ESCHERICHIA COLI GASTRO-ENTERITIS

BY

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PART I

The Incidence of Pathogenic *E. Coli* in Normal Babies in the General Community

Mild gastro-intestinal upset is common in babies, but severe disease is not now the scourge it formerly was, and part of the great improvement in infantile mortality is due to its decline in the twentieth century. The reasons for this are not clear, and many theories have been advanced. Formerly, a considerable number of cases of gastro-enteritis were thought to be due to dietetic, that is to say chemical upsets, but it is now believed that infection is the responsible factor for almost all cases. It has been known for a long time that dysentery bacilli and salmonellae cause only a small proportion of the cases, and many other bacteria have been suspected from time to time. One theory dating back to the early years of this century is that the disease is caused by the invasion of the small gut by the flora of the large gut (Moro, 1916). Adam (1922, 1923, 1927) advanced the view that there were certain varieties of *Escherichia coli* associated with the disease and based his classification upon biochemical tests. Goldschmidt (1933) showed that the strains of *E. coli* described by Adam fell into a few serological groups.

The significance of this earlier work was not at first fully appreciated when certain O groups of *E. coli*, classified according to the Kauffmann scheme, were shown to have an association with gastro-enteritis in babies. The first of these, *E. coli* O111, was described by Bray in 1945, and soon afterwards O55, O26 and O119 were described by Giles and Sangster (1948), by Smith (1949, 1953), and by Taylor and Charter (1952). The evidence incriminating these O groups was until recently epidemiological, but Thomson (1955a) showed that the whole length of the gut is colonized in the disease. The syndrome of gastro-enteritis has thus striking similarities to the syndrome of cholera: the whole length of the gut and often the gall bladder swarm with the pathogen; there is no acute

inflammation of the gut in the pathological sense; there is vomiting as well as diarrhoea, and collapse occurs because of fluid loss and electrolyte imbalance. The old name 'cholera infantum' would appear to be a very fitting one.

With few exceptions, most of the literature on gastro-enteritis associated with *E. coli* deals with hospital outbreaks, many of which have been very troublesome because infection, once introduced, may linger for a long time (Rogers, 1951; Rogers and Koegler, 1951; Wright and Roden, 1953; Jameson, Mann and Rothfield, 1954). In most areas where a study has been made of the disease the majority of cases yielding the suspected varieties of *E. coli* have arisen from cross-infection in hospitals. For example, in the Cardiff area in 1953, the year before the surveys described in this publication, 80% of the recognized cases had such an association as the following table shows.

SOURCE OF STRAINS OF *E. COLI* IN 1953

Source	Type of Organism			Total
	O55	O111	O26	
Hospitals and institutions	80	16	13	109
Other sources	21	1	6	28
Totals	101	17	19	137

Mild forms of gastro-enteritis are common in the first year of life, but the proportion of these cases caused by *E. coli* is not known as the general practitioner may not be summoned, and if summoned may not think the case serious enough to warrant laboratory investigations. There is, therefore, a suspicion that many mild cases of 'coli-enteritis' exist outside hospitals. To determine this and the number of symptomless excretors a special investigation was made of babies attending a Cardiff City infant welfare clinic.

Scope of the Survey. Babies attending one of the Cardiff City's public health infant welfare clinics were enrolled in the survey. Babies are normally

brought to the clinic when they are 4 to 6 weeks old and thus the neonatal period was unexplored. In all, 111 babies were investigated and the ages at which they first attended were: first month, 3; second month, 56; third month, 26; fourth month, 13; fifth month, 4; sixth month, 5; seventh month, 2; eighth month, 1; ninth month, 1. Most of the babies (77%) were in the survey before they were 3 months old.

Mothers were asked to send to the laboratory a specimen of faeces from their babies at fortnightly intervals. A swab was sent to the mother a few days before the next specimen was due, and on the whole the mothers cooperated well. The general practitioners of the district were informed of the investigation but not asked to take part.

The fundamental aim was to determine how many babies became infected in the first year of life, and how many developed symptoms of gastro-enteritis. The babies were not kept in the survey after they were 1 year old. The specimens were examined for *E. coli* O111, O55 and O26.

In cases of hospital gastro-enteritis it has been observed that practically the whole coliform content of the faeces consists of the suspected pathogen. This might not occur in symptomless excretors, and if the special O groups of *E. coli* are outnumbered 100:1 by other *E. coli* it would be necessary to pick and examine, on the average, 100 colonies before a positive result would be obtained (Thomson, 1955b). Thus many positives are missed, and until a selective culture medium can be found this problem will remain. The effect of this in a survey of the kind reported here must be that the number of excretors identified is a considerable under-estimate.

Results. In all, 1,681 specimens of faeces were examined from 111 babies, and 20 babies (18%) were found positive at one time or another. The following strains of *E. coli* were identified.

O26 B6 H11, 9 strains; O26 B6 H?, 3 strains;
O55 B5 H21, 2 strains; O55 B5 H7, 4 strains;
O55 B5 H27, 1 strain; O111 B4 H?, 1 strain.

The strains were identified by agglutination of their O, B and H suspensions to the full titre of antisera. At least five different varieties were identified and this might be advanced as evidence that the babies were not picking up the infection when visiting the clinic.

In nearly all positive cases a repeat specimen was taken the following day to confirm the result, but in only one case was the specimen still positive at the next routine fortnightly examination. The rate of clearance, or apparent rate of clearance, in these babies was rapid, and many more babies would

presumably have been found positive had swabs been taken at more frequent intervals. For this reason, and for the technical reasons given above, the incidence of 18% is almost certainly a considerable underestimate of the proportion of babies infected by the special O groups of *E. coli* in the first year of life. The figure of 18% might be shown as 25% per annum as the babies, on the average, were investigated for only nine months of the first year of life. In all, 1,681 specimens of faeces were examined and 21 found positive, a result which indicates that just over 1% of babies under 1 year are, at any one time, harbouring the strains of *E. coli* associated with gastro-enteritis.

The numbers were small in which to ascertain any relationship with the type of feeding, but the following analysis is given:

Number of specimens from babies receiving only breast milk (none positive)	121
Number of specimens from babies receiving breast milk and other foods (two positive)	208
Number of specimens from babies receiving no breast milk (19 positive)	1,352

No new evidence was found of the value of breast milk, but a more extensive survey of this kind might show what part, if any, is played by breast milk in protecting a baby. The immunity of the breast-fed baby may not depend upon any special immunological quality of the milk, but upon a decreased exposure to exogenous infection conveyed by other foodstuffs.

How the babies become infected is not clear. In a recent study Thomson (1956) found 1% of samples of cow's milk to be contaminated by these same O groups of *E. coli*, but none of the babies in the survey drank unheated cow's milk and only one household bought unpasteurized milk. Many babies were fed on dried milk, but this is heated before drying and is expected to be free from coliforms. Much more work will be necessary to find out how babies in their own homes become infected, and unfortunately the lack of a selective culture medium will make this a very difficult if not impossible task. The problem is to isolate the special O groups when they are present only in small numbers.

It was thought of value to ascertain if the infected babies acquired their infection shortly after the introduction of mixed feeding, including cow's milk, or if the risk remained more or less uniform throughout the first year of life. The interval elapsing between the cessation of full breast-feeding and infection was 0-1 month in 2 cases, 1-2 months in 2 cases, 2-3 months in 5 cases, 3-4 months in 1 case, 4-5 months in 2 cases, 5-6 months in 2 cases, more than 6 months, 6 cases. Having regard to the fact that examinations were made only once a fortnight,

the term 'month' as used above has no accurate meaning, but the simple analysis suggests that a baby may have a greater tendency to become infected shortly after the introduction of other foods, including cow's milk, into the diet.

There was a tendency for more positives to be identified in the summer. Of the 20 babies found positive, 14 were identified in the months April to September (818 specimens examined) and the other six from October to March (863 specimens examined).

Only eight of the 20 identified excreters had loose stools and only one baby, infected with O55 B5 H21, was sufficiently ill for the general practitioner to be called. This baby was admitted to hospital (what may happen when an infected baby is sent to hospital is described in Part II of the report). All the other babies had recovered within three days, the majority having symptoms for only 24 hours.

Another 29 babies had mild diarrhoea at one time or another, but yielded no identifiable strains of *E. coli*. Thus, from a little more than one-fifth of all cases of diarrhoea identifiable strains were isolated, but as the examinations were restricted to O groups 111, 55 and 26, leaving out 119, 128, etc., it is possible that an appreciably greater proportion might have been found positive had the bacteriological examinations been more comprehensive.

On 17 occasions it was possible to obtain specimens of faeces from other members of the family when the baby was found positive. Five family contacts were found to be excreting the same organism as the baby, and on three of these occasions it was the mother who was positive.

Discussion. In this survey of babies in the first year of life the infection rate by the special O groups of *E. coli* associated with gastro-enteritis was 25% per annum. Having regard to the technical difficulties and to the fact that specimens of faeces were examined at only fortnightly intervals, the suspicion arises that most, if not all, babies are infected in the first year of life. Most of the infected babies were not ill, approximately one half having symptoms, and only one baby was ill enough to warrant admission to hospital.

Many different varieties of *E. coli* were encountered in the survey, but all had previously been isolated in the Cardiff area. Nine babies were infected with O26 B6 H11, and though this serotype is a very common one in Cardiff and district it has not been responsible for outbreaks of severe disease. Most of the earlier strains had been isolated from mild cases and symptomless excreters in residential institutions. Four babies in the survey were

infected with O55 B5 H7, a serotype which had been previously isolated only from symptomless excreters in residential institutions. One baby was infected with O55 B5 H27, and the only strain of this serotype previously encountered in Cardiff was isolated from a chicken (Thomson, 1956). Two babies in the survey were infected with O55 B5 H21 and one of these babies was ill enough to warrant admission to hospital; this serotype had been isolated before from only two babies both of whom died.

It would appear that there might be great differences in virulence from strain to strain possibly within any O group. There may be a correlation between H antigen structure and virulence, but it is also possible that there are minor differences in the O antigens within an O group.

Babies at home are commonly infected by strains of *E. coli* associated with gastro-enteritis. The sick baby, infected by one of the more virulent varieties, is the one which is sent to hospital. What may happen after infection is carried into hospital in this way is described in Part II of this report.

PART II

The Spread of *E. Coli* Infection in Hospitals and Institutions

Gastro-enteritis is highly infectious among babies in hospital, and barrier nursing of a quality expected to prevent the spread of other intestinal diseases is commonly inadequate. How the infection spreads within institutions is not fully known.

Many hospital outbreaks of severe infantile gastro-enteritis associated with certain O groups of *E. coli* have been recorded in recent years. On the other hand it has happened not infrequently that infection by some of these O groups has spread in an institution and not caused an outbreak of serious disease. It would seem that some varieties, as in the case of the salmonellae, are much more virulent than others.

In Part I of this report evidence was advanced that many babies living at home are infected by these O groups of *E. coli* in the first year of life. One hundred and eleven babies were repeatedly examined during the first year of life and 20 of them were found to be infected at one time or another. Only one of the babies, infected with O55 B5 H21, was ill enough to be sent to hospital and it may be that our hospitals, by a process of selection, are breeding centres for the more virulent varieties. Many hospital outbreaks have lasted for a long time, since infection, once introduced, is not easily removed.

This paper reports an extensive outbreak of severe gastro-enteritis in a group of widely separated

hospitals in South Wales. Within each hospital the events followed the classical pattern frequently described in the literature in recent years and are therefore presented briefly in order that emphasis can be laid on the special evidence yielded by the South Wales epidemic, viz., the carriage of infection from one hospital to another by the transference of infected babies. The strain of *E. coli* responsible for the epidemic had the antigenic structure O55 B5 H2, and as it had a definite 'antibiotic sensitivity' pattern it could be identified with precision and followed from place to place.

Events before the Epidemic of 1954. Strains of *E. coli* associated with gastro-enteritis have been identified for some years in Cardiff. The bacteriological supervision of the disease is particularly close over the wards of the University Department of Child Health in Llandough Hospital, Cardiff. Following an outbreak in the babies' ward in 1953 a large side-ward with six cots has been set aside for cases in order to minimize the risk of spread of infection. This side-ward is part of the unit for older children and on another floor from the babies' ward proper. In addition, all babies are examined on admission to detect carriers and at weekly intervals thereafter to detect any spread of infection.

Early in 1953 there was an outbreak of gastro-enteritis in Llandough Hospital and another in Church Village Hospital which lies 10 miles north of Cardiff. The outbreaks were caused by *E. coli* O55 B5 and the limited number of strains which were examined more fully were shown to have H antigen 2. The few strains which had been preserved were shown to be sensitive to chloramphenicol, partly sensitive to terramycin and resistant to sulphonamides, streptomycin and aureomycin. The epidemic in 1954 reported here was caused by an identical organism.

The 1953 outbreaks ended in the early summer, and in Llandough Hospital where the babies' faeces were regularly examined, the epidemic strain of O55 B5 H2 was not once encountered from September to December. During these four months, in spite of weekly examinations of specimens from all babies, only two strains of O55 were isolated and both had H antigen 6.

The Outbreaks of 1954

Church Village Hospital. This hospital has 40 children's beds and cots, and on an average has 10 babies under 1 year old at any one time. Routine bacteriological examinations for the special varieties of *E. coli* were not made on all babies admitted, but cases of enteritis were so examined. Within the limits

of these clinical and bacteriological criteria the department had been free of gastro-enteritis for nearly a year, i.e., since the outbreak referred to above.

Towards the end of January, 1954, a number of babies developed gastro-enteritis; the infecting strain of *E. coli* had the antigenic pattern O55 B5 H2 and had the antibiotic sensitivities given above. The usual precautions were taken to prevent the spread of infection within the hospital and the infected wards were closed to new admissions. The infection lingered in the wards for 11 weeks; in all, 23 babies were infected, many were seriously ill and one died.

Unfortunately, in the few days before the outbreak began, and when some of the babies were presumably incubating the disease, a number were discharged and apparently carried the infection with them. These babies were responsible, in one way or another, for introducing infection into a number of institutions where outbreaks followed. The events are best described by following the babies. The three babies concerned named Susan M., aged 7 months, Philip P., aged 4 months and Howard M., aged 4 months, were discharged from Church Village Hospital at the end of January, 1954.

Baby Susan M., and Residential Nursery. Baby Susan M. had no home and lived in a residential nursery five miles away. When she had severe bronchitis she was admitted to Church Village Hospital for treatment and was returned cured to the residential nursery on January 27, 1954, i.e., on the day before cases of gastro-enteritis appeared in Church Village Hospital. Baby Susan M. remained well, but another baby (Brian E.) in the residential nursery fell ill with symptoms of gastro-enteritis so severe that he was sent to the special unit in Llandough Hospital, Cardiff. Bacteriological examinations showed both Baby Susan M. and Brian E. as well as eight other infants in the nursery to be infected with *E. coli* O55 B5 H2 possessing the antibiotic sensitivities given above. Presumably Baby Susan M. had carried the infection from Church Village Hospital to the residential nursery.

Baby Philip P., and Paediatric Unit. Baby Philip P. was also discharged from Church Village Hospital on January 27, 1954, and he went to a small paediatric unit eight miles away. Two weeks later two babies in this small hospital fell ill with gastro-enteritis and the epidemic strain of *E. coli* O55 B5 H2 was isolated. An examination of the other 15 children in the hospital revealed five more to be symptomless excretors.

Baby Philip P. had meanwhile gone home (he

went home four days before the outbreak began in the small paediatric hospital), but he was followed up and he too was found to be excreting the epidemic strain. It was thought reasonable to conclude that he had brought the infection from Church Village Hospital to the small paediatric hospital.

Baby Howard M., and Llandough Hospital. Baby Howard M. was discharged from Church Village Hospital at the end of January, 1954. A few days later he fell ill at home with vomiting and diarrhoea, and he was sent direct to the special gastro-enteritis unit at Llandough Hospital, Cardiff. This hospital thus admitted two babies both infected by the epidemic strain, viz., Baby Howard M. who had gone from Church Village to his own home and Baby Brian E. who came from the residential nursery to which infection had been carried by Baby Susan M.

In spite of the isolation afforded by the special side-ward, and the fact that the staff are constantly alert to the risks of cross-infection, there was an outbreak of gastro-enteritis within the department. The infection spread to the babies' ward on another floor of the hospital in spite of the fact that they were nursed in isolation cubicles. The infection lingered for 10 weeks. In all, 22 babies were infected, many were very ill and five died.

Thus if the outbreak in Church Village Hospital is regarded as the first generation, the outbreaks in Llandough Hospital, the residential nursery and the small paediatric hospital were second generation. Unfortunately, there were third generation outbreaks in two fever hospitals which were prevailed upon to help the other institutions to cope with their problem.

First Isolation Hospital. The problem had arisen of how to dispose of infected babies and toddlers in the residential nursery. Eventually there remained only six infected but symptomless toddlers aged 2-3 years, and in order to allow the nursery to re-open they were sent to a large isolation hospital. They were accommodated in the largest room of a cubicle block which had 10 rooms opening on to a large veranda, and the room with the infected toddlers was at one extreme end of the veranda.

In spite of the ideal conditions, and the fact that the children had no diarrhoea, and the staff were trained fever hospital nurses, infection spread within the unit. At the extreme other end of the cubicle ward were several babies suffering from whooping cough, and two weeks after the toddlers had been admitted for isolation one of these babies developed gastro-enteritis. Thereafter, the infection remained

in the ward for 12 weeks spreading from baby to baby, all of whom were infected by the epidemic strain. There were in all eight cases; some were very ill and one died.

Second Isolation Hospital. None of the babies who remained in the small paediatric unit was very ill, and in time most became free of infection as judged by bacteriological tests. At length only two babies remained infected, and in order that the small paediatric unit might re-open, these two babies were sent to an isolation hospital nearby.

This isolation hospital has a special wing of five rooms each holding one bed or two cots. These rooms were in a suite and each had a separate door. In spite of these conditions two other babies already in the ward became infected with *E. coli* O55 B5 H2 with the antibiotic stamp of the epidemic strain, one baby being infected two weeks and the other six weeks after these babies had been admitted for isolation.

Other Hospitals. All the hospitals and institutions mentioned in this report are in the county of Glamorgan, but it was known that there were extensions into hospitals in the neighbouring county of Monmouth. No serious attempt was made, however, to follow the trails into the next county where there were many cases with at least three deaths.

Part Played by Adult Carriers

To the problem of how infection spreads within an institution this report makes no contribution. When gastro-enteritis spreads in a babies' ward it is customary to suspect the adult staff of playing a part in spreading it, either by failing to observe the techniques to prevent cross infection or by acting as carriers of the infection. When children suffer from salmonella food-poisoning or dysentery, carriers are not infrequently found among the adult staff. In studies of outbreaks of gastro-enteritis nurses and other adult attendants can rarely be shown to be infected. It has been pointed out that the difficulty of finding small numbers of these special varieties of *E. coli* when outnumbered by other *E. coli* in faeces is a great one, and many excretors may thus fail to be identified.

In the outbreaks reported here, bacteriological examinations were made of nurses, doctors and other attendants. In Llandough Hospital, 19 were examined and none found positive; in the small paediatric hospital, 16 were examined and none found positive. In Church Village Hospital, 44 were examined and one male nurse was found to be excreting *E. coli* O55 B5 H2. This was the antigen

structure of the epidemic strain but the sugar fermentation reactions and the sensitivities to antibiotics differed from those of the epidemic strain. In the residential nursery 19 adults were examined and one found to be excreting the epidemic strain of *E. coli* O55 B5 H2. Four, however, were found to be excreting *E. coli* O111 B4 H6. Three weeks previously six members of the staff, including the four harbouring *E. coli* O111 B4 H6 at the time of examination, had suffered from diarrhoea, and it was difficult to avoid the conclusion that *E. coli* O111 B4 H6 was connected with this incident. *E. coli* O111 B4 H6 was isolated also from three babies in the nursery.

When Baby Philip P. was examined in his own home and found to be excreting the epidemic strain *E. coli* O55 B5 H2 (he was the baby suspected of having carried the infection from Church Village Hospital to the small paediatric unit) it was decided to examine his family. No member of the family was found to be excreting O55 B5 H2, but the father was excreting *E. coli* O111 B4.

Thus it happened that seven adult contacts were found to be harbouring pathogenic varieties of *E. coli*, but only one was excreting the epidemic strain.

If there is a moral to this investigation it is to stress the danger of admitting small babies to hospital direct from another institution and that there is much less risk of a baby contracting infection at home than in hospital.

Summary and Conclusions (Parts I and II)

Pathogenic varieties of *E. coli* were found in 1% of faecal specimens from babies under 1 year old living at home. The infection rate was shown to be at least 25% per annum.

Outbreaks of *E. coli* gastro-enteritis caused by *E. coli* O55 B5 H2 were traced through six hospitals in South Wales. Transference of infection from one hospital to another was shown to be via infected babies.

Infection by pathogenic strains of *E. coli* is common among babies living at home, but there would appear to be a great variation in virulence from variety to variety and our hospitals, by a process of selection, are breeding the more virulent ones. The breeding in hospitals of strains of bacteria of enhanced virulence is not a new observation, but *E. coli* gastro-enteritis presents yet another example.

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