MENINGOCOCCAL INFECTIONS IN BELFAST
CHILDREN 1972-1973

by

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THE incidence of bacterial meningitis in Northern Ireland has been low in recent years but small local outbreaks still tend to occur and because of a high risk of morbidity and mortality it is a condition which must continue to command the respect of physicians and parents alike.

During the winter and spring of 1972-1973 it became noticeable that many more children with meningitis were being admitted to the Royal Belfast Hospital for Sick Children (RBHSC) than in previous years. Between August 1972 and August 1973 there were 83 such admissions as compared with only 20 in the same period of 1971-1972. Closer analysis of the aetiology revealed that the majority of bacterial cases were due to the meningococcus. Included in these figures are children who developed fulminant meningococcal septicaemia with or without meningitis.

Sixty per cent of the meningococcal organisms isolated during the period under review were noted to be resistant to sulphonamides. No preventive method of control of bacterial meningitis is at present available such as has been developed for other potentially life threatening infectious diseases. The effectiveness of sulphonamide administration to contacts is now doubtful in controlling spread of the infection. Reduction in mortality is therefore dependent entirely on the early recognition of the disease and rapid commencement of rigorous therapy. Indeed 5 of the 7 fatal cases in this series died within 12 hours of admission. It is clear that every case of childhood bacterial meningitis is an acute medical emergency.

REVIEW OF MATERIAL

Eighty-three cases of meningitis were diagnosed in the RBHSC between August 1972 and 1973. In thirteen no organism was cultured from the CSF, and because of marked lymphocytosis and no reduction in CSF sugar were diagnosed as aseptic meningitis probably of viral aetiology. One case proved to be due to the tubercle bacillus. Thirteen of the remaining cases, all of whom had typical CSF changes of bacterial meningitis, i.e. polymorph leucocytosis, low sugar level, and high protein concentration, were neonatal in origin and are excluded from the series.

A total of 56 bacterial cases remained, of these 29 were due to the meningococcus as seen on gram stain of CSF sediment or on culture of blood or CSF. The incidence of other organisms isolated was haemophilus 4, pneumococcus 3, and haemolytic streptococcus 1. A final group of 19 cases in which no organism was isolated then remains. Twelve of these were thought to be meningococcal in origin on the basis of, typical findings at post mortem, presence of a purpuric rash, or close contact with a proven case, e.g. the sister of another meningitis patient with
meningococcus isolated from CSF. Of the remaining seven cases in this final group only three had a polymorph CSF leucocytosis, the cells being polymorphs and lymphocytes in the other four. Four of these seven had antibiotic therapy prior to admission.

Table I

| Basis of Meningococcal Diagnosis | Number |
|-----------------------------------|--------|
| CSF Culture                       | 17     |
| Blood Culture                     | 3      |
| Direct Microscopy                 | 9      |
| Strong Clinical or P.M. evidence  | 29     |
| Total                             | 41     |

Table 1 summarises the 41 cases of meningococcal infection and the basis on which the organism was implicated. Eighty-five per cent of cases of bacterial meningitis admitted were meningococcal. All but two children were of pre-school age and 70 per cent of infections occurred in the first two years of life (Table II) with the youngest patient from whom the organism was isolated being only 2 months of age. Seven of the 41 children had an acute fulminant meningococcal septicaemia and died, i.e. 17 per cent of the patients. Age, sex and social class in fatal cases reflected the overall pattern. The youngest fatality was 3 months of age. All these fatal cases had evidence of a fulminating septicaemia and had widespread confluent purpuric rashes at death. Autopsy was carried out on five, four had bilateral adrenal haemorrhages and one a massive pulmonary haemorrhage. Geographical

Table II

| Age     | No. of Cases | Fatalities |
|---------|--------------|------------|
| 0-1/2 yr.        | 5            | 1          |
| 1-1 yr.          | 7            | 2          |
| 1-1 1/2 yr.      | 12           | 2          |
| 1 1/2-2 yr.      | 4            | 1          |
| 2-2 1/2 yr.      | 5            | 1          |
| 2 1/2-3 yr.      | 2            | 0          |
| 3-3 1/2 yr.      | 3            | 0          |
| 3 1/2-5 1/2 yr.  | 3            | 0          |
distribution (Table III) may merely reflect the hinterland of the hospital but the possibility of a localised pocket of infection was discussed with the Medical Officer of Health. The geographical distribution was not reflected by admissions to the Northern Ireland Fever Hospital in the same period. Seasonal distribution is in keeping with reported epidemic patterns, i.e. late winter and early spring peak. The peak incidence built up from two cases admitted in December, five in January and again in February, six in March, to nine in April before falling off again to only 1 case in July. Early observations during the same period of 1973–1974 indicate a repetition of the pattern.

| Area      | No. | Area      | No. |
|-----------|-----|-----------|-----|
| Belfast   | 11  | Armagh    | 1   |
| Belfast   | 12  | Down      | 2   |
| Belfast   | 13  | S. Antrim | 2   |
| Belfast   | 14  | N. Antrim | 1   |
| Belfast   | 15  | Other Areas | 2 |

An important finding in examining the organisms isolated at the Royal Victoria Hospital Laboratory was that 60 per cent of these were sulphamamide resistant on standard testing. All these organisms were sensitive to ampicillin, penicillin and chloramphenicol. Of organisms isolated from fatal cases 50 per cent were resistant to sulphamamide. Three of the fatal cases were treated using a high dose intravenous ampicillin regime and four with traditional triple therapy. Considering all organisms isolated from the total 56 bacterial cases only one other organism showed resistance to any of the 4 mentioned antibiotics. This was a pneumococcus resistant to sulphamamide.

**CLINICAL FEATURES**

**Case 1**

A nine month old boy presented with a history of irritability and being “off his feeds”. The parents were worried because he seemed very drowsy. Hospital referral was because of an absence of a cause for his pyrexia of 101°F. Shortly after admission he was observed to have a convulsion of short duration. Lumbar puncture was performed and CSF analysis revealed a low sugar, polymorph leucocytosis and high protein concentration. Meningococci were not observed on Gram stained smears but were subsequently cultured. Intravenous triple antibiotic therapy with penicillin, sulphamamide and chloramphenicol was commenced. Within 48 hours he was obviously improved and demanding food. Parenteral antibiotics were continued for 7 days until the CSF was normal. Recovery was full and uneventful.

**Case 2**

This eight month old boy was noticed by his parents to be a little out of sorts and irritable before going to bed on the evening prior to admission. He spent a restless night and woke his parents with grunting and groaning. He had a nasal discharge in
the morning and when bathing the child the mother noticed there was a rash like red pin points on his abdomen around 9 a.m. Shortly afterwards he became very drowsy and his mother now noticed the rash had spread to his legs and buttocks. She brought him straight to RBHSC Casualty and reported his eyes had been rolling on the journey. On examination he was found to be collapsed with a widespread ecchymotic rash. He was admitted to the Intensive Care Unit at 11 a.m. Intravenous fluids, triple antibiotic therapy and hydrocortisone were administered. LP produced clear CSF with no abnormal findings, but from which meningococci were subsequently grown. One hour after admission the child suffered a cardiac arrest but was resuscitated using intracardiac calcium chloride and adrenalin. He was intubated and ventilated but 7 hours after admission again had a cardiac arrest from which he could not be resuscitated. Autopsy revealed bilateral adrenal haemorrhages.

These two cases vividly illustrate the difference between the simple case of meningitis which progresses slowly and presents with classical signs and this rapidly fatal form of the infection.

Spectrum of Disease

There is a wide spectrum of meningococcal infection ranging from asymptomatic carrier states, which have been demonstrated in 37 per cent of populations in some series, to a fatal, acute fulminant meningococcal septicaemia. When invasion from the upper respiratory tract occurs resulting in a bacteraemia, dissemination to many organs may occur. The infection most commonly presents with involvement of the meninges and the skin causing signs of meningitis and a purpuric rash. Joints, myocardium, adrenal glands, ears, eyes and lungs may also become involved by the bacteraemia.

Presentations and Progress

All practitioners recognise the classical signs of meningitis but these only occur in children past the toddler stage. The diagnosis of meningitis in infants is usually based on the analysis of cerebrospinal fluid. Lumbar puncture in this age group is carried out most often because the other common causes of a pyrexia, e.g. otitis media, tonsillitis, etc. have been excluded on clinical examination. Not only may Kernig's sign be negative and neck stiffness be absent, but there may not even be a pyrexia and bulging of the fontanelle, usually the most reliable sign in infants, may not occur. Nevertheless, the experienced physician or parent readily recognises these children are ill because they are apathetic and listless until disturbed when they become irritable and fretful. They may have vomiting and on occasions diarrhoea which can be diagnostically misleading. Without exception they feed poorly if at all. Active parenteral antibiotic therapy at this early phase in the illness usually leads to full recovery.

In the acute fulminant meningococcal infection, included in this paper under the grouping of meningococcal meningitis for simplicity, there can be a similar poverty of signs, and in our experience even C.S.F. analysis in the early hours of the illness has normal indices and is not helpful. In this situation the first diagnostic sign is the appearance of a few fine petechial spots, usually on the abdomen, chest or anterior surface of the legs. Exanths are said to occur in two thirds of all meningococcal infections and must always be sought for diligently. Its presence is
always a major cause for alarm and dictates immediate hospital admission, as in
fulminant cases it heralds or coincides with rapid deterioration, onset of shock and
convulsions which inevitably proceed to irreversible coma and death. Since treat-
ment beyond the stage of shock usually fails, early parenteral antibiotics are
imperative. Fulminating infection can occur rapidly in a healthy child within hours,
or after some time in an untreated case of meningococcal meningitis.

DISCUSSION

There was a definite increase in the number of admissions to RBHSC with
meningococcal infection during the period under review. The geographical survey
gives some support to a theory that a pocket of infection existed in the Belfast 12
area but this is not proven. To strengthen this theory it would be necessary to
demonstrate an increased carrier rate. Variable peaks of incidence occur under
normal conditions when the carrier rate is 25–35 per cent of the population but in
epidemics the carrier rate has been shown to rise to 70 per cent or more. It is
possible that the overcrowded living conditions which predispose to meningococcal
outbreaks (Ducker, 1968; Martin, 1972) exist in some areas of Belfast at present.
It is worth noting that the number of cases of acute meningitis reported to the
Registrar-General has risen sharply each year since 1967. Eleven were reported in
1967 and 51 in 1972. Certainly it will be important to watch the incidence of
meningitis over the next few years.

The case histories have demonstrated the difference in clinical presentation
between meningococcal meningitis and the acute fulminant septicaemia, emphasis-
ing the extreme importance of early diagnosis. In our series, morbidity in survivors
has been low. The commonest finding has been behaviour disturbances noted in
15 per cent at review. Most of these disturbances may occur in any group of
children in the pre-school age group after a hospital admission for acute illness.
Examples are: extreme shyness amounting almost to fear of strangers, reticence
to mix or play with other children, nightmares, bed wetting, refusal to leave
mother’s company, aggressive behaviour and temper tantrums.

TREATMENT

No clear advantage of the traditional triple antibiotic therapy over the more
modern regime of a high dose of ampicillin (400 mg/Kg. body wt. in 4 divided
doses 6 hourly) was demonstrated. The finding that 60 per cent of organisms were
sulphonamide resistant would suggest that the latter treatment should now be
preferred, especially when one bears in mind the perhaps overstated danger of
blood dyscrasias with chloramphenicol. Several studies have demonstrated the
efficacy of high dose ampicillin regimes in all types of bacterial meningitis including
that caused by Haemophilus organisms (Jenson, 1968; Werle, 1969; Mathies, 1972).
Ampicillin however has not been shown to be effective in eradicating throat
organisms in carriers and sulphonamides are obviously no longer useful in this
field. The two best drugs for prophylaxis in the families of patients are phenoxy-
methicillin and erythromycin. These will often not eradicate organisms but should
abort bacteraemia. Antibiotic therapy of patients sensitive to penicillin is difficult
and fortunately we did not have this problem. Chloramphenicol and tetracycline are recommended and for sensitive organisms sulphonamides.

The major problem which remains to be overcome is the successful treatment of fulminant septicaemia which so often results in death from the Waterhouse-Fredrichson syndrome. Current thinking is that the pathogenesis of the condition is a Schwartzman type reaction. This was first described as a reaction in animals to endotoxin in which there is clotting disorder blocking small blood vessels, vessel wall necrosis and haemorrhage. The phenomenon is thought to be unrelated to hypersensitivity and antigen – antibody reactions. The hallmark of this reaction is fibrin thrombi in small blood vessels. This has been demonstrated in meningococcal sepsis probably due to meningococcal endotoxin (Margaretten, 1958; Levin, 1965).

The condition is also associated with acute coagulation abnormalities resulting in hypofibrinogenaemia, thrombocytopenia, consumption of clotting factors, and a haemorrhagic diathesis (Evans, 1968; Manios, 1971). This was seen clinically in one of our patients. The role of this mechanism in the precipitation of adrenal haemorrhage is not proven, and when the disseminated intravascular coagulation (DIC) is controlled, as was our experience, death can still result from irreversible shock. It is important nevertheless to search for DIC and initiate early treatment with advice from an experienced haematologist, because although early intravenous heparin will arrest the process, if given at a late stage it may potentiate bleeding and fresh blood is more useful. Danger signs are (i) oozing at venepuncture sites. (ii) Sudden appearance or worsening of purpura. (iii) Shock or unexplained hypotension.

Hydrocortisone has not been demonstrated as effective prophylaxis of adrenal haemorrhages but pharmacological doses should not be withheld when shock is evident.

Death in the fulminant disease may be due to cardiac dysrhythmia and early warning can be obtained by monitoring serum potassium (Mauger, 1971). Although this is often normal at time of admission the patients often become hypokalaemic within 4–6 hours. If this situation is revealed, intravenous correction will be required with continuous ECG monitoring. In the presence of tachycardia with gallop rhythm rapid digitalisation is indicated to prevent fatal pulmonary oedema and cardiac impairment. We recorded two instances of hypokalaemia and one patient actually developed cardiac failure.

**Conclusion**

Meningitis must be considered in all children who have a pyrexia without an immediately obvious cause. In view of the increased incidence we have demonstrated, the possibility of meningococcal aetiology must be borne in mind especially where the patient is of pre-school age. A normal C.S.F. excludes this infection in most instances but continued observation is essential for 12 hours as the exception is the potentially fatal fulminant meningococcal septicaemia. Where there is any positive sign of meningitis, or in the infant group when such signs are often absent,
further investigations are important even when the C.S.F. is clear. Blood culture may grow organisms even when the C.S.F. proves sterile. A platelet count may give warning of impending disseminated intravascular clotting. Electrolyte estimation may reveal dehydration or hypokalaemia the correction of which may avoid cardiac complications. These latter tests are especially important in the fulminating disease where they probably offer the only hope of saving life. Treatment with intravenous ampicillin in high dose is recommended commencing as early as possible in the infection and is of equal efficacy for all the common organisms. This means that on occasions treatment should be started on the basis of clinical diagnosis alone where signs are unequivocal. The increased incidence of sulphonamide resistance of the meningococcus demonstrated raises problems in prophylactic treatment of contacts.

**Summary**

An increase in the incidence of admissions to the Royal Belfast Hospital for Sick Children (RBHSC) due to systemic meningococcal infection during the period August 1972 to August 1973 is demonstrated. A high mortality rate due to fulminant meningococcal septicaemia occurred. Reasons for the increase are discussed on the basis of age, sex, seasonal and geographical distribution, and the possibility of a pocket of infection in one area of Belfast, at that time, is raised. Presentation, pathogenesis and complications of the fulminant infection are described and treatment suggested, including the use of a high dose ampicillin regime as opposed to the traditional triple therapy. A high incidence of sulphonamide resistance in isolated organisms is noted. High index of suspicion, early diagnosis, hospital admission and initiation of treatment are emphasised as the most important methods of reducing fatality in what remains a serious childhood disease despite all recent advances in treatment.

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