Drug Treatment of Disease

DRUG TREATMENT OF INFANTS AND CHILDREN SUFFERING FROM PNEUMONIA

BY

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The treatment of infants with pneumonia has always differed from that of older children because of the different pathological conditions commonly encountered in the two groups—namely, bronchopneumonia in infants and lobar pneumonia in children. To-day, however, lobar pneumonia has become comparatively rare; this change is related to the higher incidence of viral infections and possibly to a decline in the prevalence of pneumococci. Viral infections of the lung tend to spread more widely and are seldom the cause of lobar consolidation. In infancy, when staphylococci, *Haemophilus influenzae*, or Friedländer's bacillus are more likely causative organisms than pneumococci, the lesion resulting is usually bronchopneumonia. The same, or similar, drugs are therefore indicated in most cases for both age groups.

It is easy to say that the drug which should be used is the one to which the infecting organism proves most sensitive, but it is singularly difficult to ascertain with any degree of certainty what the infecting organism is in young children, who notoriously swallow what sputum they produce, and it is unwise to withhold treatment pending the results of any investigations. This has naturally led to the prescription of one or more of the "broad-spectrum" antibiotics from the outset, and it is indeed difficult not to uphold this rationale on occasions. What is important is that chemotherapy should not be used merely as a febrifuge. Aspirin is just as effective in reducing fever and much less dangerous. Not every infant with a cough and fever is starting bronchopneumonia; definite physical signs should be evident before a course of antibiotic therapy is prescribed.

Lobar Pneumonia

As lobar pneumonia, though less frequently seen than formerly, still occurs and is the most straightforward pulmonary infection to be encountered, the appropriate drug therapy for affected children will be described first. "Stosstherapy," the large single dose, is the treatment *par excellence* and is nearly always successful. Sulphonamides are the first choice. Sulphapyridine is the most active against pneumococci, but, because it is more toxic than the later compounds, it is little used now. Of the later compounds, sulphadiazine, sulphathiazole, and sulphadimidine are all reliable and efficient. It is wise to combine two or more sulphonamides, because this diminishes the risk of renal complications; sulphamerazine in particular has been reported as causing crystalluria and is therefore better avoided, especially in young children, whose urinary output may be difficult to assess with any certainty. The diazine, thiazole, and dimidine compounds may well be prescribed in equal parts. At 2 years of age 1 g. of this mixture would be an adequate dose; at 3 years, 1.5 g.; and from 4–5 years, 2 g. It is seldom necessary to exceed 3 g. in childhood. Sulphafurazole is also of

value and has the advantage of more ready solubility; the dose is the same as for the triple mixture.

If vomiting is a prominent feature, or if the drug is vomited when administered, penicillin should be given intramuscularly. From 1,000,000 units at 2 years to 2,000,000 units at 5 years of age should be sufficient. In either case no further specific treatment should be necessary for acute pneumococcal lobar pneumonia.

Attention thereafter is directed solely to the child's general condition and not to the physical signs in the lungs: these will follow the normal course, and their disappearance is in no way expedited by the stoss-therapy. In other words, the continued presence of slight fever and the persistence of bronchial breathing for two to three days are not an indication for further treatment, provided the child's general condition is steadily improving.

If, in the early stages, a frequent, irritable and painful cough is present, Gee's linctus (linctus scillae opiatu *B.N.F.*) may be given in doses of 30–60 minims (1.7–3.5 ml.) until relief is obtained. No other drug therapy is required.

Bronchopneumonia

In the treatment of infants with bronchopneumonia it is always helpful if there are any indications of the nature of the causative organism. In the presence of epidemics, or of the infection previously of an older sibling or adult in the household, it is possible that the organism may be known and the most suitable antibiotic be thereby determined. Similarly, in the newborn period it is likely that the organism will be a staphylococcus or *Escherichia coli*. Pertussis, even in unimmunized infants, may not be accompanied by whooping, and the diagnosis will be suspected from the spasmodic nature of the cough, by its being worse at night, and by many of the spasms ending in a bout of vomiting.

Unfortunately bronchopneumonic infants are not good subjects for stoss-therapy; nevertheless, every attempt should be made to give maximal dosage of whatever antibiotic is chosen and to give this for the shortest possible time. No antibiotic acts selectively on the lungs and all are apt to exert unfavourable influences elsewhere in the body. In infants one special risk is that of thrush, which in the presence of antibiotics appears to have an enhanced virulence. Moreover, it may not only spread from the mouth to the gut but even enter the smaller blood vessels and become systemically disseminated, with grave risk of fatal pulmonary moniliasis. Further, it is well known that antibiotics administered for any length of time interfere with the natural intestinal synthesis of members of the vitamin-B complex, and they may induce diarrhoea, which will add greatly to an infant's task in successfully overcoming his bronchopneumonia. If, for any reason, treatment has to be

continued for more than a week, extra vitamin B should be given throughout the subsequent course.

Whether an antimonilial drug should also be given prophylactically is more debatable. It is probably preferable to exercise greater care with the oral hygiene and with the preparation of the infant's feeds, because the prophylactic use of such drugs as nystatin may indeed lead to the emergence of resistant monilia organisms if they succeed in gaining entry into the infant's mouth in his debilitated condition.

Neonatal Pneumonia

Newborn infants may acquire a pneumonic infection before, during, or immediately after birth. In the first two cases some knowledge of the infecting organism may be gained from bacteriological examination of the mother (blood culture, culture of the liquor amnii, or culture from a high vaginal swab). In the case of infection acquired in the newborn period the organism will usually be a staphylococcus or *E. coli*.

The chief difference in treatment depends on whether the infant has been born in hospital or at home, because the chances of a penicillin-resistant staphylococcus in hospital are too great to allow of the use of penicillin as the antibiotic of choice. At home, penicillin will probably be successful. In hospital, streptomycin is the most useful drug and may be prescribed in doses of 125 mg. twice a day intramuscularly (62.5 mg. for infants weighing less than 5 lb. (2.25 kg.)), usually for two or three days. At home crystalline penicillin, 250,000 units, should be injected as soon as the diagnosis is suspected, followed by procaine penicillin 250,000 units daily until the infection is controlled. If there is reason to believe that *E. coli* is the infective organism, streptomycin should be given as above. If there has been no response to penicillin, prompt change to streptomycin should be made because lack of response would suggest that the organism was either resistant or insensitive to penicillin. In older infants the choice of the main drug will be determined, as previously indicated, if there is any clue to the likely organism—for example, chloramphenicol in pertussis—the dose varying from 125 to 250 mg. every 4–6 hours. Treatment should preferably be discontinued after a week or ten days. The risks of producing aplastic anaemia are remote when compared with the good results which may be expected from this antibiotic. Chloramphenicol is likewise indicated if *H. influenzae* is suspected, but treatment does not usually need to be continued for so long.

Pneumonitis

In the recurring episodes of pneumonitis to which infants with mucoviscidosis (cystic fibrosis of the pancreas) are so often subject, chlortetracycline ("aureomycin") is the antibiotic of choice. Its dose is the same as that of chloramphenicol. It may indeed also be used, in smaller dosage, as a continuous prophylactic, but, if it is, regular bacteriological examination of the flora should be undertaken. In these cases the main infecting organism is the staphylococcus, but after continued treatment with chlortetracycline *E. coli* may become dominant, and then the antibiotic should be changed.

When infants have repeated attacks of lower respiratory infection, a search for the underlying pathological condition must not be omitted. There may be a congenital cystic lung, for example, or the infections may be due to a general disorder such as agammaglobulinaemia. Investigation should therefore

include examination of the sweat, bronchography, and plasma electrophoresis—each providing positive evidence of mucoviscidosis, cystic lung, and agammaglobulinaemia respectively.

Of the many other antibiotics available, all may be of value if resistant strains of organisms are present and should be tried if adequate response is not forthcoming after the treatment already recommended for the conditions described. There is seldom any indication for combined antibiotic therapy. Synergism is rare, and there is no great advantage in combinations which are simply additive. *Moreover, if the dose prescribed of any of the various members of a mixture is suboptimal, antagonism may occur and resistant organisms may emerge.*

Virus Infections

There remain the infections caused by viruses—an important and seemingly growing group—for which there is no specific treatment yet. Antibiotics may give rise to resistant organisms; erythromycin and novobiocin are perhaps least likely to do so, but they should be kept for special cases and not used in the first instance except in an epidemic in which other antibiotics have proved valueless and one or other of these has proved helpful. The dose is 50–100 mg. 8-hourly. A recent introduction is an intramuscular preparation of erythromycin (50 mg. of erythromycin ethylsuccinate in 1 ml. propylene glycol), which may prove of special value in acutely ill infants and children and when vomiting is a feature of the illness. Parenteral treatment should be replaced by oral therapy as soon as possible.

In the initial treatment of an infant with bronchopneumonia it is usually as well to assume a bacterial origin and to prescribe a broad-spectrum antibiotic of the tetracycline group (aureomycin, "terramycin," "achromycin"). The dose should be about 25–50 mg. per lb. body weight per day (12–25 mg. per kg.). Failure of response within two to three days would suggest that the infection was viral; the only value then of continuing antibiotics would be to prevent secondary infection, but it is probably preferable to revert to penicillin if such cover is thought necessary. A suspension of potassium phenoxymethylpenicillin (penicillin V) given by mouth may well be as beneficial as intramuscular injection and certainly makes management of the infant easier. The dose is 30–60 minims (1.7–3.5 ml.) twice a day. This is the equivalent of 100,000 to 200,000 units of crystalline penicillin twice daily. Treatment should always be continued until the infant's general condition is satisfactory and the temperature has been normal for 24 hours.

Symptomatic Treatment

Symptomatic treatment may be of value in addition to chemotherapy. Cough is often troublesome in infants with bronchopneumonia, and on auscultation there are usually copious moist rales. A mixture such as the following may then be prescribed, a teaspoonful diluted to be taken three or four times a day.

Ammonium carbonate	...	2½ gr. (160 mg.)
Sodium bicarbonate	...	2½ gr. (160 mg.)
Potassium iodide	...	1 gr. (65 mg.)
Liquid extract of liquorice	...	10 minims (0.6 ml.)
Peppermint water	...	to 60 minims (3.5 ml.)

If spasm is a feature, relief may follow the administration of an antihistaminic combined with a sedative. Suitable drugs are mepyramine maleate

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To-day's Drugs

With the help of expert contributors we publish below notes on a selection of drugs in current use.

Strepsils Antiseptic Lozenges (Boots).—Each lozenge contains 2:4-dichlorobenzyl alcohol 1.2 mg. and amyl-*m*-cresol (6-pentyl-*m*-cresol) 0.6 mg. in a hard sugar base. This also is an antibacterial preparation for local use against minor infections of the mouth and pharynx.

Iversal (Farbenfabriken Bayer (Distributors: Levmedic)).—Each troche contains ambazone (1:4-benzoquinone aminohydrazine thiosemicarbazone hydrate), 10 mg. This inhibits the growth of haemolytic streptococci and pneumococci in high dilution but has no action against coliform bacteria, and so will probably not disturb the intestinal flora.

Neither of these preparations contains any of the more generally used antibacterial agents, and organisms resistant to them are unlikely to cause trouble. They may therefore have some value in treating minor infections in the mouth and pharynx, but are not likely to be suitable if a severe buccal or pharyngeal infection develops, when antibacterial drugs given systemically would be indicated.

N.H.S. basic price: strepsils, 24 lozenges, 1s. 8d.; iversal, 15 troches, 2s. 4d.

Steroxin Ointment and Dusting Powder (Geigy).—These are chloroquinaldol 3% in an ointment (non-greasy base) and 5% in a dusting powder.

Although superficial infections of the skin are very often treated with antibiotic ointments, an antiseptic such as steroxin still has a valuable place. It is perhaps most useful in superficial infections such as intertrigo, moist infected seborrhoeic dermatitis, infectious eczematoid dermatitis, and other types of eczema with superadded secondary infection. The response of lesions of this kind to treatment is often difficult to predict, and it is easy to make the eruption worse with an application which is irritant or sensitizing. In the treatment of these difficult eruptions steroxin occupies an honourable position; in effectiveness it compares well with many of its rivals and it is very unlikely to irritate. It can be combined with other bases such as Lassar's paste and it can be mixed with hydrocortisone ointment, sometimes with great benefit.

N.H.S. basic price: 4 oz. ointment, 6s.; 30 g. powder, 1s. 8d.

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("anthisan") 5–25 mg. with pethidine 5–10 mg., the lower dose being suitable for infants of under 6 months and the higher for those between 6 months and 1 year of age. This may be repeated as necessary.

Finally, although tuberculosis is much less common in infants and children than it was, it still occurs. The value of the Mantoux test must not be overlooked, for in tuberculous bronchopneumonia the substitution of isoniazid and streptomycin for other antibiotics tried previously will rapidly improve the child's condition. But the treatment of tuberculosis will not be discussed in detail here.

In overwhelming infections, both tuberculous and non-tuberculous, steroid therapy may prove life-saving. Hydrocortisone, given by mouth in doses of 5–10 mg. twice daily for three or four days, should certainly be tried, provided always that it is accompanied by adequate antibiotic therapy.

Correspondence

Aetiology of Coronary Disease

SIR,—Dr. J. N. Morris and Dr. Margaret D. Crawford (*Journal*, December 20, p. 1485) have given us a fascinating study of the relationship between coronary heart disease and physical activity of work. I hope they will extend their inquiries, for, although other studies in which they are engaged on somatotype and occupation may add something, they have, as they themselves remark, shed no light so far on the personality factors involved both in taking exercise or, for that matter, in taking this or that form of diet.

Recently at the request of Dr. S. Savage, who for preventive purposes was seeking some quick and suitable means of recognizing people predisposed to coronary disease, I calculated the frequency per thousand of various somatotypes in the series of young men with coronary thrombosis reported by Gertler and White.¹ Next I calculated the frequency per thousand of similar somatotype groups in W. H. Sheldon's distribution of 46,000 American men. Dividing the first frequency by the second gives a ratio which indicates which somatotypes succumb most often to coronary thrombosis in early middle life, and which types are relatively free. An abbreviated list of results is given below in which the ratios have been multiplied by 100 to express the risk of coronary disease as a percentage of general expectation. Descriptions of physique in each somatotype sector may be found elsewhere.²

Somatotypes Highly Disposed		Percentage of General Expectation
Sector Mf	Near somatotype 451	1,915
	Near somatotypes 352, 353	440
	Near somatotypes 461, 361, 362	314
Sector Fm	Near somatotypes 641, 541	757
Somatotypes Less Disposed		
Sector Ml	Central	21
	Lm	51
	Lf	55
	Lm	rare
	Lf	rare
	Fl	rare

Thus, although it is a dominantly muscular build which seems most disposed, it is the fat muscular build which carries much the highest risk. The risk for lean muscular builds is lower and they may include more bus conductors than drivers in their ranks, more postmen than Government clerks. Physical disposition to coronary disease appears to vary from negligible levels of risk to levels 10 or perhaps 20 times general expectation. That this risk may be recognized in terms of physique makes it possible for men most in need to take precautions, while those of more linear build, who incidentally are more often prone to anxiety, may be exempted from unwelcome exercise, spared unnecessary restriction or alteration in their diet, and relieved of inappropriate foreboding.—I am, etc.,

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Oxford.

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REFERENCES

- Gertler, M. M., and White, P. D., *Coronary Heart Disease in Young Adults*, 1954. Harvard University Press, Cambridge, Mass.
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