

STRAMA

The Swedish Strategic Programme for the Rational Use of Antimicrobial Agents

Swedish guidelines for the treatment of
rhinosinusitis, pharyngotonsillitis and acute
media otitis in children.

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The pharmacological treatment of rhinosinusitis

Main points

- 1 Rhinosinusitis is traditionally defined as an inflammatory condition of the nasal cavity and paranasal sinuses and may have several causes. The aetiology of the rhinosinusitis is crucial to the choice of treatment and should be an integral part of the diagnosis.
- 2 Symptoms and clinical signs do not establish or exclude the presence of bacterial infection with any certainty.
- 3 Spontaneous resolution of sporadic bacterial rhinosinusitis is common.
- 4 Adults with mild to moderate pain in the maxillary area in association with a cold of less than ten days' duration should be recommended symptomatic treatment.
- 5 Patients with a high fever and swelling and/or severe pain over the sinuses should be diagnosed and treated promptly irrespective of the duration of the illness.
- 6 Antibiotic treatment should be considered for adults with cold symptoms of more than 10 days' duration and who have marked pain in the cheeks/teeth.
- 7 In doubtful cases or if the patient has had recurrent attacks, radiological diagnosis and possibly diagnostic sinus puncture may prove helpful.
- 8 Unilateral symptoms for more than three weeks require investigation.
- 9 The investigation of recurrent or persisting rhinosinusitis should focus on causative factors and associated problems, e.g. allergy, nasal polyposis and hyperreactivity.
- 10 Children with uncomplicated bacterial rhinosinusitis do not need antibiotic treatment.

The definition of rhinosinusitis

The term *rhinosinusitis* has in recent years been used increasingly as a general term for inflammation of the nasal cavity and paranasal sinuses, irrespective of the aetiology. This covers everything from viral or bacterial infection, allergies or other immunological defects, and also reduced aeration of the sinuses as a result of anatomical conditions. The diagnosis should include the identification of the probable cause, and this should be documented in the medical notes.

The diagnosis of bacterial rhinosinusitis

Diagnostic sinus puncture and culture of the aspirate is the most reliable method of establishing a diagnosis of bacterial sinusitis. A positive bacterial culture is obtainable in approximately 60% of

those cases thought to have a bacterial aetiology, mainly *Streptococcus pneumoniae* and *Haemophilus influenzae*. *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* are thought to account for some cases, but the significance of these agents remains unclear. The isolation of bacteria from nasopharyngeal swabs has low predictive value. False negative cultures occur in all diagnostic scenarios.

The presence of fluid on plain X-ray of the maxillary and possibly the frontal sinuses and on ultrasound suggests rhinosinusitis but says little about the aetiology, as fluid may also occur in viral rhinosinusitis. These methods have a specificity of 60% and therefore “overdiagnose” bacterial rhinosinusitis. Radiological evidence of mucous membrane swelling alone does not provide support for the diagnosis of acute bacterial rhinosinusitis. The absence of pathological radiological findings excludes bacterial rhinosinusitis.

The clinical examination should take place after decongestant treatment of the nasal cavity with ordinary decongestant nose drops. It is unusual to find evidence of a purulent discharge in the middle meatus or the nasopharynx, but this is a strong indication of bacterial rhinosinusitis. Evidence of purulent secretion in the nasal cavity may be a pointer. A normal ESR or CRP in an adult with a ten day history of URTI and suspected acute rhinosinusitis argues against a bacterial aetiology.

Management

The diagnosis of acute ethmoid and frontal sinusitis is based on the clinical picture which is characterised by swelling, redness, and pain around the eye in ethmoiditis, and primarily by pain around the eyebrow in frontal sinusitis. These patients are often generally unwell and require antibiotic treatment.

Patients with acute severe pain over the sinuses, swelling or oedema in the face and fever should be seen promptly for diagnosis and treatment irrespective of the duration of the illness.

Patients with cold symptoms for less than 10 days, purulent rhinorrhoea and mild to moderate pain in the maxillary area probably benefit little from antibiotics and should be recommended symptomatic treatment.

Patients with cold symptoms and purulent rhinorrhoea for more than 10 days, with marked pain in the cheek or teeth may, like patients with an obvious deterioration after five to seven days' cold symptoms, obtain some benefit from antibiotics. Antibiotics may be offered to those patients who on examination have:

Probable rhinosinusitis

- 1 Purulent discharge in the middle meatus or nasopharynx.

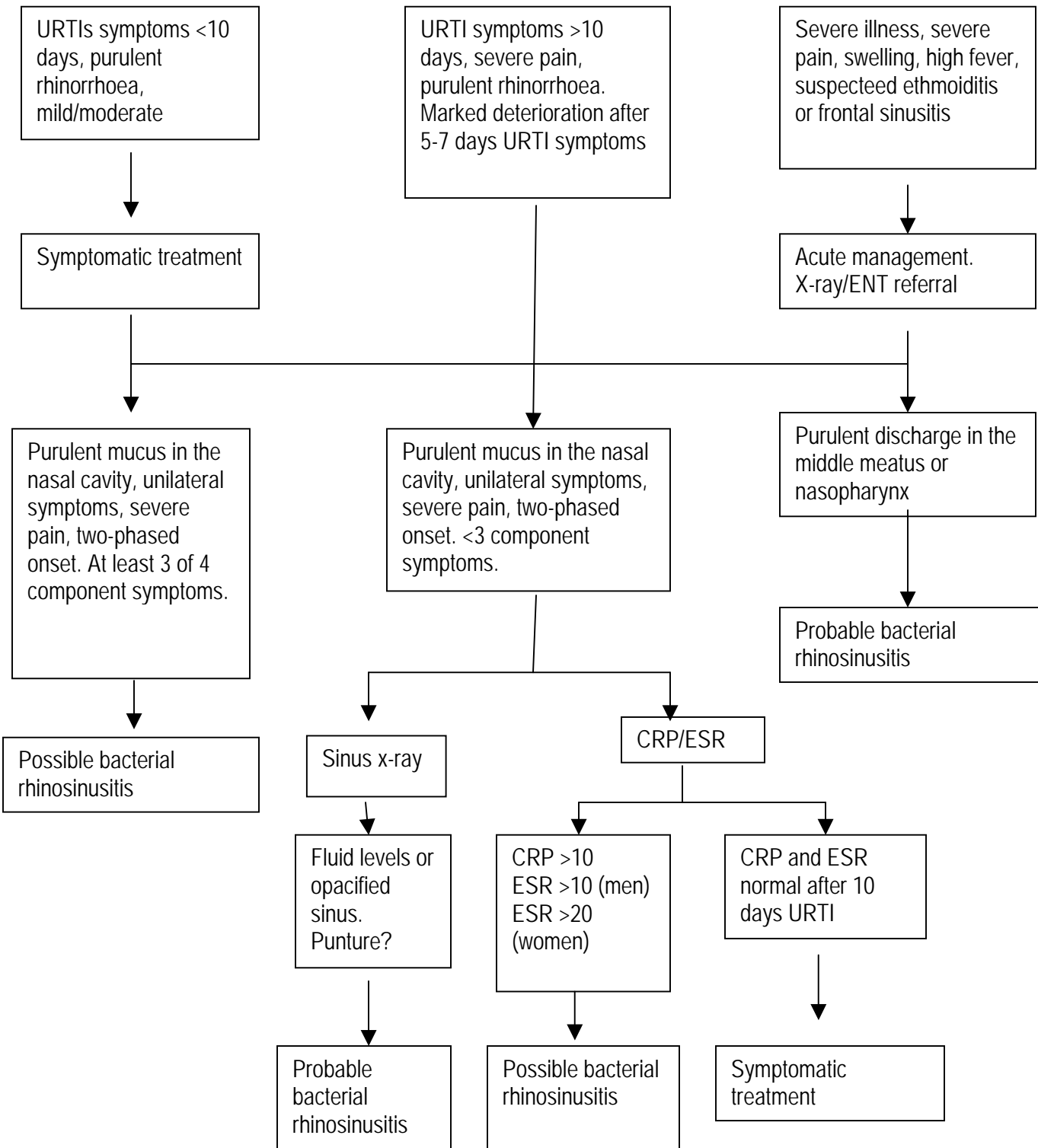
Possible rhinosinusitis

- 1 Purulent mucus demonstrated in the nasal cavity, pronounced pain in the teeth or face, unilateral symptoms and a two phase onset (at least three of four findings).
- 2 Pronounced pain in the teeth or face and raised CRP (>10) or ESR (>10 for men, >20 for women).

In doubtful cases or if the patient has had repeated episodes, radiological investigation and possibly diagnostic puncture can be carried out. Antibiotic treatment can only be justified by the presence of unequivocal ultrasound findings or plain x-ray findings of an opaque sinus cavity or fluid levels.

The potential advantages of antibiotic treatment need to be weighed against any potential adverse side effects, in discussion with the patient (see algorithm Fig. 1).

Figure 1. Algorithm – Management of rhinosinusitis in adults and older children based on symptoms and signs. For the management of patients with probable or possible bacterial rhinosinusitis – see text.



Differential diagnostic considerations

Patients who have persistent unilateral problems three weeks after the onset of the illness and after any attempted treatment need to be investigated with regard to possible dental infection, nasal polyposis and tumours.

Patients with recurrent bacterial sinusitis (>3–4 annually) and those with persistent symptoms need to be further investigated with regard to underlying causes or associated diseases e.g. allergy, nasal polyposis or hyperreactivity. The investigations may include a more detailed history, allergy testing, plain x-ray/CT scanning and endoscopy, possibly in consultation with an ENT specialist.

Antibiotic treatment

The purpose of treatment is to shorten the course of the illness. Complications of rhinosinusitis are rare and may not necessarily be prevented by antibiotic treatment. Bearing in mind the high rate of spontaneous resolution in sporadic bacterial rhinosinusitis and taking into consideration the potential side effects of antibiotics, the patient should actively participate in the decision to give or withhold antibiotic treatment. One way of achieving this is to provide the patient with a prescription with the advice to only cash it at the pharmacy in three to five days if no improvement has been experienced. There is no evidence base for recommending that treatment should last for ten days. From the point of view of the development of resistance, shorter courses may be preferable.

Treatment of choice

Phenoxymethylpenicillin in two to three divided doses for seven to ten days.

For example: 1.6 g three times a day or 1.6–2.0 g twice a day

Tetracyclines can be used in penicillin allergy.

Evaluation of effect

The evaluation of the effect of treatment should be delayed for at least five days, as response to treatment is slower in rhinosinusitis than in tonsillitis and otitis. Treatment failure should prompt a re-evaluation of the diagnosis. If the diagnosis is confirmed, the antibiotic should be changed. Persisting problems warrant referral to an ENT specialist.

Treatment failure or recurrence (new rhinosinusitis within four weeks):

Amoxicillin 1.5 g/day in two or three divided doses for seven to ten days. For pharmacodynamic reasons, thrice daily dosing (500 mg t.d.s.) is preferable.

Amoxicillin is more effective than phenoxymethylpenicillin against *H. influenzae* and pneumococci with reduced susceptibility to penicillin. In microbiologically confirmed infection with betalactamase-producing pathogens, treatment with co-amoxiclav or a tetracycline is recommended.

Patients with treatment failure or recurrence and who are allergic to penicillin can be offered co-trimoxazole or a macrolide (although the latter has an inadequate effect on *H. influenzae*).

Complications

Patients with sporadic rhinosinusitis who have signs of complications (such as spread beyond the sinus or who are markedly unwell) should be referred for a specialist ENT opinion.

Follow-up

Patients with radiologically confirmed frontal sinusitis and other seriously ill patients should be actively reviewed. Others should be reviewed only in the event of inadequate response to antibiotic treatment.

Complementary pharmacological treatment

Symptomatic treatment

Local vasoconstrictors and saline douches provide symptomatic relief but do not influence healing. There is no evidence base for the use of oral decongestants.

Analgesia is often required, paracetamol initially. NSAIDs can also be used once hypersensitivity has been excluded.

Corticosteroids

There is no adequate published scientific documentation that justifies the use of topical corticosteroids as an alternative to antibiotic treatment. Topical corticosteroids can, on the other hand, be used as a complement to antibiotics in the treatment of bacterial rhinosinusitis superimposed on pre-existing allergy or vasomotor rhinitis with hyperreactivity. Previously initiated treatment with topical corticosteroids in patients with allergic or vasomotor rhinitis should therefore be continued alongside antibiotic treatment of sporadic rhinosinusitis. Intranasal corticosteroids can also be used by patients with rhinitis medicamentosa for the relief of symptoms associated with sporadic bacterial rhinosinusitis.

Sinus puncture

Sinus puncture and irrigation is a useful diagnostic tool. It also has therapeutic benefit in the event of antibiotic treatment failure. Repeated washouts can be facilitated by the insertion of a drainage tube.

The management of pharyngotonsillitis

The following recommendations apply to acute pharyngotonsillitis in patients without serious underlying disease. The main recommendations in the guidelines may be summarised as follows:

- 1 Serious complications such as glomerulonephritis and rheumatic fever are nowadays extremely rare and do not in themselves justify the treatment of all throat infections caused by *Streptococcus pyogenes* (*S.p.*).
- 2 The clinical picture will allow the diagnosis of probable viral infection in many patients who consult for sore throat, particularly if coryza and cough are present. Aetiological tests for streptococcal infection, e.g. rapid antigen tests (RAT) should be avoided in these patients.
- 3 Diagnostic tests for bacterial infection are recommended only if the clinical picture suggests pharyngotonsillitis and the aetiological agent is in doubt.
- 4 Patients with clear-cut symptoms and definite clinical or laboratory evidence of *S.p.*-related pharyngotonsillitis should be offered treatment with phenoxymethylpenicillin (penicillin V) for ten days.
- 5 Recurrent infection is treated with a cephalosporin or clindamycin.
- 6 If treatment fails, check the diagnosis!
- 7 Frequent recurrences may justify tonsillectomy, but only after a cephalosporin or clindamycin has been tried.

Background

Streptococcus pyogenes (*S.p.*) is the taxonomically correct term for the bacteria that in ordinary medical parlance are called beta haemolytic streptococci Lancefield group A, Group A streptococci, GAS, GABHS, etc. The abbreviation *S.p.* is therefore used in this document.

Clinical diagnosis

The aim of management of pharyngotonsillitis is to identify those patients that have an infection caused by *S.p.*, for whom the advantages of treatment outweigh the disadvantages. The history should include epidemiological information about possible streptococcal infection in the close environment. The clinical examination should be carried out by a doctor and should, in the case of pronounced pain and swallowing difficulties, also include inspection of the epiglottis, especially if the patient's clinical picture is not consistent with pharyngotonsillitis.

Many patients who consult for sore throat have symptoms caused by viral infection, e.g. cough, coryza, hoarseness, generalised lymphadenopathy or blisters on the palate (Figure 1). These patients can be given a diagnosis of probable viral infection on the history and clinical picture. Aetiological tests for the presence of streptococci should be avoided as the rate of false positives is high in this group of patients.

Older children or adults, who have signs and symptoms that strongly suggest *S.p.* infection (all four Centor criteria, see text box 1) and for which further support for such an aetiology can be found (e.g. proven *S.p.* infection in the close environment), can in certain cases be prescribed antibiotics without further aetiological tests. Rapid antigen testing or throat swab cultures can provide further support, which is particularly important in recurrent infection.

Diagnostic criteria for older children and adults

1. Fever ≥ 38.5
2. Tender cervical adenopathy
3. Purulent tonsils
4. Absence of cough

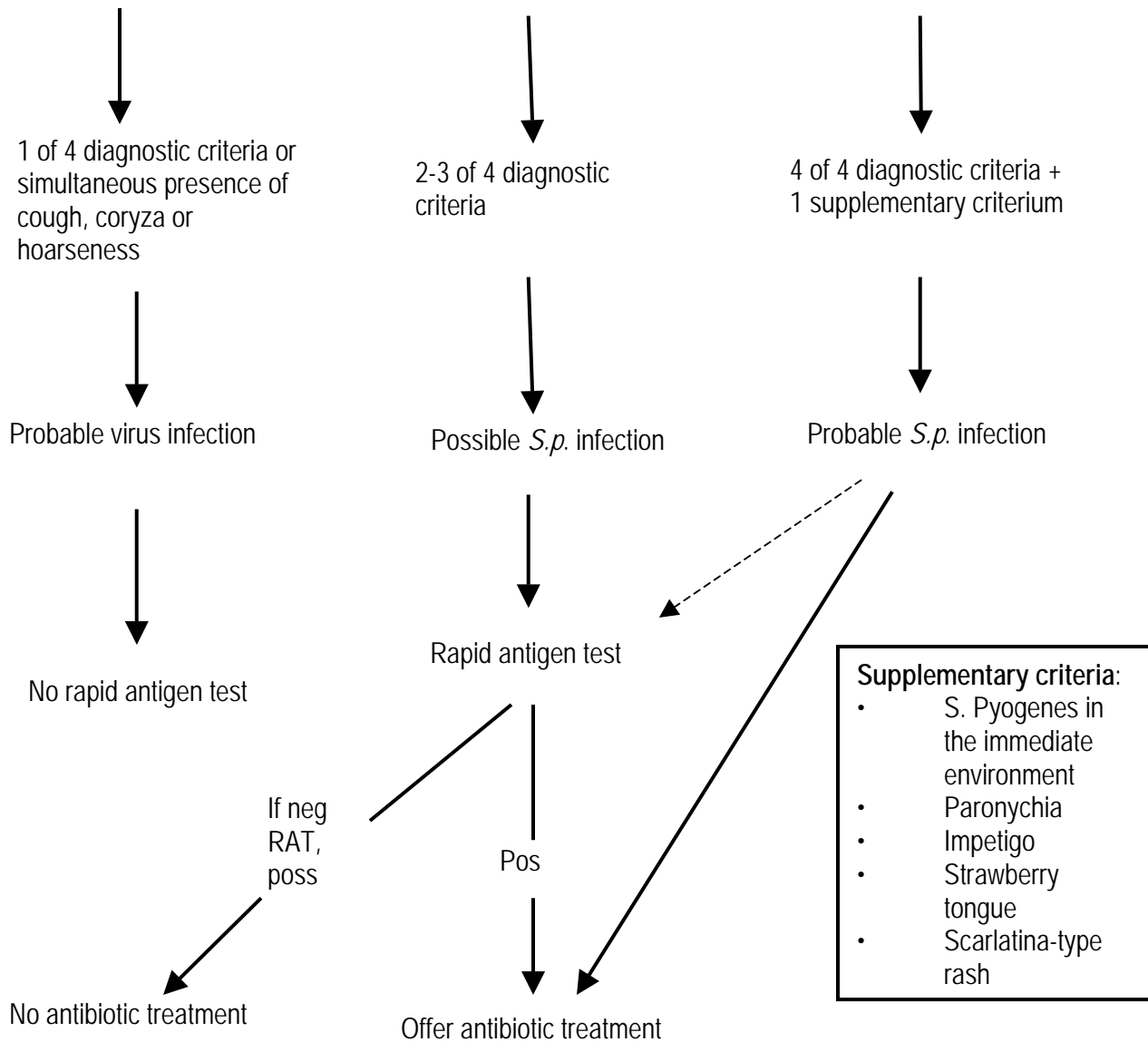


Figure 1.

In small children, pharyngotonsillitis is not a prominent feature of *S. pyogenes* infection. The presence of supplementary criteria may, in these circumstances, justify antigen testing.

Research-based diagnostic criteria according to Centor

(In older children, if all of the following four criteria are met, the sensitivity and specificity for *S.p.* infection will reach 75%).

- 1 Fever³ 38.5 degrees
- 2 Tender cervical adenopathy
- 3 Purulent tonsils
- 4 Absence of cough

Other symptoms and clinical findings that suggest *S.p.* infection

Rapid onset

Severe pain on swallowing

Palatal petechiae

Red and swollen uvula

Strawberry tongue

Circumoral pallor

Angular stomatitis

Scarlatina-type rash

Impetigo

Paronychia

In children under four, pharyngotonsillitis is not a prominent feature of *S.p.* infection, which makes clinical diagnosis more difficult. Features associated with *S.p.* infection include the simultaneous presence of impetigo and purulent rhinorrhoea with sores in the nostrils. An aetiological diagnosis should be sought. A viral aetiology is very common in this age group also. Common symptoms in children with viral infections include rhinorrhoea, cough and feeding difficulties. This group of patients needs no further bacteriological investigation. One should remember that the incidence *S.p.* carrier states is particularly high in this age group, which means that streptococci can be identified in viral illnesses although they lack aetiological significance.

Bacteriological diagnosis

It will not be possible to make a diagnosis of probable *S.p.* infection or viral upper respiratory tract infection on clinical grounds alone in a significant number of patients with pharyngotonsillitis. In addition to a good history and examination, these patients need to be investigated bacteriologically, primarily by rapid *S.p.* antigen tests. Antibiotics should be offered if the result is positive. Conventional bacterial culture can sometimes be justified on epidemiological grounds.

According to the manufacturer, the rapid antigen test (RAT) has a sensitivity of around 95% and a specificity of around 98% compared to culture. These figures are lower in ordinary practice – around 90% sensitivity and 95% specificity. However, variations occur between studies. Good testing technique is crucial to the reliability of both RAT and culture. The swab is rubbed over both tonsils. It should be taken during the clinical examination. Good illumination, e.g. with the aid of a forehead lamp, is a precondition. The result may be misleading if the test is not taken properly.

In order to check regularly that the rapid antigen test's sensitivity and specificity applies to the individual clinic, it is important that there is good collaboration with the local microbiology laboratory and that there is regular participation in an external quality assurance programme. If the RAT is negative and suspicions remain that the aetiology is streptococcal, a throat swab should be taken for culture, as the RAT is unable to detect small numbers of *S.p.* and does not detect streptococci group C or G, which can give rise to the same type of symptom as group A. A recurrence that occurs within a month of completed treatment for streptococcal pharyngotonsillitis requires an aetiological diagnostic test. The RAT can give a transiently false-positive result after antibiotic treatment for streptococcal infection, due to remaining bacterial antigens, which is why culture is preferable in this situation.

Other diagnostic tools

C-reactive protein (CRP) levels and the white cell count are of little value in establishing a diagnosis in the individual case with suspected acute *S.p.* pharyngotonsillitis. Serological tests, such as the antistreptolysin O (ASO) titre and anti-DNaseB, are not useful in the acute setting.

Treatment of pharyngotonsillitis caused by *S. pyogenes*

Primary infection

The treatment of choice is phenoxymethylpenicillin for ten days. Shorter courses carry the risk of recurrence. In penicillin allergy, treatment with a cephalosporin for 10 days (provided there is no history of type 1 allergy), clindamycin or a macrolide (preferably erythromycin) is recommended.

There is no indication for the use of ampicillin derivatives (ampicillin/amoxicillin/co-amoxiclav), tetracyclines, fluoroquinolones or co-trimoxazole. These agents are no more effective and have a higher incidence of adverse effects, resistance development or undesirable environmental consequences.

Treatment failure

In treatment failure, i.e. poor clinical response to continuing treatment, the diagnosis must be re-evaluated and patient compliance assessed. Glandular fever or other types of viral pharyngotonsillitis in combination with streptococcal carrier status, or the development of peritonsillitis must also be considered. *S.p.* is invariably susceptible to beta-lactamase antibiotics (penicillins and cephalosporins), which is why treatment failure never depends upon to resistance

to penicillin or cephalosporins. On the other hand, treatment failure due to macrolide or clindamycin resistance does occur, and in these circumstances a change of treatment should be made after taking a throat swab for culture.

Relapse of infection

A relapse, defined here as the reappearance of infection within a month of completed treatment, should be confirmed by culture or rapid antigen test. Phenoxymethylpenicillin is not suitable if it was used to treat the original infection, as it is associated with a significantly higher risk of a further relapse. A cephalosporin or clindamycin should be used instead. The course should extend to ten days. In penicillin allergy, an antibiotic of a different class to the one used for primary treatment should be used. Infection that recurs more than a month after completed treatment should be managed as a new primary infection.

In relapsing or recurrent infection it is important to try and identify any possible sources of infection in the patient's immediate environment and to swab suspected cases. One should, however, be aware that streptococci may be found in skin lesions such as ulcers, eczema and impetigo, and also in perianal dermatitis, vaginitis and balanitis.

Recurrent infections

Recurrent infection implies at least two infections per six months of which neither qualifies as a relapse. Tonsillectomy should be considered in recurrent infections (three to four per year). A cephalosporin or clindamycin should always be tried prior to any decision.

Asymptomatic carriers should not normally be treated.

Outbreaks of *S. pyogenes* infections in nurseries

S.p. infections in individual children in nurseries are managed in the standard fashion with a ten-day course of antibiotics and confinement in the home for two days or until the child has recovered. In a clustering of cases, i.e. when around one third of the children in a class have confirmed or suspected streptococcal infection, assessment and intervention according to the following points may be justified.

- 1 Confirmation of the outbreak by early evaluation by the responsible doctor/nurse, and the confirmation of a proportion of the clinical cases by rapid antigen testing or culture
- 2 Hygiene guidance for the nursery
- 3 The simultaneous treatment of all children with symptoms and clinical signs of streptococcal infection.

The treatment of acute otitis media in children

Acute otitis media is generally defined as an acute, transient and clinically verified inflammation of the middle ear. These guidelines apply to isolated episodes of acute otitis media in children under sixteen. They do not apply to children prone to acute otitis media, i.e. those who suffer recurrent attacks.

What causes acute otitis media?

Microbiological aetiology and resistance

Bacteria can be demonstrated in 50-70% of all acute middle ear infections. Since the mid-fifties, *Streptococcus pneumoniae* (referred to here as pneumococci) has been a common cause of acute otitis, whilst *Streptococcus pyogenes* (referred to as group A streptococci), which had previously been a greatly feared aetiological agent, is seldom seen nowadays. *Haemophilus influenzae* and *Moraxella catarrhalis* are other common infectious agents, whilst other species of bacteria, including anaerobic bacteria, are uncommon causes of otitis.

It is common knowledge that acute otitis is often preceded by upper respiratory tract infection. Viruses, therefore, are an accepted cause of acute otitis, usually in combination with bacteria. It has been estimated that as many as 75% of all patients with acute otitis have a concomitant virus infection, and viruses can be found in the middle ear in up to 50% of patients. Viral infection affects the ability of the epithelial cells to prevent bacterial adherence and has a deleterious effect on the patient's inflammatory reaction. The RS (respiratory syncytial) virus and the influenza virus are the most significant in this context.

Age, sex and other factors that affect susceptibility to infection

Acute otitis usually affects children and is commonest in children under two. Children that are affected during their first year are more prone to recurrent otitis. Acute otitis is somewhat commoner in boys than girls.

The course of the illness and complications

Acute otitis usually presents with sudden earache, often in association with an upper respiratory tract infection. Discharge from the ear may occur and is a sign that the eardrum has perforated. During the first few days, earache, fever, malaise, irritability, and insomnia are common. The infection often affects both ears. The symptom pattern and clinical findings may vary, depending on the bacterial aetiology.

How should otitis be diagnosed?

In strictly scientific terms, acute otitis media is an infection of the middle ear in which puncture of the eardrum has obtained fluid containing an infectious agent. For all practical purposes, another definition must be used, based on the history, symptoms and examination of the eardrum.

Diagnostic criteria

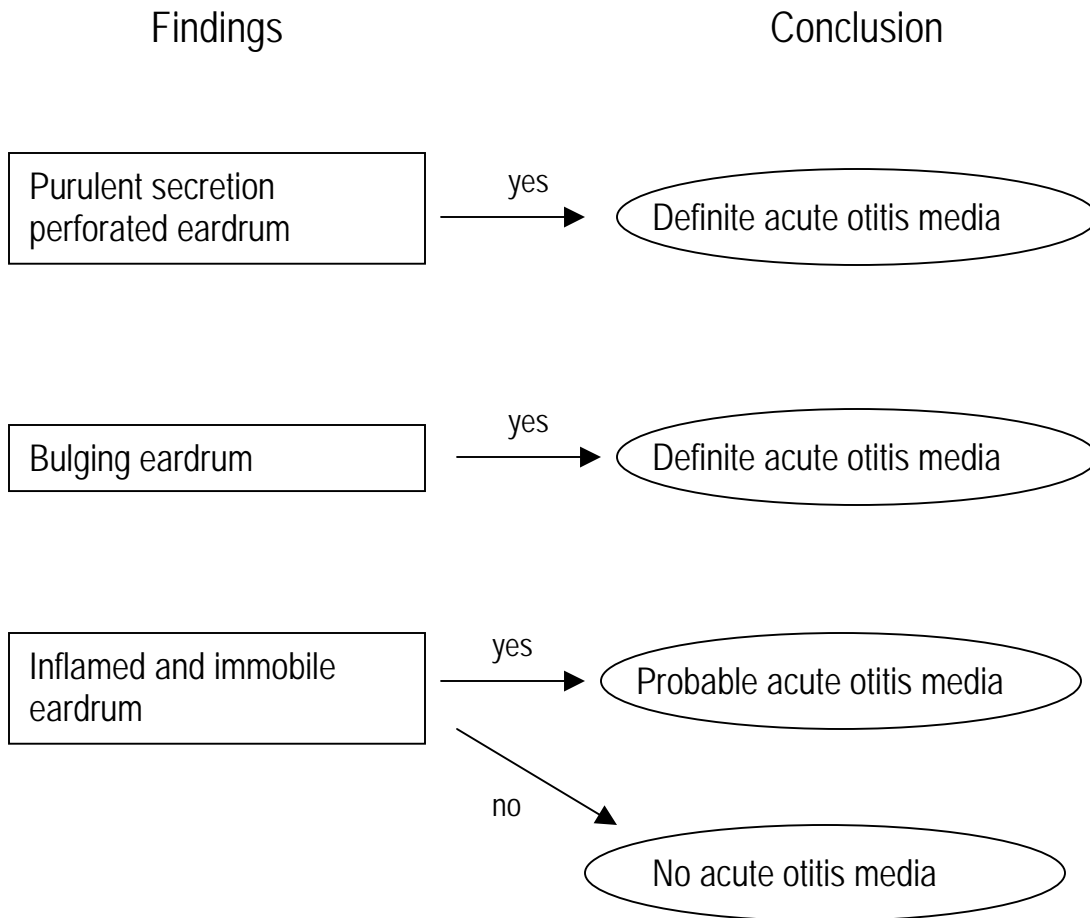
Acute otitis media can be diagnosed in the presence of symptoms of infection, and clinical findings of a bulging eardrum or discharge in the external auditory meatus. If changes in colour and form are present in the absence of a bulging eardrum, the mobility of the drum must be assessed in order to establish whether there is fluid in the middle ear. The history may show a varying pattern of a cold, fever, poor appetite, poor sleep and general irritability. Earache in a child under two is a good sign of acute otitis (high positive predictive value), but the absence of pain does not exclude acute otitis (low sensitivity).

Assessment of the eardrum

The eardrum must be visualised in order to make a diagnosis. This can be done with an otoscope or an aural microscope. If the eardrum is not bulging, but shows changes in form and colour, the mobility of the drum should be assessed with a pneumatic otoscope or a tympanometer. This increases diagnostic certainty. A red but mobile drum suggests the absence of purulent secretion in the middle ear. Situations can arise in which it is impossible to remove wax and inspect the drum. Unless the canal is completely occluded, the tympanometer can provide some information about drum mobility. History and examination alone provide an uncertain basis for diagnosis. If the child's condition permits, it may be appropriate to delay possible antibiotic treatment and give wax-softening drops pending a fresh assessment the following day.

Flow chart for diagnosis to be used when the history suggests acute otitis media

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Management

The first contact is often made by telephone. There is seldom a medical reason for examining a child with suspected acute otitis media during the evening or night. An appointment should be offered for medical examination within a day. A medical examination is not necessary if the child recovers during this time. If the nature of the symptoms is uncertain or the child is generally unwell, a prompt examination should be carried out.

All treatment decisions should be made with the active participation of patients and parents.

Analgesics should be given as necessary. Raising the head and using nose drops provide no particular benefit in acute otitis but can relieve nasal congestion. If the child is generally ill and the otological findings do not adequately explain the clinical picture, further investigations should be carried out and contact with an ENT surgeon or paediatrician considered. If the child is generally well and it proves difficult to make a definite diagnosis, the examination can be repeated the next day.

Treatment

Children under two: Antibiotic treatment is recommended for these children. A fresh medical examination should be carried out if no improvement is seen within three days, in order to reassess the diagnosis and treatment. The child should be examined earlier in the event of deterioration.

Children aged two or older: Antibiotics are recommended for children with perforating acute otitis, or acute otitis with generalised symptoms. Other children are managed in two alternative ways:

Alternative 1: If the child is not generally unwell, information is provided and the doctor recommends that antibiotics be withheld for the time being. The parents are asked to contact the doctor again (possibly by telephone) if the symptoms persists for two days beyond the onset of symptoms. If the symptoms are unchanged it is possible to agree, at this juncture, that antibiotics will be prescribed without a fresh examination. It is also possible, if one is comfortable with the situation, to wait a further day pending a further agreed contact. If symptoms persist to a third day, the child should be examined again and antibiotic therapy initiated if the diagnosis is confirmed. Any child that deteriorates should be examined earlier.

Alternative 2: the child is treated with antibiotics in a similar fashion to children under two.

Follow-up

A follow-up examination is recommended for children with confirmed acute otitis media. This would normally take place three months after the original infection. It is particularly important that the youngest children are followed up. The purpose of the examination is to confirm that the eardrum and the hearing have returned to normal.

Children to whom these general recommendations do not apply

When assessing children with acute otitis media, it is important to be mindful that the child does not belong to a group that has raised susceptibility to infection, which is associated with a greater risk of complications. These groups include children with immunodeficiency, congenital abnormalities and chromosomal defects. Children with serious underlying disease – and who are taking immunosuppressive drugs – also represent a risk group. A third group comprises of children with anatomical changes in the ear and nearby structures, e.g. skeletal abnormalities or persisting changes following a fracture of the base of the skull. A further group includes children that have had ear surgery, especially if artificial implants have been used (does not apply to grommets). These children need good continuity of care in their overall management, so that they should rarely need to be seen in the Accident & Emergency dept or by the out-of-hours service. This also applies to children suffering from recurrent otitis.

Choice of antibiotics

The treatment of choice: Phenoxymethylpenicillin (Penicillin V) for five days. Dose: 50 mg per kg body weight per day in 2-3 divided doses. On recurrence: Phenoxymethylpenicillin for ten days, or alternatively amoxicillin 50 mg per kg body weight per day in 2-3 divided doses for ten days.

In treatment failure: Amoxicillin 50 mg per kg body weight per day in 2-3 divided doses for ten days.

In confirmed penicillin allergy: Erythromycin for 7-10 days. Dose 40 mg per kg body weight per day in 2-3 divided doses.

In penicillin allergy and treatment failure: Co-trimoxazole. In treatment failure a swab culture and an ENT opinion may be helpful in further management.