Chapter 6: Acute and chronic laryngitis; leucoplakia

Paul van den Broek

Acute laryngitis

Acute laryngitis is usually of infectious origin, either viral or bacterial, but can also be due to exogenous noxious agents. In some instances autoimmune processes can manifest themselves in the larynx, simulating an acute inflammatory reaction. Swelling of the laryngeal mucosa and the underlying tissue is the common factor in all these conditions. They can be divided into several well-defined clinical entities which are discussed in this chapter.

Acute (simple) laryngitis

Aetiology

This is the most usual form of laryngitis and occurs as a symptom of a common cold. The disease is often associated with and secondary to an acute inflammation of the nose, throat or paranasal sinuses. It is an airborne infection usually caused by adenoviruses and influenza viruses. These can damage the respiratory mucosa to such an extent that secondary bacterial infection supervenes. The bacteria involved most commonly are *Streptococcus pneumonia*, *Haemophilus influenzae* and the haemolytic streptococcus, which are common inhabitants of the aerodigestive tract in some patients. Unfavourable climate and diminished resistance through undue physical and psychological strain may be predisposing factors.

Pathology

The laryngeal mucosa shows all the signs of acute inflammation. There is extravasation of fluid. In the early phase, polymorphonuclear leucocytes, and later lymphocytes and plasma cells, predominate the picture. The underlying muscles and even the perichondrium and the cricoarytenoid joints may be affected by the process.

Areas of epithelium may be destroyed and exfoliated. Full recovery is usual but, in some instances, fibrosis will result and there can be permanent damage to the laryngeal mucosa with loss of its original structure. This can be the beginning of a chronic laryngitis.

Symptoms

The main symptoms are hoarseness, discomfort and pain in the larynx; usually there is also an irritant paroxysmal cough. The voice is hardly ever completely lost, but speaking causes discomfort and phonation often results in a high-pitched husky voice. The voice varies in strength and pitch. The irritating cough may persist after the voice has returned. The degree of temperature elevation and general symptoms depends very much on concomitant infections in the other parts of the respiratory tract. The infection is often limited to the larynx with very few general symptoms.
Clinical diagnosis

The diagnosis is made by a careful history and examination of the upper and lower respiratory tracts. The presence of a generalized infection is usually apparent. It may be necessary to substantiate this further by radiographs of the sinuses and chest. The larynx is investigated by indirect laryngoscopy, which can be difficult in the presence of acute infection as a result of hypersensitivity of the surrounding structures. A local anaesthetic consisting of 4-10% xylocaine spray may be helpful.

When the larynx can be seen, a red and swollen mucosa is found which may prevent a deeper view into the larynx. The true vocal cords lose their whitish and contrasting colour and are also swollen, sometimes partly obstructing the laryngeal lumen. In adults this hardly ever results in impaired breathing with stridor; however, in children, the clinical course can be rapidly alarming. The presence of inspissated mucus, or sometimes a true purulent discharge, is pathognomonic of a bacterial infection which needs more aggressive treatment.

Treatment

The treatment of acute laryngitis depends on the presence of concomitant infections in the upper respiratory tract and the degree of local changes in the larynx. The treatment in all cases consists of simple supportive measures such as voice rest, medicated steam inhalations and the avoidance of cold, draught, tobacco and alcohol. Expectoration of mucus can be assisted by administration of mucolytic agents.

With these measures most cases of viral laryngitis subside within a few days. After a viral laryngitis, it may sometimes be necessary to suppress persisting coughs with codeine.

The presence of bacterial infections, apparent by the presence of pus and general symptoms, is usually an indication for antibiotics. These should be broad spectrum whenever they are given without prior culture and sensitivity testing. The most appropriate antibiotics are broad-spectrum penicillins 500 mg four times daily or doxycycline 200 mg/day.

Local application by sprays with astringent agents should be avoided. When professional activities occasionally prevent taking full vocal rest, the discomfort of speaking can be overcome by a local anaesthetic spray. This should, however, always be restricted to one or two applications to prevent further irritation.

Acute laryngitis is mostly a disease with a short and benign course. Adequate treatment along the lines described above is mandatory to prevent permanent damage of the laryngeal mucosa which can be the beginning of a chronic laryngitis.

In children, symptoms and signs of acute laryngitis may be much more alarming because the laryngeal lumen is much smaller and the laryngeal tissues are more prone to oedematous swelling. This applies especially to the separate entities known as acute laryngotracheobronchitis and acute epiglottitis.
Acute (fibrinous) laryngotracheobronchitis

Aetiology

In children, an acute respiratory infection may run a fulminant course spreading to the entire respiratory system. Small children up to the age of 7 years are most often affected. The infection can be caused by any of the microorganisms commonly involved in respiratory infections, but the haemolytic streptococcus is predominant. It usually superinfects on an infection by the influenza virus.

Pathology

Acute laryngotracheobronchitis affects the entire respiratory tract. The production of tenacious mucus which can hardly be expectorated, thus adding to the respiratory distress, is characteristic. The formation of pseudomembranes is also common, which, unlike diphtherial membranes, can be wiped off without causing bleeding. The inspissated secretions may cause total obstruction of the small bronchi leading to atelectasis.

Clinical features

Any mild common respiratory infection can lead to the complete picture of an acute laryngotracheobronchitis with its sometimes fulminant course. This generalization of a limited infection complicated by a bacterial superinfection must be recognized early to allow adequate treatment. The patient's temperature sometimes rises up to 41°C and toxaemia may develop rapidly.

Most commonly, during or after a common cold, the child's temperature rises further and this is combined with a dry and harsh cough, hoarseness and an evident stridor. The production of tenacious secretions which can be hardly expectorated, and the mucosal swelling are the main causes of obstruction in the airway, which is most prominent at the narrow laryngeal inlet. It is at this stage that painstaking observation is necessary to prevent the child developing respiratory failure which can be rapidly fatal. The increased muscular energy consumption required for breathing and coughing, together with the retention of carbon dioxide, leads to a combination of metabolic and respiratory acidosis which paralysis the central regulation of respiration. During the initial phase the child is restless and sometimes cyanotic; in the later stages there may be an apparent improvement when the child becomes tired and calm. The retention of carbon dioxide causes a change of colour from cyanotic to pale and these are the first and often only signs of imminent disaster.

A small child with a temperature higher than 38.5°C and stridor should be admitted to hospital for observation. The clinical picture is usually dominated by the laryngeal stridor, the degree of which can scarcely be investigated objectively. The sequelae of rapidly developing or continuing stridor can only be properly judged by objective blood analysis which gives information on the degree of oxygenation, carbon dioxide retention and acidosis. It must be realized that any value can change within a very short time. Mirror examination in these children is impossible. Auscultation of the lungs is often difficult to interpret because of the stridor and massive secretions. A chest X-ray is required to investigate the degree of
involvement of the lower respiratory system. First and most important remains sound clinical judgement based on clinical examination and laboratory investigations.

**Treatment**

Acute laryngotracheobronchitis should be treated vigorously. Treatment should start immediately with antibiotics, preferably a broad-spectrum penicillin; this can be given orally or by injection depending on the general condition of the child. The value of corticosteroids in reducing the inflammatory reaction is debatable. However, when children are in distress the use of intravenous steroids will certainly do no harm and is probably beneficial. They should not be used for longer than is required to relieve the most acute symptoms; this is usually a few days.

The child should be isolated in a room or tent with moist air. Mucolytic agents can be added by mouth or in aerosols to facilitate expectoration of the tenacious mucus. If feeding by mouth is difficult a nasogastric tube should be introduced. The child must be adequately hydrated and should be carefully monitored for cardiac or respiratory failure; regular blood samples should be taken for analysis. Any sign of deterioration should lead to consultation about the necessity of airway assistance either by endotracheal intubation or tracheostomy and, if necessary, by assisted respiration. It is outside the scope of this chapter to discuss the merits of intubation versus tracheostomy. Neither method is safer than the other. They both require good instrumentation and technique, but above all well-trained personnel to observe and nurse a child with a tracheostomy or endotracheal tube.

**Subglottic laryngitis (pseudocroup, spasmodic cough)**

**Aetiology**

Acute laryngotracheobronchitis should not be confused with the condition generally known as subglottic laryngitis (pseudocroup). Subglottic laryngitis is common in young children below the age of 3 years. The symptoms are usually alarming. The exact aetiology is unknown, but the disease is often associated with an infection by one of the influenza viruses. However, certainly in view of the clinical picture, the association with a microorganism or virus seems at least doubtful. The main intralaryngeal changes, consisting of a substantial swelling of the mucosa, are found on or near the undersurface of the true vocal cords and in the subglottic region.

**Clinical features**

An attack of pseudocroup starts abruptly in a child, who might have a mild respiratory infection with some cough. Usually after the child has gone to bed and has fallen asleep, he/she wakes up again with a dry cough and a rapidly increasing stridor. The complete clinical picture develops in a very short time and seems alarming. There is usually no or only mild fever, the voice is raw and the sound resembles the barking of seals. The cough is dry. Secretions may be present but are not marked. The child becomes restless, nervous and tends to cry. The anxiety of the parents is usually projected onto the child and the clinical signs then worsen. The child may have a red appearance from exertion and perspiration. There are
no further diagnostic aids to ensure the diagnosis of this generally benign and self-limiting condition.

**Treatment**

The child and sometimes the parents need treatment. The child should be comforted as much as possible because further exertion during crying and coughing stimulates intralaryngeal swelling. Sedatives should never be given to the child because they suppress respiratory reflexes essential for maintaining oxygen and carbon dioxide levels within normal limits. Sedatives are probably best given to the parents! The value of corticosteroids for the treatment of the child is still debated. There is no objection to parenteral administration of corticosteroids but the effect is doubtful and injection can distress the child.

If possible the child should be taken to a room with moist air which helps to ease coughing and irritation. A bathroom with running hot water to produce steam is probably the best place. The child should be observed carefully until the worst symptoms settle. If any doubt is present about the child's breathing capabilities he should be admitted to hospital. Only rarely will there be a real emergency. Occasionally there may be progression to complete acute laryngotracheobronchitis, requiring more aggressive treatment.

In an emergency the treatment of choice is endotracheal intubation which can usually be limited to 1 or 2 days. Whenever this is necessary it is of paramount importance that the right diameter of tube should be used to prevent local damage to the mucosa which may otherwise lead to permanent stenosis: it is better to use too small than too large a diameter. Siliconized tubes have the advantage of a very low friction coefficient and therefore have a less traumatic effect on the mucosa.

Although the progress of the stridor should be carefully monitored, it is hardly ever necessary to proceed to aggressive treatment. The stridor usually subsides within a few hours and the next day the child may be entirely normal. There is a tendency towards recurrence and it seems that some children have a predisposition for this condition. Possibly an allergic reaction in the subglottic region is a contributing factor.

**Membranous laryngitis**

**Aetiology**

Another rare form of laryngitis, probably closely linked with acute laryngotracheobronchitis, is known as membranous laryngitis, sometimes also called croup or pseudomembranous croup. It is not caused by *Corynebacterium diphtheriae* (Klebs-Loeffler bacillus) but by various microorganisms including streptococci, *Pseudomonas aeruginosa* or Vincent's microorganisms.

**Pathology**

The presence of a confluent membrane covering the laryngeal surface is the most characteristic sign. No bleeding occurs when this is removed and no ulceration remains. The
main site is the supraglottis or the laryngeal vestibule. Only rarely does it spread to the vocal cords. It can descend from above as part of Vincent's infection of the pharynx.

**Clinical features**

The clinical picture is similar to that of other forms of laryngitis. The constitutional disturbance is often accompanied by anorexia and thirst; there is moderate fever; swallowing is painful and coughing is usually present. Later there may be stridor due to laryngeal spasm and obstruction by oedema or obstructing membranes. The disease should be differentiated from classical diphtheria which it resembles. A bacteriological investigation will establish the diagnosis and differentiate it from other forms of laryngitis.

**Treatment**

Antibiotics or sulphonamides are given depending on the sensitivity of the microorganism. Modern chemotherapy has altered the outlook of most forms of acute laryngitis.

**Acute epiglottitis**

Acute epiglottitis is a distinct form of acute inflammation of the larynx. As the name implies the epiglottis is the main site of involvement. The inflammation of the epiglottis leads to extensive swelling in the laryngeal inlet.

**Aetiology**

Acute epiglottitis has been shown to be caused by infection with *Haemophilus influenzae* type B. In general, this bacterial disease is secondary to a virus infection which has rendered the larynx more sensitive to bacteria. The disease mainly affects children but is also seen in adults.

**Clinical features**

The history is usually short and starts with an upper respiratory tract infection. There is a rapid rise in the patient's temperature sometimes exceeding 40°C, with signs of severe illness. The patient is quiet, and has pain the throat which inhibits swallowing and appetite. There is often a rapid and potentially fatal increase of stridor which is most marked in children. Unlike pseudocroup the child prefers the sitting position, the tripod sign, and usually drools.

The epiglottis is often directly visible in the throat as a rounded swollen red mass. Care should be taken when depressing the tongue as this can cause fatal glottic spasm.

**Treatment**

Acute epiglottitis should be considered a surgical emergency and the patient should be admitted to hospital. The possibility of rapid deterioration requires careful and skilled observation in order to be able to take adequate measures when necessary. When the airway
is sufficient the main treatment consists of inhalation of moist air, and antibiotics, preferably amoxycillin, should be given. Airway obstruction may develop very rapidly and some experienced surgeons advocate direct establishment of an airway. There is still much debate whether this should be by intubation or tracheostomy (Fearon and Cinnamond, 1977; Oh and Motoyama, 1977; Kinnefors and Oloffson, 1983). Both methods seem to give equivalent results.

In general, the monitoring of patients, especially children, with airway obstruction due to laryngeal infection or other causes has become a separate speciality. The otolaryngologist should be a regular observer in intensive care wards where his endoscopic and surgical skills may be needed when the airway becomes obstructed. The observation of a stridulous patient should include constant monitoring of heart and respiratory function, temperature, and regular analyses of the gaseous content of the blood.

A child has a relatively small respiratory reserve compared with an adult; the oxygen consumption per unit of bodyweight is twice as high. Furthermore, the smaller diameter of the airways results in a higher peripheral airway resistance and a greater risk of obstruction.

The relief of life-threatening obstruction of the airways can usually be effected by passing an endotracheal tube. Except in cases of a foreign body in the airway, the laryngeal opening can be found and a tube inserted. This procedure require a laryngoscope with good light and tubes of different sizes. After the airway has been re-established a decision should be taken as to whether an indwelling tube should be left or a tracheostomy performed. Siliconized tubes of various makes cause very little local irritation if they are of the correct size. Many paediatricians and otolaryngologists have accepted prolonged intubation as the method of choice for the first 10-14 days, provided that adequate monitoring facilities are available.

Successful results with prolonged intubation have led to less frequent use of tracheostomy for short-term airway relief in many centres. Whenever long periods of assisted ventilation are foreseen, tracheostomy should still be considered as a good and probably preferable alternative. Modern synthetic semirigid materials reduce the chance of complications which were common when metal tracheostomy tubes were used.

Nowadays, tracheostomy is rarely performed as an emergency procedure, because endotracheal intubation has usually been carried out first. Yet, in most centres, a regular tracheostomy in the trachea is preferred.

The differential diagnosis of different types of acute laryngitis in children is very important for the institution of adequate treatment in cases where this is necessary. Some conditions need rapid and aggressive treatment, others can be observed without danger.

The main features of the different forms of laryngitis are summarized in Table 6.1.
<table>
<thead>
<tr>
<th></th>
<th>Simplaryngitis</th>
<th>Subglottic laryngitis</th>
<th>Laryngotracheobronchitis</th>
<th>Epiglottitis</th>
</tr>
</thead>
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<tr>
<td><strong>Age</strong></td>
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<td>1-4 years</td>
<td>1-8 years</td>
<td>3-6 years</td>
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<td><strong>Onset</strong></td>
<td>Gradual</td>
<td>Rapid</td>
<td>Gradual (after common cold)</td>
<td>Rapid</td>
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<td>&lt; 38°C</td>
<td>&lt; 38°C</td>
<td>&gt; 39°C</td>
</tr>
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<td>Hoarse</td>
<td>Harsh</td>
<td>Hoarse</td>
<td>Normal</td>
</tr>
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<td>Sitting, drooling</td>
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<tr>
<td><strong>Treatment</strong></td>
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<td>Moist air, supportive</td>
<td>Antibiotics, rarely intubation</td>
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<td><strong>Monitoring</strong></td>
<td>No</td>
<td>No</td>
<td>No</td>
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**Oedema of the larynx**

Oedema of the mucosa can accompany any inflammatory reaction of the larynx and is, therefore, not a specific disease but rather a sign. It may be a solitary reaction to different types of exogenous stimuli or to unknown factors. Trauma, infections and tobacco are the most important contributors. Another important cause of oedema is the physical trauma of radiation treatment. Most forms of laryngeal oedema persist over a prolonged period of time with only a limited tendency to spontaneous resolution. Several clinical entities require special mention.

**Reinke's oedema**

The accumulation of fluid under the epithelium of the true vocal cords is generally known as Reinke's oedema, named after the German anatomist, Reinke, who first described the loose areolar tissue in this region. The attachment of the vocal ligament along the medial edge and underneath the vocal cord by the lamellar fibres extending into the conus elasticus restricts the oedema to the superior surface of the cords (Mayet, 1961).

**Aetiology**

The precise cause of Reinke's oedema is not known. Allergy, infections and especially local irritants probably play a major role. Tobacco is one of the major culprits and it has been shown that an important percentage of patients are heavy smokers (Myerson, 1950). Chronic sinusitis has also been implicated, but most studies fail to mention this.
Clinical features

The condition is fairly common and comprises about 10% of benign laryngeal pathology. The disease is commoner in men but the percentage may vary greatly. The patients are mostly aged between 30 and 60 years old. The oedematous swelling of the vocal cords can easily be recognized with indirect laryngoscopy. The vocal cords are red and swollen and have a slightly translucent appearance. Sometimes the mucosa becomes redundant and polypoid projections are visible. Rarely these may be so voluminous as to cause stridor. The oedema prevents normal vocal cord vibrations causing hoarseness often with deepening of the voice. The vocal range diminishes and the voice become monotonous. There is frequently a dry cough or clearing of the throat.

Treatment

The treatment of Reinke's oedema should consist of a combination of surgery and vocal rehabilitative measures. Naturally all known causative factors, especially smoking, should first be eliminated. If smoking is not stopped the results of any treatment will be very disappointing.

Surgery consists of microsurgical removal of strips of vocal cord mucosa by microlaryngoscopy (Kleinsasser, 1976). First the mucosa is incised in a sagittal direction and the fluid, which may be either thin or mucoid, is sucked out. A strip of vocal cord mucosa is then removed with a microforceps and scissors.

There is some controversy whether both vocal cords should be stripped at the same session or whether an interval should be allowed. The present author agrees with Kleinsasser that it is perfectly safe to treat both cords during the same operation, but that care should be taken not to extend the incisions into the anterior commissure. After the procedure absolute vocal rest is advocated for one week. Healing is usually rapid and new epithelium develops with a firmer attachment to the vocal cord muscle which prevents recurrence. Speech therapy is instituted after 2-3 weeks and is continued for as long as it is felt to be beneficial. Recurrences are generally uncommon.

Some patients only come for treatment after a long history, often of many months. Delay of treatment for too long can result in the development of chronic laryngitis.

Angioneurotic oedema (angio-oedema)

This condition is characterized by recurring attacks of local swelling in various parts of the body particularly the face, larynx, extremities and buttocks. Death may result from life-threatening oedema of the larynx. Gastrointestinal disturbances presenting as colic, nausea and vomiting, are almost invariably associated with the oedema.

Generally, angio-oedema can be divided into an allergic and a non-allergic form which can be either hereditary and non-hereditary.
Angioneurotic oedema of allergic origin

This form is usually accompanied by urticaria. It presents as an acute allergic reaction to food, medicines or inhaled allergens. The diagnosis is based on the history and typical concomitant symptoms. The oedema rarely leads to laryngeal obstruction. The allergic reaction can be alleviated with antihistamines and corticosteroids. In severe cases, a subcutaneous injection of adrenaline (1:1000) 1 mg can be life saving. It is very important that the allergens are identified in order to prevent future attacks.

Hereditary angio-oedema

Less frequently, angioneurotic oedema is of non-allergic origin: it can be both hereditary and non-hereditary. The hereditary form with all its clinical manifestations was described by Sir William Osler in 1888. He recognized the life-threatening character of this condition. The underlying mechanism of the disease has been recognized to be a serum deficiency of the C1-esterase inhibitor protein (C1-iNH). This enzyme is one of a series of naturally occurring inhibitors of complement activation, kinin formation and fibrinolysis.

The complement system is composed of nine serum components which are activated by each other in a strict sequence leading to the release of polypeptides which enhance vascular permeability. When C1-iNH is not present as in hereditary angio-oedema, minor events such as trauma or emotional strain, can elicit a chain of reactions resulting in the release of complement. The mortality from concomitant laryngeal oedema is high if treatment is not rapidly instituted.

Blok and Baarsma (1984) described a family in which 35 members over three generations were traced, 14 (40%) of whom appeared to be affected. This indicates an autosomal dominant inheritance with a high penetrance. The typical triad (abdominal pain, peripheral non-pitting oedema and laryngeal oedema) was present in four patients. The laryngeal oedema being the least common symptom.

The treatment can be divided into that of the acute attack and short- or long-term prophylaxis. The acute attack is treated with an intravenous injection of C1-iNH 36,000 units. Patients should keep this at home for use in an emergency. This preparation can also be used as short-term prophylaxis in these patients before operations such as dental extractions.

Patients suffering from frequent attacks should have long-term prophylaxis which is best effected by the fibrinolytic inhibitor epsilon aminocaproic acid (EACA) and its derivative tranexamic acid, or by the androgen methyltestosterone and its derivative danazol. These stimulate the production of C1-iNH.

Laryngeal perichondritis

Perichondritis is an inflammatory reaction in the tissues covering the laryngeal cartilages. A primary form, usually developing as a blood-borne infection, used to be quite common when typhus, typhoid and smallpox were still prevalent. Immunization programmes have eliminated these diseases from major areas in the world. Perichondritis can also be
secondary to a superficial infection in the larynx spreading to the deeper tissues. In the presence of abscesses or cellulitis the cartilage may also be involved.

At present, one of the major causes of perichondritis is radiotherapy. Although the improved dosage schedules and the introduction of megavoltage radiation sources have greatly diminished the chances of serious complications, perichondritis remains a potentially dangerous hazard of this form of treatment. Perichondrium and cartilage can be affected by the radiation beam resulting in a sterile inflammatory reaction with very little tendency to spontaneous resolution. When the cartilage is uncovered after the tumour resolves, the cartilage with its inherent avascularity is liable to serious infection with little healing tendency.

**Clinical features**

Perichondritis usually develops slowly. The characteristic sign is dull pain over the entire laryngeal skeleton. The thyroid and cricoid cartilage are thickened and tender on palpation. The swollen red laryngeal mucosa can be seen on indirect laryngoscopy. The swelling may be so pronounced as to impair vocal cord function or obstruct the airway. Sometimes the cartilage is exposed. A foul smell indicates tissue necrosis. Occasionally pieces of necrotic cartilage are expectorated.

The clinical course is usually slow and protracted but, occasionally, the clinical signs of perichondritis develop very quickly, especially during radiotherapy, necessitating emergency treatment.

**Treatment**

Medical treatment, consisting of high doses of broad-spectrum antibiotics effective against anaerobes, should be instituted directly. Furthermore, corticosteroids should be given in high doses for one week with gradual withdrawal (prednisone 30 mg/day). Whenever airway problems predominate, tracheal intubation or a tracheostomy should be performed.

Although acute perichondritis can resolve quickly, especially with regard to airway obstruction, the laryngeal oedema may last for weeks to months. Laryngeal abscesses should be drained.

Separate mention should be made of the treatment of laryngeal perichondritis after radiotherapy (Stell and Morrison, 1973). This condition is generally serious and may be the cause of very resistant trouble. It may be necessary to maintain a tracheostomy for weeks, months, or even years. Resolution is usually slow and often leaves a gradually progressive narrowing of the larynx from scar formation.

**Relapsing polychondritis**

Relapsing polychondritis is a rare condition which was first described in 1923 by Jacksh-Wartenhorst. There is a recurrent inflammation of cartilage especially of the auricle, nose and trachea. The aetiology is unknown, but it is thought to be an autoimmune disease linked with the collagen-vascular group of diseases. Occasionally, patients with relapsing
polychondritis suffer from rheumatoid arthritis, systemic lupus erythematosus or ankylosing spondylitis.

The recurrent inflammation in the cartilages of the head and neck region such as the pinna, nasal cartilages, larynx or trachea, is the most prominent manifestation, but inflammatory lesions such as scleritis, conjunctivitis, keratitis, arthropathy and vasculitis can be found in other supportive tissues. The erythrocyte sedimentation rate is often raised except in the very early stages.

Laryngeal and tracheal lesions manifest themselves with signs of laryngitis and tracheitis. The mucosa is swollen especially around the epiglottis and aryepiglottic folds and descending down into the trachea. In the later stages the cartilage disappears and the epiglottis may be shrunken. The other laryngeal cartilages may also be soft and tender. Loss of cartilage of the larynx and the trachea can lead to segmental narrowing through collapse and fibrosis.

Histologically there is degeneration of the cartilage tissue due to invasion by inflammatory tissue. Several authors have described the microscopic aspects of these lesions. It seems that the process is preceded by a degeneration of the marginal chondrocytes (Valenzuela et al, 1980). The ground substance of the cartilage become acidophilic. Erosion by inflammatory tissue takes place around the cartilage and compression of lacunae can be found. Initially, the exudate is mainly composed of neutrophils but later lymphocytes, plasma cells and sometimes histiocytes can be found. In the end stages progressive fibrosis is found. Histochemical staining has shown a deficiency of matrix acid polysaccharide (Verity, 1963).

Although anticartilage antibodies have been found in the serum of patients with relapsing polychondritis, the exact meaning of these immunological findings in relation to the cause of the disease is not known (Michaels, 1984). This also applies to the finding of autoantibodies to type II collagen, a constituent of both eye and cartilage tissue, which have been found in cases of relapsing polychondritis. Although there is growing evidence that relapsing polychondritis is an autoimmune disease, definite proof is still lacking.

The presenting symptoms of laryngeal involvement are hoarseness and dyspnoea due to oedema of the mucosa. Usually there are signs of acute inflammation with fever and pain. Without treatment there is progression to serious stenosis of the larynx. The course can be very slow and relatively benign but can also be rapid and fatal. The mean survival of 27 patients found in the literature who died before 1971 was 5.25 years, but varied from one month to 23 years (Hughes et al, 1972).

The treatment of choice is still considered to be the administration of corticosteroids; initially high dosages are required, prednisone 30-60 mg/day. After the acute symptoms have subsided a maintenance dose is necessary to prevent exacerbation, prednisone 5-10 mg/day. The therapy can rarely be withdrawn entirely. When exacerbations occur the dose must be increased. The use of other drugs such as antimetabolites and immunosuppressive drugs seems logical if the autoimmune cause is accepted but, at present, not enough evidence for their usefulness is available.
Chronic laryngitis

Any chronic non-specific inflammatory reaction of the laryngeal mucosa may be called a chronic laryngitis. The patient suffering from chronic laryngitis complains of hoarseness over a long period of time and, on inspection of the laryngeal surface, changes in the laryngeal mucosa are always visible. The clinical picture may show variations so that over the years many descriptions have been given to clinical entities which were thought to be different. These were given separate names mainly referring to the macroscopic or microscopic appearance, and date back to the time of Virchow, the German pathologist of the second half of the nineteenth century. He introduced the term 'pachydermia' to designate local changes in the vocal cord which on microscopic appearance showed thickening of the epithelial layers. Depending on the history and the site of the lesions he further divided this entity into 'pachydermia verrucosa' and 'contact pachydermia'. Although these names are not much used today the condition is still well known to every laryngologist.

Since Virchow's time many other names have been used such as hyperplastic laryngitis, leucoplakia, keratosis and hyperkeratosis and others meant to describe chronic laryngeal disease with certain clinical and histomorphological features. However, most are so ill-defined that they are of limited value for a clinician, although they may be informative with regard to aetiology, natural history and treatment. Furthermore, the microscopic appearance of the laryngeal mucosa and the surrounding tissues may show some differences, although these are not pathognomonic for any clinical entity. On the contrary, in most of these non-specific laryngeal conditions the microscopical picture is rather uniform, being characterized by hyperplasia of the squamous epithelium with differences only at the cellular level. The mucosa of the true vocal cords is normally covered by squamous epithelium whereas the remainder of the larynx is normally covered by respiratory epithelium. During life this respiratory epithelium is subject to progressive metaplasia towards squamous epithelium. It has been known for a long time that epithelial changes in the laryngeal mucosa are enhanced by tobacco and environmental pollution and can result in the development of an infiltrating carcinoma. In 1923 the American laryngologist Chevalier Jackson stated that chronic laryngitis and what he called 'keratosis' could be precancerous. These lesions should be detected early and eradicated. Several authors (Putney and O'Keefe, 1953; McGavran, Bauer and Ogura, 1960; Gabriel and Jones, 1962; Norris and Peale, 1963; Crissman, 1979) have carried out studies to investigate the possibility of malignant degeneration, and it has been recognized that certain microscopic changes, especially at cellular level, can be regarded to be predictive for later malignant transformation.

Kleinsasser (1963) first stressed the importance of a classification system of histological grades which would help to alert the clinician to those lesions which have a higher chance of malignant degeneration and thus would need more aggressive treatment or a closer follow-up. The introduction of microlaryngoscopy by the same author around 1961 allowed well delineated and representative biopsies to be taken from the suspicious lesions in the laryngeal mucosa and was an important step towards accurate clinical assessment of these lesions. Over the past 20 years the value of this method has been repeatedly confirmed.

However, a uniform grading system has not yet been adopted and subjective interpretations of the degrees of change found in the laryngeal mucosa under pathological circumstances are an obstacle to a reliable and reproducible grading system. Perhaps more
objective means of quantification of the changes at the cellular level, for instance, morphometric or photometric evaluation (Hellquist and Oloffson, 1984; Hellquist et al, 1984), will enhance the reliability of such a system and make it more acceptable.

**Actiology**

Chronic laryngitis primarily affects middle-aged men but the variation in age is wide. The median age is approximately 57 years, that is about 5 years less than the average age of patients with laryngeal carcinoma.

Many factors, both endogenous and exogenous, have been incriminated as causative. The exogenous stimuli may be physical, chemical or infective, the most important being inhaled irritants and, notably, cigarette smoke. In many studies it has been shown that metaplastic changes in the surface epithelium of the airways in heavy smokers is more marked than in non-smokers. This also explains the sex differences observed.

The changes in the mucosa are most marked on the ventricular bands and the true vocal cords. Auerbach, Hammond and Garfinkel (1970), in a study of larynges at post-mortem found epithelial changes in 6% of non-smokers, 22% of smokers of 20 cigarettes and 44% of smokers of 40 cigarettes a day. The degree of cellular atypia is also strongly related to smoking habits. The presence of cellular atypia is observed in 85% of heavy smokers. After smoking has been stopped the hyperplasia remains, but the cellular atypia gradually diminishes.

In series of patients with chronic laryngitis the percentage of smokers is usually high (Putney and O'Keefe, 1953, 89.8%; Norris and Peale, 1963, 94%). Alcohol is also often mentioned as a causative factor (Hinds, Thomas and O'Reilly, 1979), but much less solid evidence is available. In the author's own data on smoking and drinking habits in a large number of patients with head and neck cancer, the alcohol consumption among the laryngeal cancer patients is much lower than among patients with carcinoma of the oral cavity and pharynx. This could point towards a direct surface effect. In a study by Stevens (1979), hamsters exposed to benzpyrene and alcohol were affected more frequently by laryngeal carcinoma than those not receiving alcohol.

Chronic laryngitis is more frequently found in patients suffering from a chronic infection of the upper or lower respiratory tract. Stell and McLoughlin (1976), studying a group of 58 patients with chronic laryngitis, found a history of infection in 53%. It is not clear whether this association is due to the increased incidence of coughing in these patients resulting in mechanical trauma, or whether a more generalized involvement of the respiratory mucosa including that of the larynx is the main reason. Probably both factors play a role. The stubborn nature of chronic respiratory tract infections means their elimination plays an important role in the treatment of chronic laryngitis.

Besides coughing, vocal abuse is an important physical factor which contributes to the development of inflammatory lesions of the larynx due to mechanical irritation. Muscular strain, venous congestion and forced vocal attack are probably involved. Virchow recognized the factor of vocal abuse when describing the picture of pachydermia verrucosa in a Prussian army officer. It is certain that abnormal vocal strain especially in those who use their voice
professionally can be a source of tissue changes which have a disastrous effect on the voice. These are discussed in Chapter 7.

Finally endogenous factors must also be taken into account. These may be constitutional or metabolic. Short, heavily-built people are more prone to chronic laryngitis. Diabetes, hypothyroidism and vitamin A deficiency can also be contributory.

**History and clinical signs**

Chronic laryngitis is usually of insidious onset and rarely develops after an acute laryngitis, although this may be the trigger in a larynx which has already been affected by asymptomatic epithelial changes. When no acute infection has been present it is difficult for the patient to pinpoint the exact time of onset.

There are no general symptoms and no fever. Hoarseness is the most frequent and often the only symptom. This complaint tends to vary with the time of the day and with the intensity with which the voice is used. Typically the patient complains that the voice is worse in the morning. Drying of the laryngeal mucosa during the night through mouth breathing and a decreased frequency of swallowing is probably the reason for this. Inspissated mucus which has to be cleared causes dryness and the feeling of a foreign body in the throat. When the throat has been cleared and the mucosa is moistened again the voice gradually improves. However, it remains harsh with varying pitch and volume. There can be periods of complete aphonia, although these are rare. The vocal range is reduced, especially in the higher frequencies. There may be a cough caused by local irritation as a result of mucus, dryness or intraepithelial changes, which can worsen the other symptoms. Pain is rarely present unless undue strain by coughing has damaged the mucosa.

The complaints of a patient with chronic laryngitis tend to develop slowly and then become stationary. There may be variations over short periods but, in general, chronic laryngitis remains constant over a long period.

**Clinical picture**

Chronic laryngitis is diagnosed from the history and by indirect laryngoscopy. Direct inspection of the larynx is the corner-stone of any diagnosis. Furthermore, a histopathological examination of tissue removed from the laryngeal lesions is indispensable. Without these investigations a diagnosis cannot be made.

Chronic laryngitis can be divided into several clinical conditions.

**Simple diffuse chronic laryngitis**

The patient complains of hoarseness and sometimes a slight cough over a long period of time. These complaints start insidiously, occasionally during an upper respiratory tract infection, and persist although they are not always present.

Examination shows a reddened hyperaemic laryngeal mucosa. The true vocal cords lose their white colour and become pink or red, sometimes with a glossy appearance or with
submucosal oedema. Diagnosis is made on the findings at indirect laryngoscopy. If the laryngeal mucosa is smooth and regular, a biopsy should be avoided in the early stages to prevent damage to the laryngeal mucosa.

Simple chronic laryngitis can best be treated by vocal rest, inhalations with mentholated air and, if the slightest signs of infection are present, an appropriate antibiotic should be given. Furthermore, all possible noxious agents should be avoided especially tobacco and alcohol.

This form of laryngitis is reversible within a few weeks with adequate measures.

**Chronic diffuse hyperplastic laryngitis**

The most important contributing factors are chronic infection of the sinuses and lower airway; tobacco and alcohol; occupational, chemical or physical irritants; and mouth breathing. The onset is insidious and these patients often have a history of coughing.

The laryngeal picture is determined by more conspicuous changes of the laryngeal mucosa, especially the true vocal cords, which lose their normal appearance. The mucosa is clearly swollen and the white colour replaced by red, deep red or sometimes grey. The surface of the mucosa is hardly ever completely smooth. Patches of epithelial thickening and broad-based polypod lesions can be found. The picture is much more alarming than that of simple laryngitis and it may be difficult to differentiate its appearance from carcinoma or specific laryngitis.

This form of laryngitis is usually associated with chronic respiratory infections such as sinusitis and bronchitis.

**Keratosis, leucoplakia, pachydermia, squamous cell hyperplasia**

These terms are based partly on clinical appearance and partly on histological features. They are still often used for local or more diffuse lesions of the larynx, primarily the vocal cords. Many clinicians would like to see these terms abandoned because they are ill-defined and confusing. The lesions are often well circumscribed and well demarcated from the surrounding tissue. One or both cords can be affected as well as the anterior commissure.

Very often the surface of the lesion is white in colour as a consequence of thickening of the squamous epithelium covered by excess keratin. The elevation of the lesion from the surrounding tissue can be seen clearly under the operating microscope. The surrounding mucosa may be normal or may resemble simple chronic laryngitis. The keratinization may be so abundant that the picture may simulate a benign tumour, a squamous papilloma or a verrucous carcinoma. When the lesion lies in the posterior part of the glottis where the mucosa is redundant to allow movement of the cords, it has also been named 'posterior laryngitis'. Its possible relation with nocturnal regurgitation of gastric acid has led to the name 'acid laryngitis'. At this site the epithelium is already normally slightly thickened and the transition towards abnormal is very gradual, so that care should be taken not to overdiagnose this condition. The presence of symptoms including gastro-oesophageal reflux usually helps to make a diagnosis.
Contact ulcers - contact pachydermia

These terms were coined by Jackson (1928) and Virchow (1887) respectively and are still in use today. Although Jackson later included vocal cord granuloma, this should be considered as a separate entity.

Contact ulcers are saucer-like lesions on the medial edge of the vocal cord exactly at the vocal process. They can be bilateral and symmetrical, often with a small projection on one cord which fits the saucer of the other side. There is no epithelial defect, thus the word 'ulcer' is not correct. The lesions are made up of thickened epithelium with a central indentation exactly at the site of the mucoperichondrial covering of the vocal process. Patients with a contact ulcer may complain of pain locally. This disease usually occurs in tense personalities and it is agreed that vocal overuse and abuse are important aetiological factors.

Histology of chronic laryngitis

The importance of an accurate histological diagnosis in cases of chronic laryngitis cannot be overestimated. The relation between chronic epithelial changes and carcinoma has been repeatedly demonstrated, although the percentage is generally only between 3 and 5% (Crissman, 1979).

The chances of malignant degeneration are related to certain histomorphological characteristics which can help to divide the lesions into high and low risk groups (Oldekalter, 1986). A reliable diagnosis demands two criteria to be fulfilled. The first is that the biopsy is taken from a representative site of the lesion. If the lesion is small a total removal will allow examination of the entire specimen. When the lesion is extensive, biopsies are taken from the most aggressive looking part of the lesion. Epithelial changes such as carcinoma in situ are often found in the vicinity of a squamous cell carcinoma and care should be taken not to overlook the site where a carcinoma may be present, for instance, subglottic or in the ventricle (McGavran, Bauer and Ogura, 1960). The second requirement regards the way the specimen is sent to the pathologist. If possible the removed undamaged piece of mucosa should be orientated to allow the pathologist to make sections vertical to the mucosa to avoid tangential sectioning which may simulate infiltration of tumour tissue into the underlying tissue.

Although it is recognized that squamous epithelium can undergo changes which may eventually lead to squamous cell carcinoma and that certain histological and cellular features indicate a higher chance of malignant transformation, a uniform and internationally accepted classification of these lesions is still lacking, mainly because each classification depends on a subjective interpretation. The results of objective methods such as morphometry (Oldekalter et al, 1985), photometry (Hellquist and Olofsson, 1984) and others have not yet found widespread clinical application.

In Europe the most accepted classification is that originally proposed by Kleinsasser (1963), who introduced a histological grading system. The normal squamous epithelium of the larynx is non-keratinizing in several layers. Adjacent to the subcutaneous tissue lies the basal layer (stratum germinativum), consisting of cylindrical cells with ovoid nuclei. Mitoses are frequent in this germinal layer of the epithelium. From this layer the cells move to the
surface, gradually changing from round to flat cells which are shed from the surface. Although the more superficial cells contain intracellular keratohyalin granules, there is no full development towards keratin. Under normal circumstances this maturation process follows a regular pattern with normal cells grouped in layers. A disturbance of this normal maturation underlies the pathological changes found in chronic laryngitis. The degree of disturbance of this maturation process, also called dysplasia, forms the basis of Kleinsasser's and other classification systems.

**Grade I: simple squamous cell hyperplasia or keratosi**

There is thickening of the entire epithelium. The basal cell layer becomes undulated, sometimes with deep projections in the stroma (acanthosis). There is further differentiation of cells towards intracellular keratin formation. The nuclei extend into the keratin layer (parakeratosis) and keratic covers the lesion to a varying degree (hyperkeratosis), but the regular maturation pattern is retained.

**Grade II: squamous cell hyperplasia or keratosis with atypia**

In the second stage there is early disorganization of the maturation process, but this is not very extensive; the loss of the normal organization is limited and never affects all layers at the same time. There is atypia at the cellular level, including altered nucleus/cytoplasm ratio, abnormal DNA content, abnormal mitoses and other aberrations. Acanthosis, dyskeratosis and parakeratosis are also present.

**Grade III: carcinoma in situ**

This third stage shows the most serious disorganization of the squamous epithelium identical to that of severe dysplasia. Frequent mitoses and cellular anomalies are found. The entire epithelium shows all cellular changes compatible with squamous cell carcinoma, but without infiltration through the basal membrane.

**Treatment**

It is important to make an early diagnosis and classify the lesion in order to institute adequate treatment. Squamous cell hyperplasia should be removed locally. Microlaryngoscopy as introduced by Kleinsasser is the most appropriate method. The lesion can usually be peeled off the underlying muscular tissue and vocal ligaments adequately and accurately. Both cords can be treated in the same session if the anterior commissure is left untouched. Occasionally the lesion may be so diffuse that total removal is not possible. In these cases removal is performed as far as possible (Kleinsasser, 1976).

Histological examination is always performed. Class I and II lesions normally need no further treatment. For class III lesions opinions differ. The increased chance that an infiltrating carcinoma will develop from such a lesion means that less risk can be taken. If possible, total removal by microlaryngoscopy is the method of choice and should be performed as soon as possible. A laryngofissure is rarely indicated. Furthermore, a good inspection of the surrounding mucosa is mandatory, especially in the subglottic region, in order not to overlook an infiltrating carcinoma. Radiotherapy is only indicated when removal
must be repeated for recurring or diffusely spreading lesions. Although some authors prefer radiotherapy as the primary treatment of choice, others feel that the recurrence rate after radiotherapy is too high and therefore advocate surgical removal or laser treatment.

Local removal is the method of choice in previously untreated carcinoma in situ. Radiotherapy should be given if the disease is so diffuse that local removal cannot be performed, or for recurrence of lesions previously removed.

Any patient suffering from squamous cell hyperplasia of the larynx needs careful follow-up. Class II and III lesions carry an increased risk of developing squamous cell carcinoma and need regular, life-long follow-up (Hellquist, Lundgren and Olofsson, 1982).

**Atrophic laryngitis**

This rare entity is also called laryngitis sicca. It is characterized by atrophic changes in the respiratory mucosa with loss of the mucus-producing glands. It is usually part of an atrophic rhinitis caused by *Klebsiella ozaenae*, but is much rarer.

**Pathology**

Fibrosis of the corium of the mucosa leads to anaemia and glandular atrophy. The respiratory epithelium shows squamous metaplasia with loss of cilia. Inspissated mucus adheres to the epithelium, dries and forms thick crusts. The most common sites are the false cords, the posterior region and the subglottic region.

**Clinical features**

An irritable cough and hoarseness are the most important signs. Crusts which are sometimes blood stained are expectorated. The crusts can readily be seen in the larynx and are the most important diagnostic feature. If the nose and sinuses show similar pathology the diagnosis is made easily.

In far advanced stages, when repeated crusting has led to total atrophy, there may be reactive inflammation of the cartilage structures with progressive fibrosis and eventually serious stenosis of the larynx.

**Treatment**

Treatment is directed at underlying causes such as generalized infections, poor nutrition or, rarely, syphilis. Local treatment consists of the stimulation of secretions and the removal of crusts. Secretions can be encouraged by small doses of ammonium chloride or iodide. The mucus so produced is less viscous, it softens the crusts and facilitates expectoration. The larynx can be sprayed with solutions of mucolytic agents. Local irritation especially by smoking should be strictly forbidden.
Contact granuloma (intubation granuloma)

A separate entity is formed by localized granulomata, nearly always unilateral, situated medially or superiorly on the vocal process of the arytenoid cartilage.

These lesions are often confused with contact ulcers. Jackson (1923) made no mention of granuloma when he first presented the clinical and pathological features of contact ulcers. Later he added the description of granulomata and considered them as part of the healing process. Benjamin and Croxson (1985) consider granulomata as a separate clinical entity. The granuloma has a typical polypoid appearance which is a local reaction to trauma. Granulation tissues can develop if the perichondrium is damaged either by vocal trauma or through trauma from an endotracheal tube. The granuloma may develop a long time after intubation.

Clinical features and diagnosis

Slight hoarseness is the most important symptom; the diagnosis is readily made by indirect laryngoscopy. The lesion is usually small but can become quite large and sometimes partially obstructs the laryngeal lumen. It is most restricted to one side and is usually attached on the superior edge. The granuloma can be pedunculated and move up and down between the cord. The colour is red, sometimes stained with dark areas from haemorrhage.

Treatment

These granulomata are not easy to treat. Simple removal by microlaryngoscopy seems the method of choice but local recurrences are common. The carbon dioxide laser advocated in recent years for treatment of this condition has not really improved matters; repeated treatment is often necessary. A conservative approach of 'wait and see' is sometimes as effective and should be considered in every case in view of the very resistant nature of this condition in spite of surgical removal.

Amyloidosis

Amyloid is an eosinophilic hyalin material with a strong affinity to certain dyes such as Congo red. Amyloidosis is a disease which has been known for over 140 years in which infiltration of different organs may occur.

Laryngeal amyloidosis is rare. It may be part of a generalized amyloidosis with involvement of many organs, in particular the heart, kidneys, gastrointestinal tract, blood vessels, liver. There are two main forms. Type A is the secondary type which is found in patients with long-standing inflammatory diseases; type B is the primary which is sporadically found in the larynx. This latter form may also be found in patients with multiple myeloma or macroglobulinaemia. With modern immunohistochemical methods it is possible to differentiate further the different types of amyloid, which morphologically, are all the same.

The clinical presentation of amyloid in the larynx is not characteristic. It may present as a solitary polyp on the vocal cord or as a more diffuse swelling in any region of the larynx or even trachea. Ulceration is not present. A biopsy of the lesion will lead to a diagnosis. A biopsy of the wall of the rectum is necessary to exclude a generalized form.
In rare instances there can be extensive infiltration from the larynx into the trachea, with progressive obstruction of the lumen of the airway.

Treatment is directed towards any underlying disease. The local lesion can be removed by microlaryngoscopy with sharp instruments or with the laser. The disease usually only progresses very slowly and repeated removal may be necessary.

**Granulomatous infections**

Both specific and non-specific granulomatous diseases can be found in the larynx. Sometimes the exact nature of the disease may be evident especially when a diagnosis has already been made elsewhere. However, it may be very difficult to make a diagnosis if only the larynx is involved. History, histopathological investigations and blood chemistry are essential for a correct diagnosis.

**Tuberculosis**

Laryngeal tuberculosis used to be commonly associated with pulmonary tuberculosis. In the western world, improved socio-economic circumstances and the advent of chemotherapy have resulted in a marked decline in tuberculosis, which is now rare in these areas. However, in developing countries the situation is quite different (Manni, 1982).

Laryngeal tuberculosis is almost exclusively found in patients suffering from open pulmonary tuberculosis and, in most cases, is a result of contamination by sputum containing acid-fast bacilli. Laryngeal tuberculosis only rarely develops by a blood-borne infection which causes diffuse involvement of the laryngeal mucosa with extensive ulceration. The frequency of the involvement of the larynx is difficult to estimate and varies in the different series published. Auerbach (1946) in his historic publication found laryngeal involvement in 37.5% of patients with pulmonary tuberculosis at autopsy, but today the percentage of involvement is probably much lower. There is no sex predominance. The age of patients with laryngeal tuberculosis used to be between 20 and 40, but is now generally higher.

**Pathology**

The pathway of infection is not known exactly, it is believed that contact with sputum containing tubercle bacilli plays an important role. The possibility of haematogenous or lymphogenous infection has also been suggested (Ormerod, 1939). The infection starts in the subepithelial space with exudation and hyperaemia followed by round cell infiltration. There is an inflammatory reaction of the mucosa and tubercles are found consisting of a granulomatous reaction with Langhans' giant cells, caseation and necrosis. The covering mucosa has an irregular appearance. Eventually confluence of these tubercles leads to necrosis of the overlying epithelium which sloughs and ulcerates. The ulcers are shallow with undermined edges, but there may be infiltration of cartilages, especially that of the epiglottis and the arytenoids. Acid-fast bacilli may be found with special stains, but are not always present.

Tuberculosis is to some extent self-limiting and heals with fibrosis which may result in serious stenosis of the larynx. Sometimes tumour-like swellings are found with reparative
processes called tuberculomata. Occasionally, there may be a diffuse oedematous reaction consistent with an allergic response to the tubercle bacillus.

**Clinical features**

Laryngeal tuberculosis should be suspected in any patient with pulmonary tuberculosis, especially in countries where tuberculosis is still endemic. Pain in the throat and referred earache are common. Cough, often productive, and hoarseness are nearly always present.

In advanced cases with extensive ulceration, the symptoms are very severe. The voice may be reduced to a harsh whisper. The pain and dysphagia can become unbearable. Only rarely is oedema so severe as to cause dyspnoea.

Laryngeal tuberculosis presents in many different forms. Mucosal hyperaemia and oedema are common first signs, often with irregularities of the mucosal surface. When tubercles are formed, granulomatous masses can be seen, ulceration appears later although it is relatively rare (15%, Manni, 1982). All regions of the larynx can be affected but there is a certain predilection for the posterior commissure, the arytenoids and the vocal cords.

**Diagnosis**

Patients with pulmonary tuberculosis should undergo laryngoscopic examination. A chest radiograph is performed to assess pulmonary lesions and a sputum smear for acid-fast bacilli will usually be sufficient to confirm the diagnosis.

Other forms of non-specific laryngitis and scleroma may resemble laryngeal tuberculosis as well as the ulcerative lesions found in lupus vulgaris, syphilis and carcinoma. If there is any doubt a biopsy should be performed. Tuberculosis and a malignant tumour may present simultaneously.

**Treatment**

As a result of improved socio-economic standards and the discovery of several very effective drugs, laryngeal tuberculosis is now rare. The drugs include streptomycin, para-aminosalicylic acid and rifampicin. Usually a combination of these drugs is used for maximum effect. Toxicity is still a problem, and all otologists should be aware of the serious side-effects of streptomycin on the auditory and vestibular organ. As well as these drugs, vocal rest should be advocated. Previously, application of local preparations containing local anaesthetic and astringents such as formaldehyde were advised, but these seem to be of limited benefit compared to chemotherapy.

Historically, galvanocautery was applied and even nerve blocks were performed in the superior laryngeal nerves for intractable pain. The recurrent nerve used to be injected with alcohol to immobilize the cord to promote better healing. These measures have now been abandoned.
The prognosis has altered entirely since the introduction of antituberculous drugs and nowadays a laryngeal infection with adequate treatment will subside within a few weeks, but treatment must be continued over a long period.

**Sarcoidosis**

Sarcoidosis is a chronic idiopathic granulomatous disease, also known as Besnier-Boeck disease. It may affect several organs and the mediastinal lymph nodes are usually involved. Head and neck manifestations are found in 10% of patients of whom only a minor proportion have laryngeal disease (Neel and McDonald, 1982). Symptoms are generally mild notwithstanding extensive tissue involvement. The disease is usually self-limiting. Laryngeal sarcoidosis may be the sole site in 50% of cases affecting the larynx.

**Pathology**

The pathology of laryngeal lesions resembles a non-specific granuloma similar to the lesions in other organs. The granulomata are composed of epithelioid cells with a varying number of lymphocytes and plasma cells. Giant cells with inclusion bodies are few and necrosis or caseation are not found. Later fibrosis and hyalinization and possibly encapsulation by fibrous tissue are more apparent.

**Clinical features and diagnosis**

Usually the patient has a history of hoarseness, dysphagia and dyspnoea. In most cases the main site is the supraglottis. The epiglottis and the false cords are swollen, oedematous and pale, and the rim of the epiglottis is full and rounded. The true cords and the subglottis are only rarely affected. The lesion can progress rapidly and lead to life-threatening airway obstruction. The diagnosis is made by biopsy which reveals the granulomatous nature. Further suspicion is raised by systemic manifestations. When the diagnosis is suspected, confirmation should be obtained by a full physical and laboratory investigation. This may be very difficult, especially if no other organs are involved. In rare instances sarcoidosis can present with a neuritis of the recurrent laryngeal nerve through involvement of cervical or mediastinal nodes. A positive Kveim skin test is highly suggestive but a negative reaction does not exclude the diagnosis. An elevated serum angiotensin converting enzyme (SACE) is found in about 60% of the patients. A gallium-67 scan can be very helpful in localizing enlarged lymph nodes.

**Treatment**

Opinions still differ as to whether sarcoidosis should always be treated. In general, sarcoid is very sensitive to high doses of corticosteroids, however, the recurrence rate is high and many lesions will regress spontaneously. The main indication for treatment for laryngeal sarcoidosis is airway obstruction and, to a lesser degree, severe dysphagia or hoarseness. Steroids may be given systemically or by local application, but their effect remains difficult to estimate. If the airway is seriously compromised a tracheostomy may be necessary and may have to remain in place for many months.
Syphilis

With the improvement in the treatment of syphilis, laryngeal syphilis is now rare. Involvement of the larynx is present in about 5% of cases. A syphilitic infection of the larynx should always be considered whenever an unexplained infection is present.

All stages of this disease can manifest in the larynx. A primary lesion has been described rarely. A small mucosal erosion develops into a typical primary chancre. The secondary stage is pluriform: vesicles and papular lesions often extend into the larynx from the pharyngeal mucosa. The third stage appears after a symptom-free period, sometimes of many years, and is the most important. Granulomata are found in the mucosa and form a gumma. These are characterized by a centre of necrotic amorphous tissue surrounded by an infiltrate of plasma cells and lymphocytes, sometimes with eosinophils and giant cells. There is periarterial infiltration and obliterative endarteritis.

The lesions have a predilection for the anterior parts of the larynx - the epiglottis and the aryepiglottic folds - compared to tuberculosis, which more often lies in the posterior part of the larynx. The mucosa is swollen and infiltrated and later undergoes deep ulceration with central sloughing. Abundant tenacious necrotic tissue reaches and penetrates the cartilage. The vallecula and the lateral pharyngeal wall are also involved. Considerable destruction can be found which, after healing, leaves a bizarre deformation of the larynx.

Clinical features

The presentation of syphilis in the larynx is very similar to other granulomatous laryngeal diseases. Hoarseness and sometimes dysphagia are the primary symptoms. Pain is rare and indicates very rapid destruction of deeper structures. Swelling of the mucosa causes some degree of stridor.

The laryngeal appearances vary widely. Laryngeal syphilis can easily be confused with a malignant tumour or with other chronic granulomatous infections, such as tuberculosis. At one time, the simultaneous occurrence of laryngeal syphilis and a malignant tumour was not rare. Nowadays laryngeal syphilis has become so rare that the diagnosis is usually only suspected after a biopsy has excluded carcinoma, which is so much more frequent.

Very rarely congenital syphilis can affect the larynx in the infant.

Treatment

The treatment of laryngeal syphilis should conform to the normal treatment of syphilis. This usually means prolonged treatment with high doses of penicillin. Local treatment by inhalations may be beneficial by removing necrotic tissue, which must sometimes be carried out to ensure an adequate airway. Local irritants such as tobacco and alcohol should be avoided.
**Scleroma of the larynx**

Scleroma, better known as rhinoscleroma, is a chronic granulomatous infection caused by *Klebsiella rhinoscleromatis*. The disease was recognized as an inflammatory process by Mikulicz in 1882 who described the characteristic foamy cells which carry his name. Initially it was considered as a lesion of the nose alone, but later, other sites of this infection were described which led to the change of name. The disease occurs worldwide with a low incidence but it is endemic in certain parts of central Europe, North East Africa and Central America. In a fully developed infection the pathology is characterized by Mikulicz cells, Russell bodies and Gram-negative bacteria but, in the initial stages especially, the inflammatory reaction is non-specific and can be difficult to diagnose. Repeated biopsies may be necessary before the diagnosis is made. Other granulomatous infections including tuberculosis, leprosy and granuloma inguinale can give a similar picture with the presence of macrophages resembling Mikulicz cells.

The symptoms and signs are non-specific and, as in many other chronic laryngeal infections, the diagnosis is usually first suspected after the discovery of the characteristic findings in a biopsy specimen. The presence of nasal lesions, which are found in 95% of cases will help to make a diagnosis. Laryngeal involvement is found in 14-80% of the cases. Laryngeal scleroma is rarely isolated (Jay, Green and Lucente, 1985).

Treatment consists of prolonged administration of bactericidal drugs. The spore forming properties of the organism necessitate the combination of an aminoglycoside, such as gentamicin, with an antimetabolite, such as tetracycline. Occasionally, endoscopic removal of granulomatous tissue is necessary to prevent obstruction. Relapse is common and makes close observation for longer periods necessary.

**Wegener's granulomatosis**

Wegener's granulomatosis is a diffuse systemic disease of unknown cause. It includes a triad of necrotizing granulomatous lesions in the upper and lower respiratory tracts manifesting themselves as a sinusitis or rhinitis, generalized vasculitis involving arteries and veins, and a necrotizing glomerulonephritis (MacKinnon, 1970). Probably about 25% of the patients also develop laryngeal manifestations during the course of the disease. The larynx is rarely the source of primary manifestation (Terent et al, 1980).

The lesion usually lies in the subglottis and may cause laryngeal obstruction. The mucosa is swollen, has a granular appearance, bleeds easily and is sometimes ulcerated.

If untreated Wegener's granulomatosis can be rapidly fatal. Corticosteroids can change the course of the disease if given early. Nowadays there is strong evidence that immunosuppressive drugs, especially cyclophosphamide, are very active against this disease and they are the treatment of first choice. In view of the toxicity of these drugs they should be used with proper precautions and only under medical supervision. Cures lasting up to 10 years have been reported.
**Leprosy**

Lepromatous lesions can be found in the larynx and these resemble the tuberculoid and syphilitic granulomata. The disease, caused by *Mycobacterium leprae* (Hansen's acid-fast bacillus), still holds many secrets with regards to the mode of infection. There are two forms - lepromatous and tuberculoid - both of which can arise in the larynx.

The epiglottis and aryepiglottic folds are most often affected. There is granulomatous swelling, and often ulceration and destruction, primarily in the supraglottic region. The epiglottis may be curled into a hollow rod. The mucosa may be studded with tiny nodules which may also occur in the trachea. Microscopically, the mucosa is thickened and foamy histiocytes are found (Virchow cells).

Modern chemotherapy can alter the otherwise fatal outcome to a certain extent. Dapsone, clofazimine and rifampicine are commonly used. The treatment should be prolonged over many years.

**Mycosis of the larynx**

Fungal infections have become much more common, partly through the widespread use of antibiotics and cytotoxic agents, which may influence the bioequilibrium allowing fungi, some of which are normal saprophytes, to spread. Also, generalized diseases such as diabetes, hypovitaminosis, malnourishment, hepatic disease and disseminated malignant disease predispose to fungal infection. It is likely that these infections will become increasingly important with the increasing incidence of acquired immune deficiency syndrome (AIDS).

Other mycoses have become more common as a result of the increase in worldwide travel, which has spread fungal infections from regions where they are endemic (Lyons, 1966).

An isolated involvement of the larynx is very rare. Contamination of the larynx is usually part of a fungal infection of the aerodigestive tract or of a systemic infection. These infections may be either superficial and limited to the mucosa, or infections spreading deep into all tissues.

The following mycoses can also affect the larynx.

**Candidiasis (moniliasis)**

Laryngeal involvement by *Candida albicans* is usually secondary to candidal infection of the oropharynx or of the lower airways. *Candida albicans* is essentially a saprophyte commonly found in the mouth and pharynx which can assume pathogenic properties under altered circumstances.

Manifestations of candidiasis in the larynx include oedema and erythema of the mucosa, a whitish-grey adherent fibrinous pseudomembrane and superficial ulceration.
surrounded by squamous cell hyperplasia. Microscopically the yeast, with its hyphae and pseudohyphae, is easily recognized.

Treatment is primarily directed towards correction of the underlying causes. Drugs containing nystatin or miconazole are given by topical application, as lozenges or as an aerosol.

**Coccidioidomycosis**

This infection, caused by *Coccidioides immitis*, is endemic in certain parts of California, especially the San Joaguin Valley. Primary infections are common and present as mixed respiratory infections. The disseminated form is very rare.

There have been incidental reports of involvement of the larynx presenting as a granulomatous lesion clinically identical with other granulomata such as tuberculosis. The fungus can usually be seen in biopsy specimens. Administration of amphotericin B is the treatment of choice.

**Paracoccidioidomycosis (South American blastomycosis)**

*Paracoccidioides brasiliensis* is the causative organism of this fungal infection, also called South American blastomycosis. It is endemic in Central and South America.

The disease manifests itself with oropharyngeal or skin lesions and bronchopulmonary infections. Laryngeal involvement is quite common.

Ulcerations of the larynx can sometimes lead to strictures. The organism can be identified in a smear or in sputum. Amphotericin B is the treatment of choice.

**Histoplasmosis**

Histoplasmosis is caused by *Histoplasma capsulatum*: it is worldwide and is endemic in certain regions of the USA such as in the valleys of the Ohio and Mississippi rivers. Many people have been infected with *Histoplasma* during a previous respiratory infection leaving pulmonary calcification which can be found on a chest radiograph. There is also a disseminated form attacking organs such as the liver, spleen and bone marrow. Mucosal lesions are described with increasing frequency.

In the larynx the characteristic lesions of a chronic granulomatous infection are indistinguishable from tuberculosis. Oedema, erythema and granulomata are present, but the lesions lie more anteriorly.

It is not always easy to identify *Histoplasma*, especially in the chronic forms. Special staining tests with methenamine-silver or culture in Sabouraud's medium can be helpful. Further confirmation can be obtained by skin tests or complement fixation tests. The clinical course is variable and characterized by exacerbations and remissions.
The most important drug is amphotericin B 30-50 mg, four to six times a day. Careful monitoring is necessary as serious nephrotoxicity may occur. A newer drug, ketoconazole, is less toxic but needs further investigation into its efficacy.

Other mycotic infections

Other fungal infections which have been described in the larynx include: North American blastomycosis caused by Blastomyces dermatitidis, cryptococcosis caused by Cryptococcus neoformans, rhinosporidiosis caused by Rhinosporidium seeberi, and aspergillosis caused by Aspergillus niger. The diagnosis can be made by using fungal staining techniques.

Actinomycosis

Actinomycosis israelii is the causative agent of actinomycosis. It is not a true fungus and, according to most pathologists, should be classified in the group of the higher bacteria (Michaels, 1984). Involvement of the larynx is rare (Brandenburg, Frisch and Kirkham, 1978) and is usually secondary to a suppurative cervical lymph node. The characteristic yellow 'sulphur granules' are seen and under the microscope Actinomyces are identified as long slender Gram-positive branching filaments.

Parasitic infections

Parasitic diseases in the larynx are very rare. Leishmaniasis, trichinosis, schistosomiasis and ascariasis are all parasitic infections which can be found in the larynx. The diagnosis is suspected by the general manifestations of the disease, the lesions in the larynx being of the granulomatous type. Detailed descriptions can be found in textbooks of tropical diseases.