Prophylactic antibiotics in children

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IT HAS BEEN estimated by some authorities that as much as 90 per cent of antibiotics are prescribed unnecessarily and in themselves cause adverse reactions ranging from trivial to fatal in 21 to 29 per cent of cases (Hobart, Reiman and D'Ambola 1966). One of the main reasons for wastage of antimicrobials is unnecessary prophylactic use.

The term prophylactic antibiotics refers to the administration of antibiotics to uninfected individuals who, for some reason or other, are in danger of acquiring a bacterial infection. The paediatrician has to decide whether to prescribe or withhold antibiotics in these cases, and it is unfortunate that in many instances, there are inadequate data on which to base a firm decision.

It is the purpose of this paper to study critically the evidence for and against prophylactic antibiotics and suggest an approach that seems rational for specific situations in which clear guidelines are not available. In this paper, antibiotic prophylaxis in the foetus and newborn, infancy and childhood and in paediatric surgery will be reviewed.

Antibiotic Prophylaxis in the Foetus and Newborn

Antepartum infection and prolonged rupture of foetal membranes

Smith, Jennison and Langley (1956) gave streptomycin and oxytetracycline to mothers with presumed intra-partum infection, while they were either in labour or after their membranes had ruptured, and claimed this reduced the perinatal mortality by preventing infection of the foetus. The number of cases they studied was small and birth weight and gestation were not mentioned. In a later communication, Langley & Smith (1959) were unable to show that perinatal mortality was reduced.

Eastman (1958) found that the perinatal mortality rate during a period when penicillin was given to mothers with prolonged rupture of membranes was not different from the rate observed before the advent of penicillin. Lebherz et al. (1963), in a double-blind study involving 1,896 women, found that antibiotics do not alter the perinatal mortality of infants of mothers with premature rupture of membranes.

There is an increased risk of infection in infants born after protracted rupture of the foetal membranes (Pryles et al., 1963) but there is no conclusive evidence that the incidence of infection in the infant is influenced favourably by treatment of the mother. The routine administration of antibiotics to infants born after prolonged membrane rupture has also not been found beneficial nor desirable (Pryles et al. 1963).

Reasonable recommendations for infants who emerge from an apparently infected environment would be to give antibiotics only to those infants who appear ill at birth after swabs are obtained from the nose, throat and umbilicus, and after C.S.F., urine and blood are examined and cultured. The rest should be labelled suspect and observed closely for signs of

possible infection and if this appears, treatment should be started after appropriate culture materials are obtained. In infants of febrile mothers, it may be wiser to collect all culture material before signs appear so this information might then be available, without undue delay, should treatment become necessary.

Prematurity

Small premature infants usually exhibit few clinical signs early in the course of serious infection, and treatment is often not successful. In an attempt to improve survival, antibiotics are prescribed routinely in some nurseries. The effectiveness of this policy has not been established by a critical trial.

The aim should be to prevent infection by keeping the infant's environment as bacteriologically clean as possible by effective handwashing rather than by the widespread use of antibiotics, as this may alter the balance of flora and encourage resistant organisms. Any infant who develops vague non-specific signs which indicate possible infection, particularly after a period of well-being, should be treated after appropriate culture materials have been taken.

Epidemic staphylococcal infections and coliform diarrhoeas in nurseries

Staphylococcal colonisation of the newborn occurs at a high rate but is infrequently associated with disease (Wolinsky, Gonzaga, & Mortimer, 1962). Occasionally, an epidemic strain may appear and cause high rates of major and minor clinical staphylococcal disease, and may be difficult to terminate especially when complete closure of the unit may not be possible. Under these circumstances, mass prophylaxis with appropriate antibiotics to all babies in the nursery and those subsequently admitted to the unit until the infant population has been turned over completely at least twice, has been found usually effective in terminating the epidemic (Mortimer 1968). Mortimer has recommended that any infant shown by culture to have acquired the organism should be treated for at least 10 days in the hope of eradicating the strain.

Outbreaks of epidemic diarrhoea in nurseries are usually due to enteropathogenic E. coli. Effective antibiotic therapy has been shown to be of value in controlled trials (Medical Research Council, 1953) and is useful in the prevention of cross-infection and relapse and stopping epidemics. Effective therapy rapidly reduces the number of enteropathogenic E. coli organisms and decreases the manifestations of clinical illness (Yow 1963). Although the findings of Riley et al. (1964) cast doubt on the advisability of administering antibiotics to every person from whose stool enteropathogenic E. coli is isolated, it is recognised that although many cases of E. coli disease are mild, the course is unpredictable in newborns. Mortimer (1968) recommends closing the unit completely or mass prophylaxis along the lines described for epidemic staphylococcal disease. In both instances, he has emphasised that the institution of mass prophylaxis does not eliminate the need for other control measures, including efforts to identify carriers of the offending organisms.

Respiratory distress and meconium aspiration

There is no clear evidence to support the use of antibiotic prophylaxis in respiratory distress. But in some cases, it may be difficult to distinguish pneumonia from respiratory distress and antibiotics may then be offered as treatment for possible pneumonia and not merely as prophylaxis.

The use of antibiotic prophylaxis in meconium aspiration is controversial as no controlled studies are available. Avery (1968) recommends prophylactic antibiotics as the differential diagnosis between bacterial pneumonia and meconium aspiration is difficult and also because intra-tracheal meconium has been shown to enhance the susceptibility to E. coli infection in rats. Although the reaction in the lungs is a chemical pneumonia, the lungs at autopsy often show evidence of both aspiration and pneumonia.

Antibiotic Prophylaxis in Infancy and Childhood

Rheumatic fever and sub-acute bacterial endocarditis

It is generally accepted that rheumatic fever is casually related to streptococcal throat infections in childhood. There is proof from large scale trials that treatment of streptococcal throats by penicillin reduces the consequent rheumatism (Houser & Eckhard 1952). There is no evidence, however, that rheumatic fever, after a streptoccal infection, can be prevented in all cases by treatment of such patients, and continuous prophylaxis in patients who have experienced one attack is recommended (Cantanzaro et al. 1958). Continuous prophylaxis can be best achieved by benzathine penicillin and oral penicillin, or sulphonamides to a lesser extent, because of failture to take the drug (committee on prevention of rheumatic fever and bacterial endocarditis 1965). Accordingly, all children with rheumatic fever, with or without valvular heart disease, should receive prophylaxis. The duration of prophylaxis is uncertain but it is accepted

that the risk of carditis becomes negligible in adult life.

It has been found that 48 per cent of cases of sub-acute bacterial endocarditis follow dental infection or dental extraction (Cates and Christie 1951). The infection is preceded by a bacteraemia caused by organisms which are nearly always sensitive to penicillin. One injection of penicillin prior to operation should deal with the bacteraemia and prevent the disease. The penicillin umbrella was accepted on theoretical grounds without clinical proof. It is now too late to test the theory as it would be considered unethical to expose patients as controls to such a disease. Penicillin cover is now mandatory during dental procedures in susceptible patients. Patients already on continuous penicillin prophylaxis for rheumatic fever are liable to have penicillin resistant streptococcus viridans or staphylococci in the mouth and should be covered by a different antibiotic, such as erythromycin.

Acute viral respiratory disease

In a double blind study of 60 infants with undifferentiated respiratory disease (i.e. rhinorrhoea, nasal congestion, pharyngeal erythema, cough, rhonchi or noisy breathing but excluding pneumonia, croup, bronchiolitis, exudative tonsillitis, otitis media), antibiotics (penicillin, tetracycline) were found to be of no benefit either in shortening the mean duration of the illness or in preventing secondary complications (Ackerman 1968). Davis and Wedgwood (1965) reviewed the subject of antibacterial prophylaxis in common cold, influenza, measles and other viral respiratory disease. They concluded that antibiotics have no effect on the primary course of viral respiratory disease and thus have no place in their primary treatment. Prophylactic antibiotics have not been shown to prevent bacterial complications and since certain risks are associated with their use, they are contraindicated.

Anatomical abnormalities of urinary tract and recurrent urinary tract infections

Children with obstructive urinary tract lesions are predisposed to pyelonephritis. The routine administration of antibiotics can only be expected to provide resistant flora which is more refractory to treatment. Therapy should be directed at correcting the underlying abnormality and vigorously treating any infections after appropriate bacteriological investigations.

Petersdorf et al. (1957) found that prophylactic antibiotics neither prevented nor ameliorated infection of the bladder in patients with indwelling urethral catheters. They served only to ensure that the infection, when it develops, will be by a highly resistant organism, even more refractory to antibiotics. These data suggest that antibiotic prophylaxis is of no benefit and is distinctly hazardous.

There are no established criteria for determining how long medical treatment should be continued in children with recurrent urinary tract infections. The usual practice is to treat those with an anatomically normal urinary tract who have suffered two or more relapses for a minimum of six months, and if infection recurs after six months, treatment is re-instituted and continued for a year or more. The same regime is also followed in children with chronic infection complicating an inoperable anatomical anomaly. In many cases, it is difficult to control the infection completely but it may be possible to reduce the bacteriuria and control symptoms by continuous antibiotic therapy.

Freeman et al (1967) reported a study concerning the treatment of 225 adult patients with chronic bacteriuria.

Relapses occurred after 13 months in 50, 42, 21 and 87 per cent of patients receiving sulphamethizole, nitrofurantoin, methenamine mandelate and a placebo respectively. This study suggests that significantly better control of infection was achieved using methenamine mandelate than with other compounds. Practitioners will undoubtedly encounter difficulties in giving long-term treatment in Malaysia, but reasonable explanation should win their co-operation.

Kerosene poisoning

There are no controlled studies concerning the effects of prophylactic antibiotics administered to children with kerosene poisoning. It is difficult to differentiate superimposed bacterial infection on kerosene pneumonitis. Mortimer (1968) is of the opinion that the early administration of antibiotics as prophylaxis would do nothing more than alter the flora thereby predisposing to infection with resistant organisms.

Unconscious patients

Petersdorf et al (1957) have shown that the administration of antibiotics to unconscious patients is of no benefit as 45 per cent of prophylactically treated patients developed pulmonary complications whereas pneumonitis occurred in only 15 per cent of the controls. They concluded that antibiotic prophylaxis was

distinctly hazardous owing to the emergence of resistant strains.

Nephrotic syndrome, steroids, haematological disorders, X-radiation and antimetabolic drugs

Children with nephrotic syndrome, those receiving steroids, X-radiation or antimetabolic drugs and those with certain haematological disorders, like leukaemia and agranulocytosis, are extremely vulnerable to bacterial infections because of compromised defences. Continuous antibiotic prophylaxis will not prevent such infection which will instead occur with resistant organisms more refractory to treatment. Antibiotic prophylaxis is, therefore, not recommended; instead careful observation for infection should be conducted and appropriate antibiotic therapy instituted when bacterial infection is recognised.

Local therapeutic measures

Tracheostomies, intravenous canulae and umbilical catheters create portals of entry for infection. Although antibiotics are routinely given to infants in certain centres, the value of this practice is questionable. Bhatt et al (1970), in a recent study of infants with umbilical catheters, found no difference in the incidence of infections in a control group and a group given antibiotics prophylactically. Prophylactic antibiotics can only be expected to produce infection with resistant organisms.

Antibiotic Prophylaxis in Paediatric Surgery

Burns

Parenteral antibiotic prophylaxis has not been efficacious in the treatment of burn patients. But topical application of mafenide (sulphamyion) or 0.5 per cent silver nitrate or gentamycin has been shown to be effective. Teplitz and Moncrief (1964) have shown a reduction in the infection rate (mainly with pseudomonas) from 88 per cent to 22 per cent and also a significant reduction in mortality from 42 per cent to 0 per cent in a 30 to 40 per cent burn and from 59 per cent to 30 per cent in a 40 to 50 per cent burn following the use of sulphamylon.

Cerebrospinal fluid rhinorrhea and otorrhea

This usually follows trauma to the head. Some close spontaneously after a few days or weeks while others persist for months or years and predispose to recurrent attacks of meningitis. Close medical supervision is required in cases where attempts to correct the fistulas are unsuccessful. As the most common cause of meningitis in these cases is the pneumococcus (Whitecar, Reddin & Spink, 1966), it has been considered reasonable to institute continuing penicillin prophylaxis.

Post splenectomy

Horan and Colebatch (1962) reviewed the literature and then followed up with a study of 142 patients on whom splenectomy was performed in childhood. They found the incidence of subsequent serious infection (meningitis, septicaemia, pneumonia, sub-phrenic abscess, etc.) was 12 per cent, and 80 per cent of all serious infections occurred in infants within two years of surgery. The infecting organism is usually pneumococcus and the course of the infection is usually fulminating with high mortality. Following splenectomy, long-term penicillin prophylaxis is considered advisable as almost 75 per cent of recorded infections were due to penicillin sensitive organisms.

Clean surgical operations

Barnes et al (1959) conducted one of the large trials reported. Long-acting penicillin and streptomycin were given post-operatively to 45 per cent of 1,007 cases while the remainder served as controls. The infection rate was 11.4 per cent in those receiving antibiotics and 9.8 per cent in the controls. They concluded that prophylactic antibiotics did not reduce the incidence of post-operative infection. Tachdjian and Compere (1957) reported similar findings.

Potentially infected operations

Johnstone (1963) found the wound infection rate amongst patients who were having potentially infected operations, such as colostomies, was 38.5 per cent in those who had antibiotics and only 17.6 per cent in those who received no prophylactic treatment. But he still recommends selective use of prophylactic penicillin to prevent clostridial infection. McAdams (1960) considers sterilisation of the gut unnecessary as it tends to lead to other organisms, such as pseudomonas and proteus, becoming pathogenic.

Traumatic wounds

Experiments have failed to clarify the effects of antibiotics administered to patients with potentially infected surgical wounds. Burke (1961) has shown that wound sepsis in guinea pigs may be averted by the administration of antibiotics before surgery and to a lesser extent if administered an hour or two later. Penicillin is useful in reducing the danger of infections of wounds by gas gangrene and possibly tetanus

and is therefore used in most cases of accidental wounds in clinical practice (Walker 1966).

Discussion

The dangers of antibiotic therapy have been extensively reviewed (Murdoch 1966). Indiscriminate and widespread use of antimicrobials, especially in hospitals, not only leads to outbreaks of serious hospital-acquired and antibiotic-resistant infections but also increases the incidence of iatrogenic disorders and adds to the cost of medical care.

Prophylactic antibiotics are used for a wide variety of reasons based more often on impression rather than the results of controlled trials. A critical review of the literature reveals that antibiotic prophylaxis is generally not effective in preventing infection, except in a few specific situations. It is useful in patients who have had acute and transient exposure to a specific organism and also in patients who are chronically or recurrently at risk from a specific organism which has continuing sensitivity to an antibiotic of limited spectrum. Patients, whose defences are compromised over prolonged periods and who are susceptible to infection with multiple organisms or organisms known to develop resistance readily, usually do not benefit from prophylaxis.

The situations in which antibiotic prophylaxis is useful are limited. The use of silver nitrate or penicillin in the prevention of gonococcal ophthalmia is well documented (Barsam 1966). Recurrent attacks of rheumatic fever can be prevented by continuous prophylaxis. Penicillin cover during dental extractions is useful in patients susceptible to sub-acute bacterial endocarditis. There is evidence that prophylaxis is useful following splenectomy in infants and in cases of cerebrospinal fluid rhinorrhoea in whom surgery has not been successful. Penicillin can be used in serious accidental wounds to prevent gas gangrene or tetanus, while topical applications of sulphamylon, silver nitrate or gentamycin have a definite place in the management of burns.

In most other instances, there is no clinical evidence to indicate that antibiotic prophylaxis is useful and is generally contra-indicated.

Summary

A critical review of the literature reveals that prophylactic antibiotics are generally not effective in preventing infection except in a few specific situations.

Prophylaxis is useful in preventing:—

1. Recurrent attacks of rheumatic fever.
2. Sub-acute bacterial endocarditis following dental procedures.
3. Gonococcal ophthalmia.
4. Post-splenectomy infections.
5. The spread of staphylococcal infections and coliform diarrhoeas in nurseries.

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