PAPERS AND ORIGINALS

Neonatal Bacteriuria: A Prospective Study in 1,460 Infants

G. D. ABBOTT

British Medical Journal, 1972, 1, 267-269

Summary

In a prospective study of 1,460 virtually consecutive neonates 14 (1%) were found to have bacteriuria, established by bladder puncture. Eleven were boys and three girls. Five of the infants with bacteriuria had symptoms suggestive of infection and were treated with antibiotics. The remaining nine were asymptomatic and remained so during a period of observation—five cleared their urine of bacteria without treatment, and four received antibiotics. Only one infant with bacteriuria had bacteraemia. Six infants had more than 10 white blood cells per mm³ in the bladder puncture urine and three had proteinuria. The blood urea was slightly raised in only two of the infants. The intravenous pyelogram was normal in all infants with bacteriuria but eight had slight or moderate vesicoureteric reflux when examined by micturating cystourethrography.

Introduction

The incidence of neonatal urinary infection varies in the experience of different authors. O'Brien *et al.* (1968) found an incidence of 0.1% in 1,000 newborns, Littlewood *et al.* (1969) an incidence of 1.4% in 600 consecutive births, and O'Doherty (1968) an incidence of 1.08% in 830 infants. These authors found that the majority of infants with urinary infection had only a mild illness. Most earlier retrospective studies, however, indicated that many infants with urinary infection were severely ill and often jaundiced. The jaundice was frequently associated with positive blood cultures (Bernstein and Brown, 1962; Hamilton and Sass-Kortsak, 1963).

Since 1966 the extensive use of bladder puncture in the diagnosis of urinary infection in infants presenting to the department of paediatrics in Christchurch Hospital, New Zealand, led to an increased interest in and awareness of this problem. It was therefore decided to carry out a prospective study in order to establish the incidence of neonatal urinary

infection in a representative population in New Zealand. In addition, full investigation and follow-up of those infants with infection was planned.

Patients and Methods

A total of 1,460 infants born virtually consecutively at Christchurch Women's Hospital were studied between March 1968 and December 1969 (757 were males and 703 females). All were born to women who had attended the antenatal clinic. They represent about 65% of the live births in this hospital. Infants on antibiotics were excluded and a random loss took place during the survey, so that 80% of clinic infants were studied.

Each infant received a physical examination and any congenital abnormalities were recorded. A true "clean catch" specimen of urine was obtained by a similar method to that described by Cruickshank and Edmond (1967). The urine was collected in most instances between the third and sixth days of life, by a nurse employed solely for this purpose. The urine obtained was placed immediately at 4°C and cultured within four hours of collection on MacConkey medium for 24 hours at 37°C. If bacterial growth occurred a quantitative bacterial count was carried out by means of a pour plate technique (Mackie and McCartney, 1960). A bladder puncture was then performed if certain levels of bacteriuria on the voided urine culture were exceeded. The criteria for bladder puncture are given in Table I.

TABLE I—Criteria for Bladder Puncture

No. of Infants	Bladder Puncture Performed if:
270	>10 ⁴ organisms/ml (pure growth)
900	>50,000 organisms/ml (mixed growth)
212	>10 ⁴ organisms/ml
78	Any growth on culture
	No prior voided urine

The technique of bladder puncture was that of Abbott and Shannon (1970). The urine obtained in this way was cultured on blood agar and MacConkey medium. Bacteriuria was diagnosed if any bacterial growth was obtained from the bladder puncture urine. Micro-organisms were identified with a standard reference (Cowan and Steel, 1965). The infected bladder puncture urine was also examined for cells and protein. Cell counts were made in a Fuchs-Rosenthal counting chamber, and the presence of protein was determined by Albustix.

Christchurch Hospital, Christchurch, New Zealand

G. D. ABBOTT, M.B., CH.B., M.R.A.C.P., Senior Paediatric Registrar

If bacteriuria was diagnosed blood was taken from the external jugular vein and inoculated into standard blood culture media. Blood was also taken for urea estimation by autoanalyser.

If the infant had symptoms suggestive of infection antibiotic therapy was begun. If the infant was asymptomatic antibiotics were withheld and the infant was closely observed. Regular recordings of temperature, feeding, and weight were made and the infant was examined frequently. In this group the blood cultures and bladder punctures were repeated after a period of time (5-10 days), and if bacteriuria persisted until the end of the period of observation antibiotics were given.

All infants with bacteriuria had an intravenous pyelogram and a micturating cystourethrogram about one month after the initial episode of bacteriuria. Before micturating cystourethrography was performed it was ensured that the infant's urine was sterile.

Results

The results reported concern only those infants with bacteriuria. The results of urine cultures obtained from infants without bacteriuria on bladder puncture will be reported elsewhere.

Incidence of Bacteriuria.—Fourteen infants (11 males and 3 females) had bacteriuria, an incidence of 0.95%.

Clinical Presentation.—Five of the 14 infants had symptoms suggestive of infection. The different signs and symptoms observed were: failure to thrive and poor feeding in five, vomiting in three, fever in two, diarrhoea in one, convulsion in one, and jaundice in one. The remaining nine infants were asymptomatic.

Organisms Identified from Bladder Puncture Urine.—The organisms isolated and the correlation with colony counts on voided urine culture are given in Table II.

TABLE II—Organisms in Bladder Puncture Urine

Organism	No.	Colony Count on Voided Urine
<i>E. coli</i>	10	{ > 10 ⁴ orgs/ml (pure growth) in 6 50,000 orgs/ml (mixed growth) in 1 No quantitative culture in 3
<i>Klebsiella</i> species	1	No voided urine
<i>Staph. aureus</i>	1	35,000 orgs/ml (mixed growth)
<i>Staph. epidermidis</i>	1	35,000 orgs/ml (mixed growth)
<i>Enterobacter</i> sp. and <i>Str. viridans</i>	1	50,000 orgs/ml (mixed growth)

Clinical Course of Infants with Bacteriuria.—The five symptomatic infants were treated with appropriate antibiotics. The other nine were closely observed and none developed symptoms suggestive of infection. Four of them had persistent bacteriuria with the same organism when the bladder puncture was repeated after 5 to 10 days, and antibiotics were given. The remaining five cleared their urine spontaneously of bacteria without treatment; four of them had sterile urine at the time of the first repeat bladder puncture, but one infant had persistent bacteriuria for 10 days before the urine was found to be sterile. The organisms identified from the urine of those infants with persistent asymptomatic bacteriuria were all *Escherichia coli*. In the infants with transient asymptomatic bacteriuria the organisms identified were *E. coli*, *Staphylococcus aureus*, *Staph. epidermidis*, and the mixed infection with an *Enterobacter* species and *Streptococcus viridans*.

Blood Cultures.—Blood was taken for culture from all infants when bacteriuria was diagnosed. In those cases in which the bacteriuria persisted without treatment further blood cultures were taken. A *Klebsiella* species was isolated from the blood of one symptomatic infant and the same organism was present in the urine. Jaundice was not present in this infant.

Blood Urea.—In all infants with bacteriuria the blood urea was estimated. In two instances it was slightly raised (55 and 65 mg/100 ml) but in the others it was within normal limits (20-40 mg/100 ml in this laboratory). Both infants with raised blood urea were asymptomatic.

Pyuria and Proteinuria in Infected Bladder Puncture Urine.—Six infants with bacteriuria had more than 10 white blood cells per mm³. Three had proteinuria by Albustix.

Radiological Studies.—The intravenous pyelogram was normal in all infants with bacteriuria. The micturating cystourethrogram was normal in six and abnormal in eight (slight reflux in two and moderate reflux in six, as graded by Rolleston *et al.* (1970)). One of the latter had a large-capacity bladder.

TABLE III—Relationship between Abnormal Radiological Findings and Other Studies

	Micturating Cystourethrogram	
	Slight Reflux	Moderate Reflux
Symptomatic bacteriuria	1	..
Asymptomatic bacteriuria { Persistent	..	4
Transient	1	2
Blood urea > 40 mg/100 ml	..	1
Proteinuria	1	1

Discussion

The incidence of bacteriuria in this study is about 1%. This is similar to the 1.4% obtained by Littlewood *et al.* (1969) and the 1.08% of O'Doherty (1968). The male preponderance is again noted, there being 11 males and three females with bacteriuria. Infants with bacteriuria may either be asymptomatic or present with a mild illness. Though the more severe form of urinary tract infection with jaundice and septicaemia is more often reported, this is probably a reflection of case selection.

Transient bacteriuria in this age group has already been reported (Abbott, 1970). Of the 14 infants with bacteriuria, five cleared their urine spontaneously of bacteria.

The organisms responsible for bacteriuria were predominantly *E. coli* (71%). The presence of *Staph. aureus* and *Staph. epidermidis* in the urine aspirated from the bladder is suggestive of contamination by skin flora. However, Mabeck (1969) and Bailey (1970) thought that these organisms could be true urinary pathogens. Moreover, Bailey (1970) found that women with *Staph. epidermidis* urinary infection were more likely to have an underlying anatomical abnormality. Mabeck (1969) also observed that urinary infections with *Staph. epidermidis* were more likely to undergo spontaneous cure. The presence of a mixed infection (*Enterobacter* species and *Str. viridans*) is unusual. While *Str. viridans* may have been a contaminant, its presence in the virgin urethra has been reported (Shackman and Messent, 1954).

Only one infant with bacteriuria had a positive blood culture. The organism identified from both blood and urine was a *Klebsiella* species. In those asymptomatic infants where bacteriuria persisted for up to 10 days blood cultures were repeatedly sterile. It seems unlikely therefore that bacteriuria is of haematogenous origin. Littlewood *et al.* (1969) did not find positive blood cultures in their infants with bacteriuria.

The blood urea was raised in two of the 14 infants with bacteriuria. Both were asymptomatic. Littlewood *et al.* (1969), however, found that all infants with bacteriuria had blood urea levels above 40 mg/100 ml.

Pyuria and proteinuria were not a constant finding in the infected bladder puncture urine in this study. Pyuria (more than 10 white blood cells per mm³) occurred in six infants with bacteriuria and proteinuria in three. O'Doherty (1968) found that all infants with bacteriuria on bladder puncture had more than 50 white blood cells per mm³ in a preceding bag urine specimen. He mentioned that leucocytes were present in the bladder puncture urine also, but did not state the number. Littlewood *et al.* (1969) found pyuria in the voided urine specimens in most instances where there was thought to be significant bacteriuria. In two out of eight instances the presence of bladder bacteriuria was confirmed by bladder punctures. Whether white cells occurred in the bladder puncture urine was not stated.

Vesicoureteric reflux occurred in eight infants with bacteriuria. This was regarded as being slight in two instances and moderate in six. There seemed to be no relation between the presence of vesicoureteric reflux, raised blood urea levels, proteinuria, and symptomatic infection. All cases of moderate vesicoureteric reflux were associated with asymptomatic bacteriuria in the neonatal period. Three to four weeks were allowed to elapse after the episode of bacteriuria before the radiological studies were performed.

The screening of 1,460 consecutive infants for bacteriuria did not reveal any examples of obstructive uropathy on further investigation. Moreover, while vesicoureteric reflux was often found, it was not of the gross variety (see Table III). Recently, it has been shown that probably only this gross variety of vesicoureteric reflux is associated with progressive renal damage in a high proportion of cases (Rolleston *et al.*, 1970).

I would like to thank the following: the Royal Australasian College of Physicians and Glaxo Laboratories (England) for financial support; Sisters J. Worrall, L. Bugden, and G. Dann

for technical help; and Dr. F. T. Shannon for advice and encouragement.

References

- Abbott, G. D. (1970). *British Medical Journal*, 1, 207.
 Abbott, G. D., and Shannon, F. T. (1970). *Clinical Pediatrics*, 9, 277.
 Bailey, R. R. (1970). *New Zealand Medical Journal*, 71, 216.
 Bernstein, J., and Brown, A. K. (1962). *Pediatrics*, 29, 873.
 Cowan, S. T., and Steel, K. J. (1965). *Manual for the Identification of Medical Bacteria*. London, Cambridge University Press.
 Cruickshank, G., and Edmond, E. (1967). *British Medical Journal*, 4, 705.
 Hamilton, J. R., and Sass Kortsak, A. (1963). *Journal of Pediatrics*, 63, 121.
 Littlewood, J. M., Kite, P., and Kite, B. (1969). *Archives of Disease in Childhood*, 44, 617.
 Mabeck, C. E. (1969). *Lancet*, 2, 1150.
 Mackie, T. J., and McCartney, J. E. (1960). *Handbook of Bacteriology*, ed. R. Cruickshank, 10th edn., p. 303. Edinburgh, Livingston.
 O'Brien, N. G., Carroll, R., Donovan, D. E., and Dundon, S. P. (1968). *Journal of the Irish Medical Association*, 61, 267.
 O'Doherty, N. J. (1968). In *Urinary Tract Infection: Proceedings of the First National Symposium*, ed. F. O'Grady and W. Brumfitt. London, Oxford University Press.
 Rolleston, G. L., Shannon, F. T., and Utley, W. L. F. (1970). *British Medical Journal*, 1, 460.
 Shackman, R., and Messent, D. (1954). *British Medical Journal*, 2, 1009.

Immunoglobulin Levels in Newborn Infants with Hepatosplenomegaly

K. L. TAN, Y. C. CHAN

British Medical Journal. 1972, 1, 269-270

Summary

Serum IgM and IgA levels were measured in 97 newborn infants with and 141 without hepatosplenomegaly. All were considered normal at birth and had no apparent disease on clinical examination. Thirty per cent. of the infants with hepatosplenomegaly were found to have IgM levels of 20 mg/100 ml or greater, a level established as abnormal when compared with the control group. The number of infants with raised IgM level and the geometric mean level were significantly different ($P < 0.001$) from those in the control group. No difference, however, was found in serum IgA levels between the two groups of infants. The results suggest that intrauterine infections may sometimes be the cause of hepatosplenomegaly in newborn infants without apparent disease.

Introduction

The liver is palpable in almost all, and the spleen in some, normal newborn infants (McNicholl, 1957; Nelson, 1969). In some infants the liver is enlarged beyond normal limits and the spleen is obviously palpable. Except for the hepatosplenomegaly these infants show no other abnormalities and were considered to be normal at birth.

Hepatosplenomegaly in the normal newborn infant probably has a varied aetiology, including infection in utero. It is a common, and may be the only, clinical manifestation in intrauterine infections (Stern and Tucker, 1965; Overall and Glasgow, 1970). Intrauterine infections have been shown to be associated with raised IgM levels in infants, and the quantitation of this immuno-

globulin in cord sera has been shown to be a useful screening test for detecting mild or "silent" infections (Alford, 1971). This communication describes the results of immunoglobulin determinations in a group of newborn infants with hepatosplenomegaly and shows that this abnormality at birth, in some infants at least, may be associated with a clinically inapparent intrauterine infection.

Patients and Methods

Ninety-seven newborn infants delivered in the Kandang Kerbau Hospital in Singapore between December 1968 and March 1970 were studied. These infants were considered to be normal at birth except that they presented with an enlarged liver (≥ 3 cm below the right costal margin) and spleen (≥ 1 cm). They included both sexes in the three major ethnic groups (Chinese, Indian, and Malay) and their ages ranged from 6 hours to 3 days. One hundred and forty-one normal newborn infants who had no hepatosplenomegaly were also studied. These control infants were delivered in the same hospital from February to July 1970 and they were matched for ethnic group, sex, and age.

A complete blood count was made and radiological examination of the long bones was carried out on the infants with hepatosplenomegaly. Umbilical cord blood or blood obtained by venepuncture within three days after birth was examined for immunoglobulins IgM and IgA by a modification of Mancini's single radial immunodiffusion (Mancini *et al.*, 1965). Standard human serum and specific antisera were supplied by Hoechst Pharmaceuticals Ltd. The details of the method will be published elsewhere. The coefficients of variation for the standard serum determined from 40 estimations over a nine-month period were 6.3% for IgM and 6.2% for IgA. In this study cord sera in which IgA levels were higher than IgM levels were thought to be contaminated with maternal blood due to placental leak and were excluded from analyses. Immunoglobulin concentrations were converted to logarithms for statistical analyses.

Faculty of Medicine, University of Singapore, Singapore 3

K. L. TAN, M.R.C.P.ED., D.C.H., Senior Lecturer, Department of Paediatrics
 Y. C. CHAN, B.SC., PH.D., Senior Lecturer, Department of Bacteriology