

UPPER RESPIRATORY INFECTIONS IN CHILDREN

Different syndromes require different approaches to therapy

Each infant and child under six years of age may suffer up to five episodes of upper respiratory infections per year, with a peak incidence in children aged less than two years. The majority of these infectious episodes are due to the simple cold, but nearly one-third may result in otitis media or sore throat combined.

Besides social and economic factors associated with high infection exposure such as nursery school attendance, inadequate housing and crowding, recognised independent risk factors include passive smoking and lack of breast-feeding.

The clinical approach to children with an upper respiratory infection includes asking questions to identify the particular syndrome of localising infection: eg. is there a blocked or runny nose with nasal stuffiness, is there sore throat or earache. Mothers have been shown to be accurate in their description of difficult or rapid breathing in children with acute lower respiratory infection.

You need to find out also the systemic effects of that infection, such as fever, poor feeding, vomiting or lethargy. Thereafter a careful clinical examination will serve to categorise the infection as "non-specific" or localisable to pharynx/tonsils or middle ear.

The reason for differentiating the various syndromes of upper respiratory infections lies in the different approaches to therapy. In the common cold, the host response to the infecting virus is mediated by inflammatory cytokines and is an important contributor to pathology and symptoms. Therapy is directed against the specific symptoms that are most bothersome to the patient. Fever should be treated with antipyretics, but decongestant or antihistaminic preparations have been shown to be useful only in children over five years, adolescents and adults. Antibiotics are not necessary unless fever persists or returns and symptoms change to include worsening cough, sore throat or earache.

In general, antibiotic therapy of upper respiratory infections has not been shown to shorten the duration of the disease or to prevent the development of otitis media, lower respiratory infection and pneumonia. Furthermore, cost-effectiveness studies have shown an advantage in withholding antibiotics in the treatment of acute bronchitis and treating only those whose cough does not resolve^{1,2,3,4,5}.

Upper respiratory symptoms do not

necessarily imply an infection, even if they appear to have started acutely. Many children with upper respiratory allergy present with complaints of nasal discharge, blocked nose, mouth breathing and a dry sore throat. There may be persistent cough. The differentiating clues consist of absence of fever in the usual case, a generally well child despite the respiratory symptoms and the pale glistening nasal mucosa of allergic rhinitis. There may be a family history of atopy, and the tell-tale signs of dark rings around the eyes and transverse crease on the bridge of the nose may be present.

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The symptom of cough has a multifactorial origin including secretions in the upper and lower airway, airway narrowing by spasm or mucosal oedema, irritation by chemical or physical inhalants or foreign bodies, as well as referred and psychogenic causes. Accordingly, antitussive medication should be carefully selected for its intended effect. Cough suppressants are inappropriate where expectoration of secretions is the aim and decongestants should not be used if the lower airways are involved, owing to the risk of inspissated secretions plugging small airways.

Where a *sore throat* is the presenting symptom without much other evidence of upper respiratory infection, the treatment strategy is aimed at identifying and eradicating Group A beta haemolytic streptococcal infection (GAS)^{6,7,8,9}. This infection is more common in children than in adults with sore throat. Even though the majority of sore throats are not caused by streptococci, the risk of rheumatic fever or post-streptococcal glomerulonephritis exists in untreated or partially treated patients even in affluent communities. All patients with pharyngitis or tonsillitis must therefore have an adequate throat swab taken for the following reasons:

- The diagnosis of streptococcal infection can not be made clinically with a high enough degree of accuracy. More

than 50% of patients with exudative tonsillitis, tender lymphadenopathy, fever and absence of cough will have GAS infection, but in the absence of the above signs, the differentiation of viral and bacterial throat infection is not possible.

- Most patients are poorly compliant with drug-taking once they are symptomatically improved, commonly by the third day. It has, however, been demonstrated that less than a five-day course of macrolides and cephalosporins or a 10-day course of penicillin is not sufficient for adequate bacteriological eradication of GAS infection. A positive throat swab culture accordingly serves to reinforce compliance and reduce the risk of recurrence.
- In culture-negative patients the antibiotic can be stopped early to reduce unnecessary antibiotic exposure and the development of resistant bacterial populations. Where direct GAS antigen detection tests are available, it is recommended that antibiotic therapy can be deferred in the presence of a negative test till the culture result becomes available.
- In recurrent sore throats, throat swabs are mandatory to identify chronic GAS carriage, possible resistance and their eradication by treatment.

In treatment of the sore throat, symptomatic therapy with antipyretics and locally-acting analgesic mouth washes or lozenges is probably as important as antibiotic therapy. The rational choice of antibiotic rests on a number of considerations, including the bacteriological diagnosis, local resistance patterns to penicillin, compliance and cost. There is no difference in clinical response rates between penicillin and the cephalosporins, though bacteriological cure rates are reported to be a little higher for the cephalosporins. Intramuscular benzathine penicillin remains a good option where compliance is suspect. Apart from the benefit of infrequent doses in a short course of therapy, the newer macrolide antibiotics offer no clinical advantage over penicillin, but they are useful in penicillin-allergic patients. Where tonsillitis recurs frequently, tonsillectomy should still be considered, but it is important to remember that enlarged tonsils do not necessarily imply infection.

The diagnosis and management of acute otitis media remains controversial^{10,11,12,13}. While otalgia is an important symptom, not all children with acute otitis media complain of earache. A careful otoscopic examination is therefore essential in

patients with upper respiratory infection. The child with a uni- or bilateral dull red bulging tympanic membrane can be differentiated from the child with general hyperaemia of the upper respiratory mucosa of nose, conjunctiva and also the ear canal in viral upper respiratory infection. There is a tendency to over-diagnose the latter patients as having otitis media and introduce antibiotic therapy with little clinical effect.

Bacteria can be identified in the middle ear fluid of about two-thirds of patients with acute otitis media, these consist of *Streptococcus pneumoniae*, *H aemophilus influenzae* and *Moraxella catarrhalis*. Clinical studies suggest that only about one-third of these patients would require antibiotics to clear their signs and symptoms; these are usually infected by *S.pneumoniae*, but are not identifiable on clinical grounds. As routine tympanocentesis for microbiological culture is not feasible in patients with otitis media, antibiotic therapy is therefore still recommended with the aim of eradicating pneumococcal infection. Unfortunately, increasing resistance to penicillin and cotrimoxazole amongst community-acquired pneumococci requires the use of second-line drugs such as cephalosporins, amoxicillin-clavulanate or macrolides.

All cases of acute otitis media require follow-up, as *middle ear effusion* develops and persists for a considerable time, leading to the risk of persisting infection and conductive hearing loss. The results of medical therapy for persisting middle ear effusion with antibiotics, nasal decongestants to maintain Eustachian tube patency, or with steroids, are inconsistent and therefore controversial. Patients whose middle ear effusion has not improved by 4-6 weeks should be referred for audiological assessment. Tympanostomy tubes are successful in establishing middle ear drainage and restoring hearing, but the criteria for placement are controversial.

Some children appear to suffer from upper respiratory infections more frequently than should be expected. The cause is to be found in the environment (recurrent exposure, smoking) or in the host (chronic underlying condition). Further evaluation and investigations are mandatory if the child's symptoms never clear up completely in between the exacerbations, if there is loss of weight or failure to thrive, if the child develops new symptoms and signs, and if her clinical response to standard management is slower than usual or otherwise complicated. In such cases, the initial investigations should include a chest X-ray, tuberculin skin test and full blood count including ESR. ●

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CHOLESTEROL

Dr Saville Furman
talks to Dr Dave Marais

We seem to be living in an age of "cholesterolomania" where everybody seems fixated about having their cholesterol checked. People go for finger pricks to the pharmacist and consult us saying they have high cholesterol and someone suggested they should be on Zocor, Prava, Lescol, etc. Can we look at some of the things that influence either false low, or false high readings, and does one really need fasting levels?

Let's first talk about the fasting state. If we consider only the plasma cholesterol test and not the triglyceride, then it's quite okay to test the blood without being in the fasted state, because the meal will add very little cholesterol to the plasma in the immediate post-prandial effect. Of course, a high fat diet over several weeks will change the blood cholesterol. For screening purposes, the non-fasted random sample is quite acceptable.

We should also ascertain that the person is in their usual lifestyle and health state when we are assessing that, otherwise we should do repeated measurements to get round recent travel with altered diet or a recent illness, giving different cholesterol concentrations to the usual. In terms of illnesses there can be quite a striking lowering of cholesterol, sometimes even up to 30% with severe illnesses, ranging from influenza to surgery and even myocardial infarction. These changes usually take about a day or two to come into effect, so if one tests somebody immediately after a myocardial infarction, one can still get a reasonable value. If one is testing, for example, at the chemist, then that sort of perspective is not often given, because the focus is really on the fingerprick and the result that comes from it.

That in itself is another problem because poor technique often results in diluting the cholesterol or the blood in the process of trying to obtain the sample and then one gets a false low value.

Would you treat a patient on one reading?

One should never. I think one can take action, especially if the reading is extremely high, but if one is looking at the more usual cholesterol ranges, it is better to have an idea of two or three readings so that one can be more certain about the baseline. It is usually better in that second to do more detailed testing including triglyceride, HDL and probably Lpa at least once.

Talking about little "a", what really is the value of little "a"? You mentioned we should do it as a once-off only.

Little "a" is becoming established as an independent risk factor which seems to increase the risk by two- to threefold for coronary artery disease in Westernised subjects. If one has a borderline decision about instituting treatment, additional information such as little "a" can be quite useful and the cut-off there is usually about 300 units per litre.

Can we now look at HDL ... Should we be particularly worried if we see a patient with a raised HDL?

The dogma is that the more HDL cholesterol there is, the less the risk of heart disease, and I think that still holds true. However I would like to make some remarks to put it in a bit more perspective. The first is that the rest of patient's information is important. HDL can be falsely low with acute phase response similar to the total or LDL cholesterol going down after anything from severe influenza to myocardial infarction. But if there is an inherited low HDL that predisposes to coronary artery disease, the family history will usually support that. There are some conditions with low

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HDL cholesterol where the risk for coronary heart disease is not increased and one is thinking particularly of rare conditions such as fish-eye disease where the cornea is opacified and the patient has a low HDL cholesterol but no increased risk of coronary artery disease. There is another setting of a very low HDL cholesterol called Appo A 1 Milano where a mutation in Appo A 1 renders the reverse transport of cholesterol through HDL so rapid that the concentration drops and this associated with longevity and the clue in both of these instances is that the family history is not supportive of a high risk of coronary artery disease.

Between HDL cholesterol levels of about 0.9 and 1.6 there is very good evidence that the HDL plays a role in determining the risk of heart disease. HDLs of about 1.6 to about 2.5 are likely to protect further. However when one gets to HDL cholesterol levels of more than about 3, one has to consider a couple of obvious secondary causes and then some rare genetic disorders causing that. The secondary causes would be alcohol excess and taking microsomal inducing agents like Phenytoin or the other secondary disorders, hypothyroidism which may be having an effect on the lipoprotein profile without necessarily having clinical manifestations. Then there are the rare genetic disorders giving HDL cholesterol more than 3. They are not very well understood.

Let's turn our attention to the clinical evaluation.

You mentioned that looking at the Achilles tendon was quite an important clinical factor. Please comment.

A thick Achilles tendon due to a xanthoma is a serious physical finding in the sense that it is associated with significant metabolic errors in sterol metabolism. Although it is generally held that the disorder is due to an LDL receptor defect such as is well established in several communities in our country, it's also possible that the defect lies in the Appo B which carries the cholesterol in LDL. In both cases the internalisation of LDL back into the cell will be retarded and with this reduced clearance the plasma cholesterol will build up. Normally these patients have total cholesterol levels of more than 8 or frequently even higher, such as 10 or 11 mm per litre and the risk of heart disease is very high. Men generally die of coronary heart disease in their forties and women in their fifties.

The new buzz words are "body mass index" and "waist-hip ratio". How important are these?

I think it is becoming increasingly important to consider obesity as a risk factor because it confers insulin resistance. The higher insulin concentrations can promote atherosclerosis as well as hypertension and some dyslipoproteinaemia and obesity is an influence on it. The body mass index is probably a poorer guide because it does not take into account where the adipose tissue lies. Generally people believe that body mass index is unimportant until it's in the range of 28 to 30, at which stage obesity is diagnosed, but survival figures show that an ideal body mass index is approximately between 20 and 24, and the average probably 22kg/m². There is evidence that obesity also alters the vascular endothelial reactivity and it is also associated with mild hypertriglyceridaemia and a mild reduction of HDL cholesterol, both of which are also more atherogenic. It has more latterly become fashionable to discriminate between male or central obesity and the gynoid or peripheral obesity. In the central obesity there is a higher prevalence of the metabolic abnormalities outlined for obesity and the waist-hip ratio should ideally be less than 0.85.

What sort of diet are you advocating your patients follow and at what level, when it does not work, do you think about adding medication?

I think it is important always to address the lifestyle factors, among which I think diet is one of the most important. Apart from looking at the impact of diet on body weight, it is also important to look at the impact it has on the lipid profile. What is generally not appreciated is that the recommended diet for the prevention of heart disease is being applied for the treatment of dyslipopro-

teinaemia. The usual measures that we all know, which are to remove the skin from the chicken and the visible fat from the foods and to prefer fish and poultry, are correct in that they will reduce the plasma cholesterol a small amount and this will impact in a population on quite a lot of prevention of coronary heart disease. But when one is dealing with an identified dyslipoproteinaemia, it is important to be more aggressive and more specific about the dietary modification. In this context, one will usually benefit much from using a professional dietician and a quantitative analysis. This takes time but really pays dividends in the response that the patient will get and he or she will very quickly realise that a lot of the fat can still come hidden in the diet. It is not obvious to the person consuming the diet that there is a high fat intake and it is particularly a problem because many of our foodstuffs are not particularly labelled according to their fat content. If such a diet is done quantitatively and intelligently then certain preferred foods with higher fat content can actually be calculated into the diet so that the daily amounts of fat that influence the metabolism remain satisfactory.

Now, if all these lifestyle measures fail, one has to still decide on certain concentrations of LDL cholesterol according to which one will respond. In the setting of primary prevention, the patient can either be in a low risk category, that is fewer than two risk factors, or in a high risk category, which is more than three risk factors. The risk factors include being a male over 40 or a post-menopausal female or having a low HDL cholesterol below 0.9 or persistent smoking or diabetes or hypertension or a family history of premature ischaemic heart disease. In the low risk setting the target LDL cholesterol is 4.2 but one will accept an LDL cholesterol of up to 4.9 as not being significant predisposition to coronary artery disease. In the high risk primary prevention category the target LDL cholesterol is 3.5 and one could well accept an LDL cholesterol up to about 3.2 but higher than that it may be necessary to take action with drugs. In secondary prevention it is recommended that the target LDL cholesterol is 2.5mm/litre. According to more recent studies, however this is not always easy to obtain and *one should insist on at least a 25% reduction of cholesterol if the target cannot be achieved.*

Do you know of any non-drug way of raising the HDL level?

HDL can increase with losing weight, with exercise and it may also increase with the consumption of alcohol, but the exercise has to be quite regular for a significant amount, in the sense that one has to have a decent acceleration of the heart rate, approx. 45 minutes at least three times a week.

Finally, a lot of patients feel that once they are on cholesterol-lowering drugs, they do not have to worry about diet. Can you comment on this?

I think certainly being on a good fat-modifying diet will reduce the household budget for food, as basically those foodstuffs are cheaper. It would also result in weight loss which has other beneficial effects as well and a very low fat diet would also influence platelet behaviour and other aspects of haemostasis in a better fashion, as well as reducing the LDL cholesterol, which is one of the main aims of treatment. So for the same change in cholesterol the diet I suspect is of more benefit than the drug. Obviously it is ideal to combine diet and drug for the best benefit of the patient.

If a patient regularly takes medication, can they eat what they like without affecting their cholesterol level?

The diet will still change the plasma lipoproteins even if a person is on lipid modifying medication. This can lead to a lot of confusion if the patient changes the diet and the drug is introduced because the efficacy of the drug can then not be established. But the two modes of treatment have their action independently, so that the one does not really modify the other. They do however add together in reducing the risk for heart disease. ●

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