100	22	100

1·2 c.mm. If we take 15 cells/1·2 c.mm. (or 12 cells/c.mm.) as the upper limit of normal, then this would include 89% of newborn infants, 78% of infants under 3 years, and 94% of older children.

Stansfeld (1962) found that the inaccuracies of high-power field count could largely be eliminated by resuspending the deposit of centrifuged urine

(4000 r.p.m. for 10 minutes) in fixed quantity (1 ml.) of original urine and then using a counting chamber. Little (1964) found good correlation between using centrifuged urine and uncentrifuged urine in doing urine white cell excretion rate. Gadeholt (1964), however, pointed out that centrifugation recovered only 50% of leucocytes at 2500 r.p.m. for 5 minutes,

but he did not mention the errors that may have been due to incomplete mixing of the uncentrifuged specimen of urine. In the present study, a comparison on cell count between centrifuged and uncentrifuged urine was made on 50 specimens of urine with various cellular concentration, and close correlation was found between the two methods (Fig.). It is clear that examining uncentrifuged urine is easier and less time-consuming, and is therefore suitable for the out-patient clinic and the general practitioner's surgery. However, it is reassuring that no significant difference was found between the results using either methods, both of which are subject to experimental errors.

FIG.—Correlation of urine white cell counts between uncentrifuged urines and centrifuged urines. The diagonal line is the line of perfect correlation.

James (1959) suggested that 50 and 25 cells/c.mm. should be the 'normal' for female and male newborns, respectively, and Lincoln and Winberg (1964b) supported her suggestion. In the present study the normal urine white cell counts in newborn infants did not differ significantly from those in older children, and therefore no special value of 'normal' seems necessary.

Dukes (1928a, b) concluded that less than 10 leucocytes/c.mm. is normal, between 10 and 100 as 'excess of leucocytes', and above 100 as pathological. He further pointed out that more than 500 cells/c.mm. were usually present in acute urinary infection, and in most chronic infections urine white cell counts were between 100 and 500 cells/c.mm. Stansfeld and Webb (1953) found pyuria in chronic

pyelonephritis slight and intermittent. Houston (1963) regarded pus cell counts of 10-100/c.mm. as of doubtful significance, but suggested 50/c.mm. as the dividing line between contamination and probable infection. In our experience the urine white cell count is almost always more than 300/1.2 c.mm. in untreated cases of acute pyelonephritis, but counts in excess of 15 cells/1.2 c.mm. merit repeat examinations in order to elucidate their significance.

Bacteriuria. McCarthy and Pryles (1963) obtained bacteriologically negative urine (0-1000 organisms/ml.) in 78% healthy newborn infants, but Lincoln and Winberg (1964a) had to use special irrigation techniques in order to reduce the 30% male newborns with significant bacteriuria to under 7% in a large series. Boehm and Haynes (1966) found only 30% of newborn infants had less than 1000 organisms/ml. when urine was collected in plastic bags, but their results improved to 70% when the urine collection was changed to 'mid-stream catch' technique. About half of the newborn infants in our series had bacteriuria of more than 10,000 organisms/ml. Repeat urine culture, using the same method in cleansing and collection, did not improve the result. Irrigation of the preputial folds and vulva as suggested by Lincoln and Winberg (1964a) did not seem to influence our results, though the number actually receiving this kind of preparation was small.

Infants under 3 years of age, who are not co-operative enough to produce a mid-stream specimen, also present a problem in urine collection. In these infants, urine may be collected in attached plastic bags. Using this method, various workers have shown that bacteriologically false-positive results are common. Virtanen, Oksanen, and Peltonen (1962) found that 19% of the bag urine was bacteriologically false positive, Houston (1963) found that 12% (4 out of 34 of 'non-infected' children) had colony count of more than 100,000 organisms/ml., and Braude, Forfar, and Gould (1964) found that 48% had significant growth (100,000 organisms/ml.). Randolph and Greenfield (1964), however, had a contamination rate of only 0.5-1%. Our results lie between the two extremes, with 60-64% bag urine sterile or growing less than 10,000 organisms/ml., and 12-14% growing more than 100,000 organisms/ml. Repeat urine culture, using the same method of cleansing and collection, gave negative results in two-thirds of those previously growing more than 100,000 organisms/ml., while the remaining one-third still gave the same results as before.

Mid-stream urine culture is considered reliable in

older children. Pryles and Steg (1959) found a 96% correlation between 'clean voided' and catheter specimens, Virtanen *et al.* (1962) found only 6% false positive in clean-voided specimens, and Houston (1963) found that 86% (75 out of 87) of 'non-infected' children gave negative results (less than 10,000 organisms/ml.) in mid-stream urine culture. Our results show that 91% of mid-stream specimens in older children gave negative results, and 3% gave a doubtful and 6% a significant growth. In repeat cultures, using the same method of cleansing and collection, definite negative results were obtained in all those with significant growth.

Correlation between bacteriuria and pyuria.

Stansfeld (1962) found that only 3 out of 57 specimens of urine with more than 100,000 organisms/ml. had less than 10 cells per c.mm. of uncentrifuged urine, but he cultured only urine from those children having pyuria in their ordinary specimens, so that his results cannot represent the true incidence of bacteriuria without pyuria. Pryles and Eliot (1965) found that 90% of those with sterile urine, and 39% of those with more than 100,000 organisms/ml. had less than 10 cells/c.mm. While the former figure is the same as ours (89% had less than 10 cells/1.2 c.mm), it is difficult to compare the latter because we were unable to take the meticulous care these authors employed in preparing the perineum which had reduced contamination to a minimum. Hence a growth of more than 100,000 organisms/ml. would represent true bacteriuria in their series, whereas it cannot be so accepted without further clarification in ours. It is interesting to note that Pryles and Eliot's series was carried out in their renal clinic, and may, therefore, have included a higher proportion of bacteriuria without pyuria. Clarke (1960) and Turck, Browder, Lindemeyer, Brown, Anderson, and Petersdorf (1962) suggested that bacteriuria without pyuria is not uncommon in chronic and recurrent urinary infection, and our experience has substantiated this. However, in the present series no attempt was made to correlate pyuria and bacteriuria in children with known renal tract pathology. Our results have shown that in non-renal cases bacteriuria without pyuria usually represents contamination, because repeat culture yielded negative results in over half of these cases. It would be ideal to be able to achieve 96% correlation between 'clear voided' and catheterized urine (Pryles and Steg, 1959). However, in routine paediatric ward practice, the urine white cell count is very helpful in identifying those 'positive' cultures due to contamination.

It has been well known that in many conditions

other than urinary infection urine white cell excretion is increased (Chown, 1927; Pryles, 1960). The diagnosis of urinary infection, therefore, cannot be based solely on the presence of pyuria without bacteriological evidence. On the other hand, the determination of pyuria by an accurate quantitative method remains an easy and simple screening test when clinical suspicion of urinary tract infection arises.

Gram-stained film of unspun urine. It has been recognized that Gram-stained films of a loopful of uncentrifuged urine give close correlation to colony counts. Kass (1956) found organisms in Gram films in 80% of those with more than 100,000 organisms/ml. and only 20% of those with 100 to 10,000 organisms/ml. Pryles and Steg (1959) found that 95% of those with colony counts over 100,000 had organisms in Gram films, and only 3.7% in those with colony counts between 1000 to 100,000. In the present series, we found that all specimens with colony counts over 100,000 organisms/ml. had organisms in the Gram films, whereas only 2% of those with a colony count under 10,000 showed organisms in the Gram film. It appears, therefore, that Gram-stained film is a reasonably reliable method of forecasting the result of a colony count.

Summary and Conclusions

Urine white cell counts and bacterial counts were carried out on 168 infants and children without known urinary infection or renal disease.

The urine white cell count was found to be a useful screening test for urinary infection in children. 92% of the bacteriologically negative urines (sterile or less than 10,000 organisms/ml.) from all age-groups contained 15 or less cells per 1.2 c.mm. (equivalent to 12 or less cells per c.mm.). Quantitative white cell count on centrifuged urine is a simple and satisfactory technique which can be easily performed in the side-room.

Bacterial counts were found to be reliable in older children, from whom a mid-stream specimen of urine could be obtained without much difficulty.

In younger infants, if plastic bags were used for urine collection, only 60% gave bacteriologically negative results. Repeat urine cultures confirmed negative results in two-thirds of those with initial significant colony counts (100,000 organisms/ml.) but normal urine white cell counts.

Urine culture remains difficult in the newborn infant. Only half of the specimens were bacteriologically negative. Repeat culture tends to give a similar result if the method of cleansing is not

altered. Improved methods of cleansing the perineum and of urine collection in these young infants are required if catheterization is to be avoided.

The diagnosis of urinary infection may have a sounder basis if the quantitative urine white cell count is considered together with the bacterial count. A white cell count below 15 cells/1.2 c.mm. (or 12 cells/c.mm.) on a fresh urine specimen is strong evidence against an acute infection of the urinary tract.

Gram-stained films are confirmed to be a quick and reliable method of forecasting bacterial counts.

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