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Serum IgM in Diagnosis of Infection in the Newborn

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Haider, S. A. (1972). *Archives of Disease in Childhood*, **47**, 382. **Serum IgM in diagnosis of infection in the newborn.** Serum IgM levels were determined at weekly intervals from birth in 100 normal low birthweight and 100 normal birthweight infants during the first 4 weeks of life. The dynamics of serum IgM was also studied in 36 newborn infants with different types of infection and in 19 infants with probable infection. The behaviour of serum IgM in the infants with systemic infection and also in those suffering from superficial infection with systemic symptoms was significantly different from the normal. Serum IgM rose within two days of appearance of symptoms and the rise persisted as long as the infection was 'active'. With the eradication of infection the IgM level tended to fall. This characteristic dynamic pattern of serum IgM may be of considerable help in the diagnosis of neonatal infection, especially the clinically inapparent and atypical varieties that may have serious sequelae later in life.

The diagnosis of infection in the early days of life is inherently difficult. During pregnancy asymptomatic infections in the mother may affect the fetus, which may be clinically inapparent in the neonate and the consequences of such an infection may not be detected even for years. Infections acquired by the neonates postnatally may pass undetected and could later be responsible for considerable morbidity and mortality.

Recent studies have shown the usefulness of raised IgM levels in the umbilical cord serum in the diagnosis of intrauterine infection of the newborn infants (Stiehm, Ammann, and Cherry, 1966; Jones and Tobin, 1969). It has also been suggested that IgM readings on the cord and neonatal sera may permit screening neonates for congenital infections (Alford, 1969). Alford and others (Alford *et al.*, 1967) have demonstrated the role of serum immunoglobulin determinations in the diagnosis of neonatal infections.

The Study

A study of the behaviour of serum IgM was undertaken in newborn babies. This paper presents a part of the same study and examines the value of serum IgM in the diagnosis of infection in neonates.

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Material and Method

Studies were made on infants admitted to one unit of the Bolton District General Hospital. Into this unit were admitted all low birthweight babies born on the maternity block or outside, all the neonates requiring special care and treatment, and as there were 22 lying-in beds, a number of normal birthweight babies were also admitted because their mothers required hospitalization. A few cases were from the Paediatric Infectious Diseases Unit of the Hulton Hospital, Bolton, and the Special Care Nursery of the Moorgate General Hospital, Rotherham. The period of study was from February 1969 to August 1971.

The babies were examined on admission. An attempt was made to classify the neonates as full term, early-for-dates, or small-for-dates; but among the low birthweight babies the number of those strictly premature or dysmature was small, and in the majority there were signs of both prematurity and dysmaturity. The neonates were, therefore, classified according to birthweight irrespective of the period of gestation; those weighing 2·5 kg or less as 'low birthweight' (LBW) and those weighing over 2·5 kg as 'normal birthweight' (NBW) infants. Babies with no clinical abnormality (excluding the birthweight) and no laboratory evidence of bacterial infection of urine or faeces were considered normal.

Urine (in plastic bags) and faeces were collected from every baby routinely at weekly intervals during their stay on the units concerned and examined for bacterial infection. A specimen of blood was also collected weekly for Hb, haematocrit, leucocyte count, and IgM

estimation. However, the routine weekly examination of blood was discontinued when readings from 100 NBW (50 female and 50 male) and 100 LBW (50 female and 50 male) normal babies were obtained. Thereafter the weekly blood tests were made only on those babies who had an abnormality, clinical or otherwise. Serum IgM estimation and leucocyte count were also performed within 24 hours of appearance of symptoms.

Conventional techniques were used for the common laboratory tests. Serum IgM estimations were made by radial diffusion technique (Mancini, Carbonara, and Heremans, 1965) using the antisera supplied by Hyland Laboratories, Los Angeles, California.

Results

No cases were selected which might have produced biased effects on the results. Behaviour of serum IgM during the neonatal period was studied in 340 babies (100 normal NBW, 100 normal LBW, 36 with established infection, 19 with probable infection, 6 with haemolytic disease of the newborn, 21 with neonatal jaundice syndrome, 17 with neonatal hypoglycaemia, 5 with neonatal hypocalcaemia, 13 with asphyxia neonatorum, 11 with idiopathic respiratory distress syndrome, 3 with intracranial haemorrhage, 5 with haemorrhagic disease of the newborn, 2 with Down's syndrome, 1 with trisomy 18 syndrome, and 1 with trisomy 13 syndrome). The purpose of this paper is to assess the value of serum IgM in the diagnosis of infection in newborn infants. What follows therefore is a report on the results of investigations of the 36 neonates who had no other clinical abnormality except infection of some sort. The normal infants have been included as control. The results of the study on other cases may be reported in another communication, but a brief remark relevant to the subject here will be made during discussion.

Normal NBW infants (Fig. 1 and 2). Of the first 100 normal NBW babies (50 female and 50 male) studied the IgM levels in 89 (46 female and 43 male) infants varied from 5 to 31 mg/100 ml serum during the neonatal period. The dynamics of IgM showed a characteristic pattern—the levels rose serially with time since birth without showing a significant drop (shown by hatched area in Fig. 1 and 2). No significant difference was observed in the two sexes. In 11% (4 female and 7 male shown in dots and lines in Fig. 1 and 2) the IgM levels appeared to differ significantly from the 'normal' (89%). However, on closer observation it was noted that in 7 of the 11 babies the IgM levels were higher yet the dynamic pattern of IgM was not different from the 'normal'. 76 (68 of the 89 and 8 of the 11) infants were followed for an average period of 8 months and were found to be thriving without any clinical abnormality.

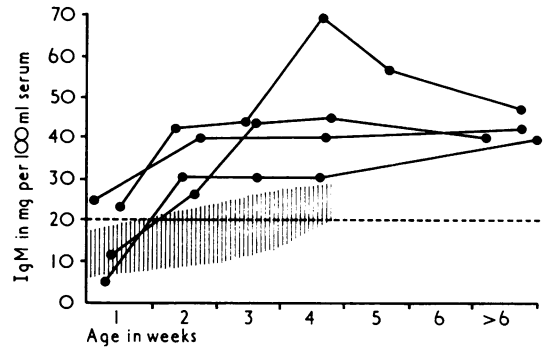

FIG. 1.—*Serum IgM in 50 NBW normal female neonates. In 46 of the babies the IgM fell in the hatched area. 4 of the babies, shown in dots and lines, differed from the general pattern (see text).*

Normal LBW infants (Fig. 3 and 4). In 92% (45 female and 47 male) of the normal LBW infants the IgM levels varied from 0 to 26 mg/100 ml serum during the neonatal period. The dynamic pattern of IgM was similar to that of the 'normal' (shown in hatched area). There were no significant differences in the two sexes. In 8% (5 female and 3 male shown in dots and lines) of the neonates the IgM levels were significantly higher than 'normal', and in 5 of these the dynamic pattern was also characteristically different from the

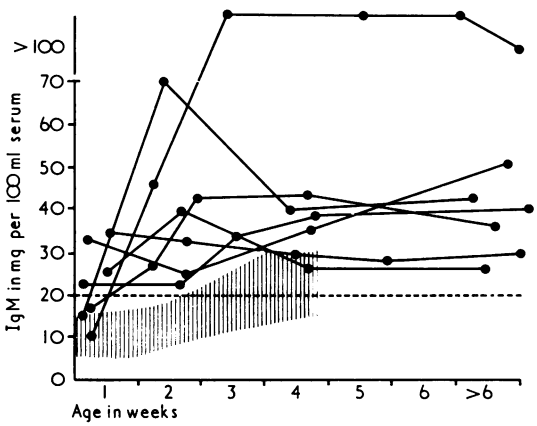

FIG. 2.—*Serum IgM in 50 NBW normal male neonates. In 43 of the babies the IgM fell in the hatched area. 7 of the babies, shown in dots and lines, differed from the general pattern (see text).*

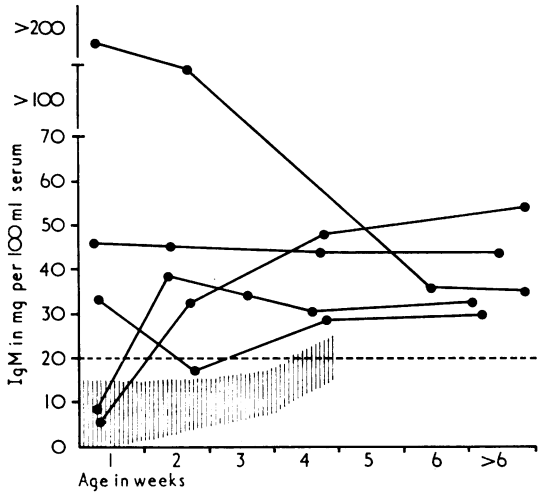

FIG. 3.—*Serum IgM in 50 LBW normal female neonates. In 45 of the babies the IgM fell in the hatched area. 5 of the babies, shown in dots and lines, differed from the general pattern.*

'normal'—the IgM curves showed a fall after a rise. 87 infants (84 of the 92 and 3 of the 5) were followed for an average period of 11 months. Of the 84 infants followed, 1 died at the age of 28 weeks after an attack of gastroenteritis (no pathogenic organism isolated), and 3 showed retarded development. Of the 3 babies who had markedly raised serum IgM, 2 were showing signs of cerebral palsy.

Neonates with offensive cord (Fig. 5 and Table I). The term omphalitis has been avoided

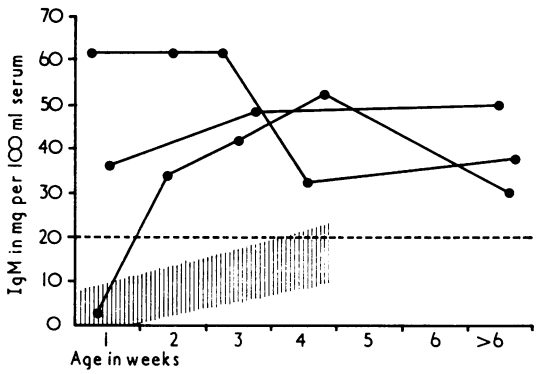

FIG. 4.—*Serum IgM in 50 LBW normal male neonates. In 47 of the babies the IgM fell in the hatched area. 3 of the babies, shown in dots and lines, differed from the general pattern.*

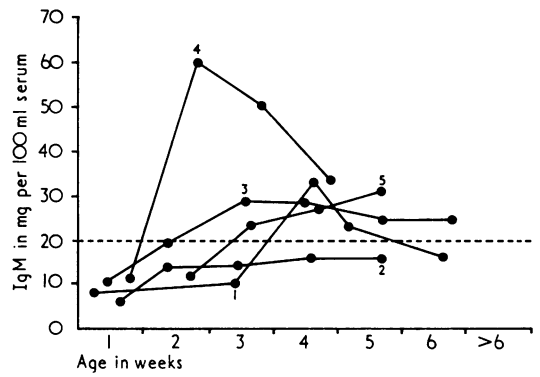

FIG. 5.—*Serum IgM in the neonates with 'offensive cord' before and after treatment.*

TABLE

Summary of Relevant Clinical Data from

Case No.	Birthweight (kg)	Sex	1st Week of Life	2nd Week	3rd Week
1	2·16	M	No clinical abnormality TPC* = 7200	Offensive cord; *Staph. aureus* from cord; local antibiotic and hygiene TPC = 6500	Moist, sticky offensive cord; local therapy TPC = 8900
2	2·9	M	No clinical abnormality TPC = 8100	Offensive cord; *Staph. aureus* from cord; local therapy TPC = 7600	Offensive cord; local therapy TPC = 7800
3	3·45	F	No clinical abnormality TPC = 7160	Offensive cord; *Staph. aureus* from cord; local therapy TPC = 6300	Offensive sticky cord; local therapy TPC = 5600
4	3·16	M	Sticky offensive cord; *Staph. aureus* and *Esch. coli* from cord; local therapy TPC = 5600	Cord ISQ; vomiting; jaundice; blood culture negative; systemic antibiotic TPC = 5960	Clinical improvement TPC = 6300
5	2·3	F	No clinical abnormality TPC = 4600	Offensive cord; *Staph. aureus* and *Esch. coli* from cord; local therapy TPC = 5680	No clinical abnormality TPC = 5600

*TPC = Total polymorphonuclear leucocyte count per mm^3.

as the picture may not be considered complete for such a diagnosis in all 5 cases. In 3 of the 5 cases (Cases 2, 3, and 5) neither the levels nor the dynamic pattern of IgM was different from the 'normal'. In the other 2 (Cases 1 and 4) serum IgM rose to higher levels with the establishment of infection. This rise was followed by a significant fall in the IgM levels with the eradication of infection. It was also of interest to note that Cases 1 and 4 had systemic symptoms.

Neonates with oral thrush and breast abscess (Fig. 6 and Table II). Behaviour of serum IgM in the 3 newborn infants with oral thrush was not different from the 'normal' pattern. The infant with breast abscess (Case 9) had a significantly raised serum IgM which rose still higher till the abscess was drained. When the infection was brought under control the IgM tended to fall.

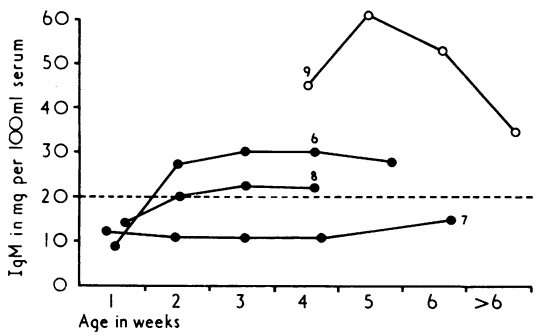

FIG. 6.—*Serum IgM in the neonates with oral thrush (shown as dots) and breast abscess (shown as clear circles) before and after treatment.*

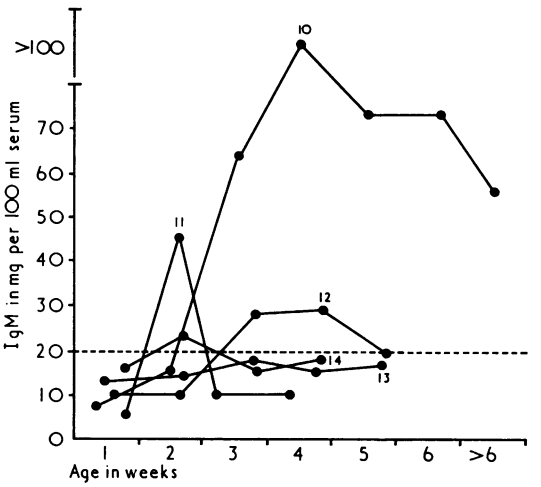

FIG. 7.—*Serum IgM in the neonates with 'sticky eyes' before and after treatment.*

Neonates with 'sticky eyes' (Fig. 7 and Table III). Serum IgM was markedly raised in 2 of the 5 infants (Cases 10 and 11). However, the dynamic pattern in 4 of the 5 may be considered different from the normal serum IgM rising with the infection and falling with its eradication.

Neonates with superficial skin infection (Fig. 8 and Table IV). Behaviour of serum IgM in 3 of 4 cases was not different from the 'normal'.

I

5 Neonates with 'Offensive Cord'

4th Week	5th Week	6th Week	Follow-up
Cord ISQ; slow to feed; lethargic; blood culture negative; systemic antibiotic TPC = 8260	Clinical improvement TPC = 7900	No clinical abnormality TPC = 6500	Followed for 7 mth; no clinical abnormality
No clinical abnormality TPC = 6980	No clinical abnormality TPC = 5800		Not followed
No clinical abnormality TPC = 6300	No clinical abnormality	No clinical abnormality	Not followed
No clinical abnormality TPC = 5800	No clinical abnormality		Not followed
No clinical abnormality TPC = 5900	No clinical abnormality		Followed for 10 mth; no clinical abnormality

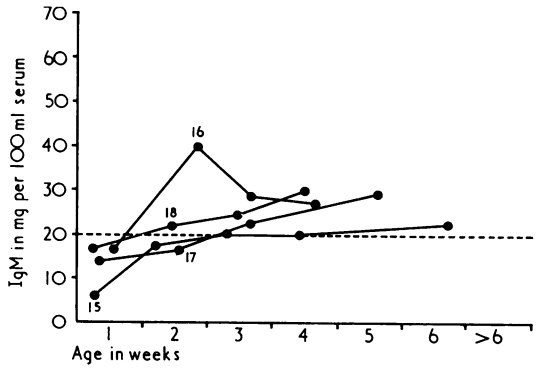

FIG. 8.—*Serum IgM in the neonates with superficial skin infection before and after treatment.*

In Case 16 the rise of IgM was higher and the level tended to fall with the control of infection.

Neonates with enteropathogenic *Esch. coli* infection (Fig. 9 and Table V). In 8 of the 9 cases serum IgM was markedly raised. The IgM rose serially till the infection was controlled. Eradication of the organism was followed by a significant fall in the IgM. In one case (22) however, the IgM tended to fall while *Esch. coli* 0126 were still being isolated from the faeces.

Neonates with infected urine (Fig. 10 and Table VI). It was realized that urinary infection should be diagnosed on clean-catch specimens, but the shortage of staff and time made it virtually impossible to get such specimens of urine. When the routine urine (bag specimen) examination showed at least 2 of the following 3 features, infection was suspected. (1) Pus cell count of 10 or more/mm^3 in male and 50 or more in female

TABLE

Summary of Relevant Clinical Data from 3 Neonates

Case No.	Birthweight (kg)	Sex	1st Week of Life	2nd Week	3rd Week
6	2·25	M	No clinical abnormality TPC* = 6960	No clinical abnormality TPC = 5700	Oral thrush; nystatin therapy TPC = 6100
7	1·7	M	No clinical abnormality TPC = 8600	No clinical abnormality TPC = 7300	Oral thrush; nystatin therapy TPC = 7860
8	2·45	F	No clinical abnormality TPC = 7360	Oral thrush; nystatin therapy TPC = 6200	No clinical abnormality
9	3·2	F			

*TPC = Total polymorphonuclear leucocyte count per mm^3.

TABLE

Summary of Relevant Clinical Data

Case No.	Birthweight (kg)	Sex	1st Week of Life	2nd Week	3rd Week
10	1·9	M	No clinical abnormality TPC* = 7100	Sticky eyes; *Staph. aureus* and *Proteus vulgaris* from eyes; chloramphenicol eye drops TPC = 5300	Purulent discharge from eyes; lethargic; poor appetite; blood culture negative; systemic antibiotic TPC = 8860
11	3·28	M	No clinical abnormality TPC = 6800	Purulent discharge from eyes; poor appetite; loss of weight; *Staph. aureus* from eyes; blood culture negative; systemic and local antibiotic TPC = 6300	Clinical improvement TPC = 8700
12	1·67	F	No clinical abnormality TPC = 7660	No clinical abnormality TPC = 6400	Sticky eyes; *Staph. aureus* from eyes; chloramphenicol eye-drop TPC = 6000
13	4·1	M	No clinical abnormality TPC = 6100	Sticky eyes; *Staph. aureus* from eyes; local chloramphenicol TPC = 6360	No clinical abnormality TPC = 5900
14	2·5	M	No clinical abnormality TPC = 7300	Sticky eyes; *Esch. coli* from eyes; chloramphenicol eye-drops TPC = 6360	No clinical abnormality TPC = 5900

*TPC = Total polymorphonuclear leucocyte count per mm^3.

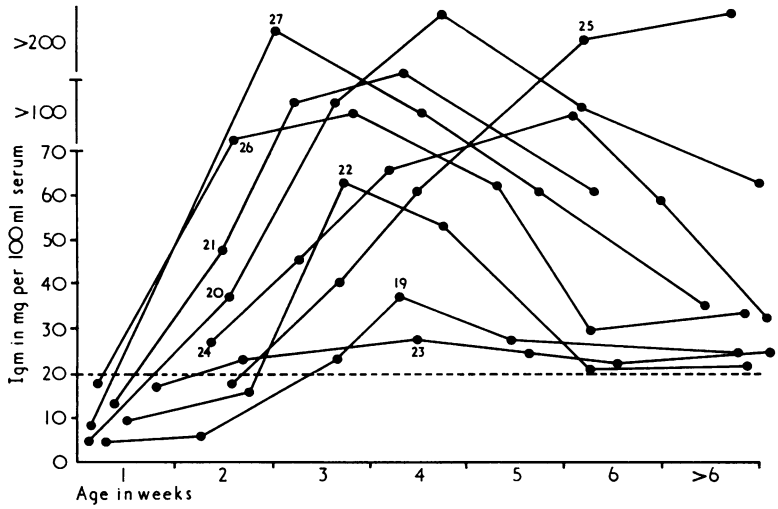

FIG. 9.—*Serum IgM in the neonates with enteropathogenic* Esch. coli *infection before and after treatment.*

II

with Oral Thrush and One with Breast Abscess

4th Week	5th Week	6th Week	Follow-up
No clinical abnormality TPC = 5300	No clinical abnormality		Followed for 10 mth; no clinical abnormality
No clinical abnormality TPC = 7900	No clinical abnormality TPC = 7300	No clinical abnormality	Followed for 13 mth; no clinical abnormality Not followed
Admitted with nonfluctuant left breast swelling, pyrexia, and poor appetite; blood culture negative; systemic antibiotic TPC = 7600	Breast abscess incised and drained; *Staph. aureus* from pus; antibiotic continued TPC = 8600	Clinical improvement; antibiotic discontinued TPC = 6360	Last IgM at 8 wk of age; no clinical abnormality TPC = 5160

III

from 5 Neonates with 'Sticky Eyes'

4th Week	5th Week	6th Week	Follow-up
Clinical improvement TPC = 7600	No clinical abnormality TPC = 6360	No clinical abnormality TPC = 5860	Last IgM at 12 wk of age; followed for 6 mth; no clinical abnormality
No clinical abnormality TPC = 6360			Not followed
No clinical abnormality TPC = 5200	No clinical abnormality TPC = 5600		Followed for 11 mth; no clinical abnormality
No clinical abnormality TPC = 5900			Not followed
			Not followed

TABLE

Summary of Relevant Clinical Data from

Case No.	Birthweight (kg)	Sex	1st Week of Life	2nd Week	3rd Week
15	1·8	M	No clinical abnormality TPC* = 6900	6 pustules in axilla; *Staph. aureus* from pustule; local therapy TPC = 6300	No clinical abnormality TPC = 6480
16	2·95	M	No clinical abnormality TPC = 6100	Pustular eruption axillary and cervical region; pyrexia; poor appetite; loss of weight; *Staph. aureus* from pustules; blood culture negative; systemic and local antibiotic TPC = 7300	No clinical abnormality TPC = 5760
17	2·25	M	No clinical abnormality TPC = 5900	No clinical abnormality TPC = 5600	Multiple pustules; *Staph. aureus* from pustules; local antibiotic TPC = 6900
18	2·68	F	No clinical abnormality TPC = 6300	Multiple pustules; *Staph. aureus* from pustule; TPC = 5700	No clinical abnormality TPC = 6700

*TPC = Total polymorphonuclear leucocyte count per mm^3.

TABLE

Summary of Relevant Clinical Data from

Case No.	Birthweight (kg)	Sex	Ist Week of Life	2nd Week	3rd Week
19	2·05	F	No clinical abnormality TPC* = 7100	No clinical abnormality TPC = 7300	No clinical abnormality; *Esch. coli* 0128 isolated from faeces TPC = 9360
20	2·6	M	No clinical abnormality TPC = 7100	Not feeding well; weight loss TPC = 7000	Poor appetite; weight loss; watery explosive stools; *Esch. coli* 0128 from faeces; clear fluids orally; TPC = 716
21 (Twin I)	2·7	M	No clinical abnormality TPC = 5600	No clinical abnormality; *Esch. coli* 0126 isolated from faeces; TPC = 6200	No clinical abnormality; *Esch. coli* 0126 from faeces TPC = 6000
22 (Twin II)	2·4	F	No clinical abnormality TPC = 7360	Poor appetite; weight loss; *Esch. coli* 0126 from faeces; clear fluids orally TPC = 7600	Watery explosive stools; *Esch. coli* 0126 from faeces; neomycin orally; TPC = 7800
23	3·3	M	No clinical abnormality TPC = 3960	No clinical abnormality; *Esch. coli* 0128 from faeces TPC = 6100	No clinical abnormality; *Esch. coli* 0128 from faeces TPC = 7100
24	2·3	M		Admitted with poor appetite and losing weight TPC = 6900	Watery stools; dehydration; I.V. fluid and oral neomycin TPC = 9800
25	1·9	M	No clinical abnormality	Watery stools; poor appetite; weight loss; oral clear fluids TPC=9600	Watery stools; weight loss; dehydration; I.V. fluids; oral neomycin; TPC=10600
26	2·25	F	No clinical abnormality TPC = 6300	Poor appetite; weight loss TPC = 7600	Watery stools; weight loss; *Esch. coli* 0128 from faeces; neomycin orally; TPC = 7300
27	1·8	M	No clinical abnormality TPC = 6900	Poor appetite; weight loss; *Esch. coli* 0127 from faeces TPC = 7600	Watery stools; *Esch. coli* 0127 from faeces; neomycin orally TPC = 9100

*TPC = Total polymorphonuclear leucocyte count per mm^3.

IV

4 Neonates with Superficial Skin Infection

4th Week	5th Week	6th Week	Follow-up
No clinical abnormality TPC = 6500	No clinical abnormality	No clinical abnormality	Followed for 8 mth; no clinical abnormality
No clinical abnormality TPC = 5600			Not followed
No clinical abnormality TPC = 6300	No clinical abnormality		Followed for 6 mth; no clinical abnormality
No clinical abnormality TPC = 5360			Not followed

V

9 Neonates with Specific Esch. coli *Infection*

4th Week	5th Week	6th Week	Follow-up
No clinical abnormality; *Esch. coli* 0128 from faeces; neomycin orally; TPC = 5600	No clinical abnormality TPC = 5280	No clinical abnormality	Last IgM at 10 wk; followed for 15 mth; no clinical abnormality
Clinical improvement; *Esch. coli* 0128 from faeces TPC = 7400	No clinical abnormality; *Esch. coli* 0128 from faeces; neomycin orally	No clinical abnormality TPC = 5900	Last IgM at 12 wk; no clinical abnormality; not followed further
No clinical abnormality; *Esch. coli* 0126 from faeces; neomycin orally; TPC = 6200	No clinical abnormality	No clinical abnormality TPC = 8600	Not followed
Clinical improvement TPC = 7300	No clinical abnormality TPC = 7000	No clinical abnormality TPC = 7200	Last IgM at 8 wk; not followed further (mother had *Esch. coli* 0126 in faeces)
No clinical abnormality; *Esch. coli* 0128 from faeces TPC = 8660	No clinical abnormality; *Esch. coli* 0128 from faeces	No clinical abnormality; *Esch. coli* 0128 from faeces TPC = 5960	Last IgM at 8 wk age; not followed
Clinical improvement; neomycin continued; oral feed reintroduced; TPC = 8600	Recurrence of watery stools; *Esch. coli* 0114 from faeces, resistant to neomycin; oral Colomycin and oral Streptomycin therapy TPC = 7660	Clinical improvement; antibiotics continued TPC = 7100	Last IgM at 12 wk age; followed for 10 mth; no clinical abnormality
Slight clinical improvement; *Esch. coli* 0114 from stool, resistant to all common antibiotics; TPC = 10900	Clinical deterioration; I.V. feeding; *Esch. coli* 0114 from faeces, resistant to antibiotics; multiple antibiotic therapy TPC = 10,800	Slight clinical improvement; *Esch. coli* 0114 from faeces; antibiotics continued; oral feeding reintroduced TPC = 9100	Last IgM at 10 wk of age; diarrhoea kept on recurring on introduction of oral feeds; *Esch. coli* 0114 could not be eradicated from stool; died at 15 wk age
Clinical improvement TPC = 7800	No clinical abnormality TPC = 6900	No clinical abnormality TPC = 5600	Last IgM at 14 wk; followed for 6 mth; no clinical abnormality
Clinical improvement TPC = 9000	No clinical abnormality TPC = 7100	No clinical abnormality	Last IgM at 10 wk; followed for 3 mth; no clinical abnormality

TABLE

Summary of Relevant Clinical Data from

Case No.	Birthweight (kg)	Sex	1st Week of Life	2nd Week	3rd Week
28	2·4	M	No clinical abnormality TPC* = 6760	Poor appetite; weight loss; vomiting; urine infected with *Esch. coli;* antibiotic therapy TPC = 6400	Clinical improvement TPC = 8600
29	2·15	F	No clinical abnormality TPC = 7100	No clinical abnormality TPC = 8200	Lethargic; no weight gain; suspected urine infection with *Esch. coli* TPC = 6600
30	1·9	F	No clinical abnormality TPC = 6300	No clinical abnormality TPC = 6060	No clinical abnormality; urine infected with *Esch. coli* TPC = 8600
31	3·4	F			Admitted with poor appetite, vomiting, and not gaining weight; suspected urine infection with *Esch. coli*; blood culture negative TPC = 5150
32	2·9	M			
33	2·2	F	No clinical abnormality TPC = 6700	No clinical abnormality TPC = 6600	No weight gain; suspected urine infection with *Esch. coli* TPC = 6900

*TPC = Total polymorphonuclear leucocyte count per mm^3.

infants. (2) Bacterial count of over 100,000/ml. (3) Pure growth of pathogenic organism.

When an infection was suspected, urine was examined on 3 consecutive days. If at least 2 of the 3 specimens of urine showed at least 2 of the 3 features a diagnosis of urinary infection was made.

In all the 6 cases serum IgM rose serially to very high levels with infection, and tended to fall with successful treatment. It is of interest to note that 2 of the infants (Cases 30 and 33) had no

TABLE

Summary of Relevant Clinical Data

Case No.	Birthweight (kg)	Sex	1st Week of Life	2nd Week	3rd Week
34	2·1	M	No clinical abnormality TPC* = 6580	Lethargic vomiting; *Esch. coli* from turbid CSF; blood culture positive for *Esch. coli*; local and systemic antibiotics TPC = 6300	No clinical improvement; CSF = ISQ; antibiotics changed TPC = 7600
35	3·2	M		Admitted with vomiting and twitching; CSF turbid and *Ps. pyocyaneae* grown; blood culture negative; local and systemic antibiotics TPC = 7960	No clinical improvement; CSF = ISQ; antibiotics changed TPC = 7300
36	2·8	M		Admitted moribund from home at 2 dy; CSF turbid with β-haemolytic streptococci; same organism from blood and also from vaginal swab of mother; died after 3 hr TPC = 9100	

*TPC = Total polymorphonuclear leucocyte count per mm^3.

VI

6 Neonates with Infected Urine

4th Week	5th Week	6th Week	Follow-up
No clinical abnormality TPC = 5900	No clinical abnormality	No clinical abnormality	Last IgM at 10 wk; followed for 7 mth; no clinical abnormality
Anorexic, lethargic; weight loss; urine infected with *Esch. coli*; blood culture positive for *Esch. coli*; antibiotic therapy TPC = 7660	Clinical improvement; antibiotics continued TPC = 5900	No clinical abnormality	Last IgM at 7 wk; followed for 8 mth; no clinical abnormality bifid pelvis on IVP
No clinical abnormality; urine infected with *Esch. coli*; antibiotic therapy TPC = 6300	No clinical abnormality TPC = 6100	No clinical abnormality	Last IgM at 12 wk; followed for 13 mth; no clinical abnormality
Symptoms persisting; urine infected with *Esch. coli*; antibiotic therapy TPC = 6360	Clinical improvement; antibiotic continued TPC = 6000	No clinical abnormality	Last IgM at 12 wk; followed for 4 mth; no clinical abnormality
Admitted with lethargy and loss of weight; urine infected with *Esch. coli* and *Ps. pyocyanea*; antibiotic therapy TPC = 7800	Clinical improvement; antibiotic continued TPC = 6900	No clinical abnormality	Last IgM at 10 wk; followed for 8 mth; recurrence of urinary infection at 5 mth; ureteric reflux on radiology
No weight gain; urine infected with *Esch. coli*; antibiotic therapy TPC = 6300	No clinical abnormality TPC = 6200	No clinical abnormality	Last IgM at 12 wk; followed for 8 mth; no clinical abnormality

symptoms and, in fact, rising IgM levels led to repeated investigation and ultimately to the diagnosis.

Neonates with bacterial meningitis (Fig. 11 and Table VII). Serum IgM was markedly raised in all 3 cases. In the 2 surviving ones, serum IgM rose serially with infection. Here again serum IgM tended to fall with clinical and bacteriological improvement.

VII

from 3 Neonates with Meningitis

4th Week	5th Week	6th Week	Follow-up
Slight clinical improvement; CSF less turbid no organism; antibiotics continued; subdural taps normal TPC = 7300	Clinical improvement maintained; CSF returning to normal; antibiotics continued TPC = 6960	Improvement maintained; CSF normal; subdural normal	Last IgM at 10 wk; followed for 9 mth; no definite clinical abnormality
No clinical improvement; CSF = ISQ; subdural tap normal; antibiotics continued TPC = 8300	Some improvement in general condition but appearance of rt. hemiplegia; CSF less turbid without organism; subdural tap normal; antibiotics continued TPC = 6700	General improvement maintained but rt. hemiplegia established; CSF back to normal; subdural normal	Last IgM at 9 wk; followed for 8 mth; left with rt. hemiplegia

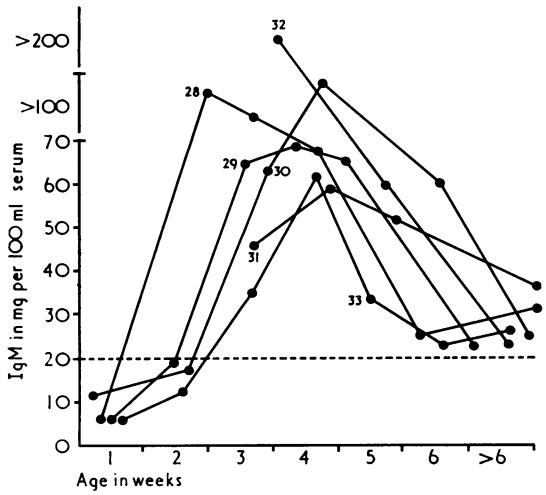

FIG. 10.—*Serum IgM in the neonates with infected urine before and after treatment.*

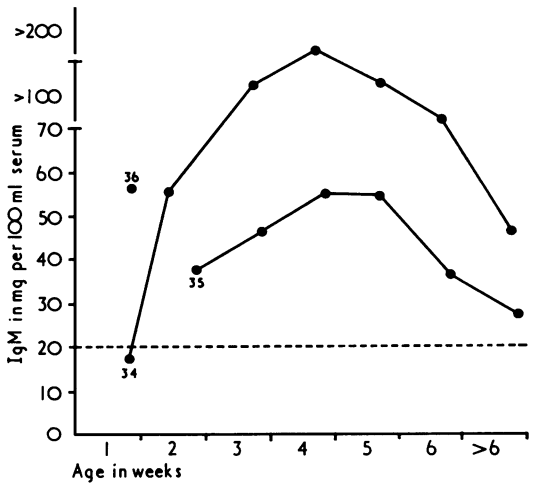

FIG. 11.—*Serum IgM in the neonates with meningitis before and after treatment.*

Neonates with probable infection (Fig. 12). During the period of observation a clinical diagnosis of infection was made in 19 cases but no pathogenic bacteria or viruses were isolated to establish the diagnosis. Behaviour of serum IgM was however found to be very similar to that observed in the neonates with established systemic infection.

Discussion

The human fetus has been found to be capable of producing immunoglobulins (Stiehm and Fudenberg, 1966; Johansson and Berg, 1967; Rhodes *et al.*, 1969). Synthesis of γ-globulin in the newborn infant begins in response to contact with infection or immunization. IgM is produced as the first humoral response to antigenic stimulation. Half-life of IgM is 5 days. It is generally agreed that the babies with infections commonly have raised serum IgM levels, but it has not been clearly shown how safely one can infer that a raised serum IgM level in the newborn signifies infection rather than some other form of stimulation of an immune response.

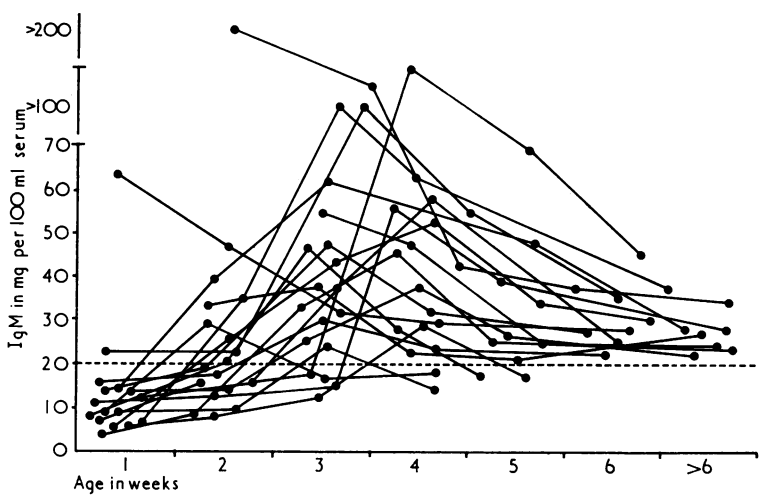

FIG. 12.—*Serum IgM in the 19 neonates with probable infection before and after treatment.*

An increasing number of medical publications show varying levels of serum IgM in the neonates. Maturity, birthweight, and the environment in which the infant is nursed are some of the factors believed to influence the serum IgM levels in the early days of life (Stiehm and Fudenberg, 1966; Washburn, 1966; Johansson and Berg, 1967; Berg, 1968).

It was considered appropriate to establish the general pattern of the dynamics of serum IgM in the normal infants during the newborn period on the units connected with the study (Fig. 1–4). Serum IgM continued to rise after birth in both the NBW and LBW infants. The rate of rise was slower in the LBW infants as was observed by others (Norton, Kunz, and Pratt, 1952; Washburn, 1966; Berg, 1968). However, this does not imply that LBW babies are not as capable of producing IgM. It should be evident from the results of this study that LBW neonates have as good a capacity for early IgM synthesis as NBW babies.

The dynamics of IgM in the newborn infants had a characteristic pattern (hatched area in Fig. 1–4). Serum IgM levels serially rose after birth at variable rates. The most significant feature, however, was that the IgM curve did not show any drop.

On examining the dynamics of IgM in the babies who had infection the following 3 groups seemed to emerge.

Group I. Babies with local/superficial infection, without any significant local reaction or systemic symptoms. In these newborn infants the behaviour of IgM was not different from the 'normal'. It appears that the 'infection' was strictly localized and could not reach the immunologically competent cells. This explanation is perhaps too simple but not too unreasonable.

Group II. Babies with local/superficial infection, considerable local reaction, and systemic symptoms. Serum IgM in these cases rose to higher levels followed by a fall with eradication of infection. This dynamic pattern was characteristically different from the 'normal'.

Group III. Babies with internal/systemic infection. Serum IgM rose to considerably high levels with the establishment of infection. The rise was followed by a significant fall with clinical and bacteriological response to treatment.

It would be reasonable to assume that an 'antigenic stimulus' for the synthesis of IgM appeared with infection. The rise in serum IgM was detectable within 48 hours of the appearance of the symptoms. This 'antigenicity' persisted with the 'infectivity' and serum IgM continued to rise till the infection was controlled. Eradication of infection corresponded to the disappearance of the 'antigenic stimulus' and the IgM tended to fall by the end of the week after the control of infection.

In the 19 cases in which a clinical diagnosis of infection (6 respiratory and 13 gastrointestinal) was made but no organism was isolated, the behaviour of serum IgM (Fig. 12) was similar to that observed in Group III cases. However, in the 85 cases with 11 different noninfective conditions the dynamics of IgM was not like that seen in Groups II and III.

The rate of formation of serum IgM in the neonates with infection was apparently independent of age, birthweight, the type of organism and its pathogenicity. Instead, the site of infection was found to affect the dynamics of IgM.

In conclusion, a rise in serum IgM with the onset of an illness followed by a fall with an effective treatment may be considered indicative of an infective aetiology of the illness.

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