Surgical pathology of the mouth and jaws

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2. Major infections of the mouths, jaws and perioral tissues

Severe oral and perioral infections are uncommon, but may take any of the forms discussed in the text. Oral bacteria can also cause dangerous metastatic infections or septicaemias and these are sometimes a significant hazard, particularly in immunodeficient patients, as discussed later.

Acute osteomyelitis

Acute osteomyelitis of the jaw has a different aetiology and microbial causes from long bone infections. The latter are largely a disease of childhood as a result of haematogenous spread of bacteria. By contrast, osteomyelitis of the jaws is a disease of adults and the infection typically originates from the mouth. The source of infection can be any of the following:

- periapical infection

- a periodontal pocket when the jaw is fractured

- acute gingivitis or pericoronitis (even more rarely)

- the skin or other external sources (open fractures or gunshot wounds).

Predisposing causes

Now that apparently spontaneous severe infections in or around the jaws have become rare in the general population, predisposing conditions have become relatively more important. The main examples include:

1. Local damage to or disease of the jaws:
    (a) open fractures including gunshot wounds
    (b) radiation damage
    (c) Paget's disease or osteopetrosis (Chapter 6).

2. Impaired immune defences. Examples include acute leukaemia, immunosuppressive treatment, poorly controlled diabetes mellitus, sickle cell anaemia, chronic alcoholism or malnutrition. In such cases, and particularly in alcoholics, serious infection of the bone is typically precipitated by injury, sometimes of a minor nature. Acute osteomyelitis of the jaw has been described in HIV infection but appears to be uncommon in this group; indeed it has been shown by Robinson et al (1992), that in such patients healing is normal after extractions and the incidence of localized osteitis is no more frequent than in a control group.

In a review of 35 cases, Koorbusch et al (1992) found that odontogenic infections and trauma each accounted for 36% of osteomyelitis of the jaws. Immunosuppressive treatment

was associated in only 9% of cases. None of the patients was diabetic, but this may reflect better control of the disease. Alcohol and tobacco use were recorded in 46% and 51%, respectively, but their contribute to the infection is unclear.

Clinical features

The great majority of patients are adult males and the mandible is usually affected. Acute osteomyelitis of the maxilla is usually a disease of neonates or infants and follows either birth injuries (due to forceps, for example) or uncontrolled middle ear infection. It is also therefore rare now in developed countries. In adults is is also a rare complication of trigeminal herpes zoster.

Early complaints are severe, throbbing, deep-seated pain, and swelling. The external swelling is initially due to inflammatory oedema. Later distension of the periosteum with pus, and finally subperiosteal bone formation, cause the swelling to become progressively firmer. The overlying gingiva is red, swollen and tender.

Associated teeth are tender to percussion. In severe cases they may become loose and pus may exude from an open socket or from round the necks of the teeth. Muscle oedema causes difficulty in opening the mouth and swallowing. Regional lymph nodes are enlarged and tender, and anaesthesia or paraesthesia of the lower lip is characteristic.

During the acute phase there may be fever, malaise and leucocytosis, but infrequently the patient remains surprisingly well. A severely ill or very pale patient suggests underlying disease which should be investigated.

Radiography

Bony changes do not appear until after at least 10 days. The sharp trabecular pattern of the bone is lost where bone has been resorbed and areas of radiolucency indicate bone destruction. These areas have ill-defined margins and have a fluffy or moth-eaten appearance. Areas of dead bone appear relatively dense. These become more sharply defined as they are progressively separated as sequestra. Later, there is subperiosteal new bone formation which is most often seen in young patients. It typically appears as a thin, curved strip of new bone below the lower border of the jaw.

Microbiology

Unlike osteomyelitis of long bones, which is usually a haematogenous infection, staphylococci are only likely to cause osteomyelitis of the jaw when they come from an external source, such as the skin, as a result of an open fracture. In such cases *S. epidermidis* is more frequently the cause than *S. aureus*. In most cases, oral bacteria, particularly anaerobes such as Bacteroides, Porphyromonas or Prevotella species, are the main cause and it is often a mixed infection (Table 2.1). Strict care in sampling is necessary to isolated anaerobes which may not be found unless the isolation technique is adequate. Gram-negative infections have also been reported, particularly in sickle cell disease and in alcoholics.

Pathology

The mandible has a relatively limited blood supply, dense bone with thick cortical plates and coarse trabeculae. Osteomyelitis is likely only to follow a straightforward extraction if the patient is immunocompromised and has a neutrophil defect as in acute leukaemia.

Table 2.1 Important bacteria implicated in osteomyelitis of the mandible

Eikenella corrodens	Klebsiella
Staphylococcus aureus	Actinomyces
Staphylococcus epidermidis	Bacteroides (various)
Pseudomonas aeruginosa	*Fusobacterium nucleatum*
Viridans streptococci	Anaerobic or aerophilic streptococci
Salmonellae	*Serratia marescens*
Streptococcus pyogenes	

Fractures of the tooth-bearing regions of the jaw are usually open to the oral cavity through torn mucoperiosteum, but there is little risk of infection from the saliva. However, periodontal pockets form a reservoir of virulent bacteria and if the fracture line involves a periodontal ligament, infection can spread from this source, unless controlled by prophylactic antibiotics. In the case of gunshot wounds there may be the combined effects of gross trauma and implantation of foreign material together with staphylococci or other bacteria from the skin.

Once infection involves the medullary soft tissue it provokes an acute inflammatory response. Outpouring of inflammatory exudate carries infection through the marrow spaces. However, the rigid boundaries of the vascular canals cause exudate to compress the blood vessels; thrombosis and obstruction then lead to further bone necrosis. Bacteria can proliferate in this dead tissue and are then relatively inaccessible to some antibiotics such as the penicillins. Dead bone is readily recognizable microscopically by the lacunae empty of osteocytes but filled with neutrophils.

Pus formed by liquefaction of necrotic soft tissue and inflammatory cells is forced along the medulla, but is eventually able to reach the subperiosteal region by resorption of bone. Distension of the periosteum by pus stimulates subperiosteal bone formation, but perforation of the periosteum by pus and formation of sinuses on the skin or oral mucosa is rarely seen now.

At the boundary between the infected and healthy tissue, osteoclasts resorb the periphery of the dead bone which eventually becomes separated as a sequestrum. Once the infection starts to localize, new bone forms around it, particularly subperiosteally. In the past this could lead to involucrum formation and enclosure of sequestra; however, no more than a rim of new bone below the lower border of the mandible is usually seen now.

Where bone has died and been removed, healing is by granulation with formation of coarse fibrous bone in the proliferating connective tissue. Gradually fibrous bone is replaced by compact bone and remodelled to restore normal morphology.

Management

The following are main requirements:

1. *Bacteriological diagnosis.* A specimen of pus or, failing that, a swabb fro the depths of the lesion should first be obtained for culture and sensitivity testing.

2. *Antimicrobial treatment.* Once a specimen has been obtained, vigorous antibiotic treatment should be started. Initially, penicillin, 600-1200 mg daily can be given by injection, provided that the patient is not allergic, with metronidazole 200-400 mg 8-hourly. Clindamycin has unusually good penetration of poorly vascular tissue and has beeneffective for the treatment of osteomyelitis of the mandible as well as of long bones. The precise regimen will be determined a few days later by the bacteriological findings.

3. *Debridement.* If there has been a gunshot wound or other penetrating injury, careful debridement, removal of foreign material and immobilization of any fracture is necessary.

4. *Drainage.* Pressure within the bone must be relieved by tooth extraction, burr holes or decortication, as necessary, and exudate drained into the mouth or externally.

5. *Removal of sequestra.* This should be delayed until the acute phase has been controlled. Dead bone should not forcibly be separated and vigorous curetting is inadvisable, but in the later stages a loosened sequestrum may have to be removed. Teeth should be extracted only if loosened by tissue destruction.

Complications

- Involvement of the inferior dental nerve may cause anaesthesia of the lower lip, but sensation should recover with elimination of the infection.

- Pathological fracture may be caused by extensive bone destruction and requires immobilization, but is unusual.

- Chronic osteomyelitis may rarely follow inadequate treatment.

- Cellulitis due to spread of exceptionally virulent organisms is also rare.

- Septicaemia is only likely to be seen in an immunodeficient patient.

Osteoradionecrosis and radiation-associated osteomyelitis

Osteoradionecrosis is death of irradiated bone which is highly susceptible to infection. Watson and Scarborough (1938) reported an incidence of 13% in a series of 1819 patients with oral cancer treated by irradiation. With modern techniques and antimicrobials, the incidence is considerably lower.

The mandible is usually affected. It has a far more dense cortical plate and trabeculae than the maxilla and its blood supply in the elderly is poor, being predominantly via the

periosteum. Infection can enter, particularly via injuries such as tooth extractions, and can spread to cause widespread necrosis of bone, periosteum and mucosa. However, radiation-associated osteomyelitis is highly unpredictable and can occasionally develop even in the absence of obvious infection or trauma.

The role of dental disease in the aetiology of bone infection after irradiation is uncertain. Clinically significant radiation necrosis of the mandible is usually associated with open mucosal wounds. Dental disease is the usual cause of disruption of these tissues and allows the ingress of microorganisms. There is a clear relationship between the dental state before radiation and subsequent infection. All dental disease should be treated thoroughly before radiotherapy, but removing teeth before radiotherapy is a subject of some controversy. One unsettled point is the interval between the time of extractions and the initiation of radiotherapy, and many authors have indicated the risks of irradiating mandible shortly after extractions. Others have just as strongly advocated that all teeth in the beam should be extracted before starting radiotherapy. In practice, with modern high-energy beams it is safe to leave healthy teeth, but any non-vital or periodontally involved teeth in the radiation field should be removed before radiotherapy.

Jansma et al (1992) in their protocol for prevention of oral complications after radiotherapy, consider that a delay of 3 weeks is necessary after extractions.

Management

The approach should be conservative. Any intraoral wounds should be regularly irrigated and the patient must maintain meticulous oral hygiene. Dilute eusol, hydrogen peroxide or chlorhexidine solutions are suitable, but the nature of the irrigation fluid is less important than the mechanical dislodgement of food debris and necrotic tissue. The patient should be shown how to irrigate the cavity and at the very least should rinse the mouth thoroughly with a chlorhexidine mouthwash, after any food.

Sequestra should be allowed to separate spontaneously. Active curettage only encourages extension of the infection. Only loose bony sequestra should be removed. Any sharp edges or spicules of bone should be smoothed off with rongeurs to prevent irritation of the tongue. Spontaneous healing is accomplished in approximately 50% of cases by natural sequestration and granulation. Because of its avascular nature, resorption of non-vital bone may take many months or even years, and great patience is required to resist the temptation to intervene surgically even after pathological fracture.

Osteoradionecrosis is usually relatively painless and any discomfort may be controlled with antiinflammatory analgesics. Persistent severe pain is an indication for surgical intervention.

The avascularity of the tissues makes antibiotic therapy unlikely to help, though clindamycin diffuses well into poorly vascular areas and is the drug of choice for some anaerobic infections such as *Bacteroides fragilis.* However, in long-term treatment, the risk of pseudomembranous colitis becomes significant. Long-term low-dose tetracycline therapy (oxytetracycline 250 mg bd) or long-term sodium fusidate (500 mg tds) may, therefore, be more appropriate. It also seems logical to include metronidazole (200 mg tds) to help combat

anaerobes. Healing takes many months, even when antibiotics are given, so that their value is difficult to assess.

Hyperbaric oxygen therapy has been shown to encourage healing by accelerating revascularization and increasing both osteoblastic and osteoclastic activity. Hart and Mainous (1976) reported on 46 patients with osteoradionecrosis of the mandible who had been treated at 2 atm for 2 h each session. A course of treatment consisted of a total of 120 h of hyperbaric therapy. Daily irrigation and long-term tetracycline were also employed. After such treatment, 37 of thr 46 patients were symptom free, with complete intraoral soft tissue healing. Nine of the patients had dental extractions and trimming of the alveolar bone without complications. A further 4 patients required bone grafts to restore mandibular continuity - all were successful. Marx (1983) reported successful treatment of 27 cases of osteoradionecrosis with hyperbaric oxygen, combined with surgery in 5 of them. By contrast, van Merkesteyn et al (1984) had limited success with it for chronic osteomyelitis. The procedure is generally safe, but Foster (1992) had described the contraindications and a formidable range of possible complications.

If pain or infection persists despite conservative measures, surgical intervention is required. Failure of conservative measures to bring about healing should prompt investigation for residual or recurrent tumour. Often when the necrotic bone is removed, active tumour becomes apparent. When surgery is undertaken, all heavily irradiatedbone must be removed and the line of resection must be within healthy bleeding bone. Failure to achieve this will result in further necrosis. In patients who have been treated for large tumours or even small anterior tumours, both sides of the mandible may have received high-dose irradiation. Bilateral mandibular resection may then be necessary and considerable susequent deformity can result.

Long-term management. No reconstructive surgery should be attempted until the lesion has undergone fibrosis and contraction for at least a year. Often this will result in extra-articular ankylosis which makes subsequent intubation for general anaesthesia hazardous. Ankylosis must be released before soft tissue reconstruction (using local and distant flaps) can be attempted. Ankylosis often recurs due to the strong tendency to fibrosis and osteogenesis in the affected tissues. Active jaw movement exercise postoperatively for an indefinite period is therefore essential.

Chronic osteomyelitis

Inadequately treated osteomyelitis may become chronic. Rarely, chronic osteomyelitis may develop without any apparent acute episode. The infection is localized, but persistent because of the inaccessibility to host defences of bacteria growing in dead bone. There is intermittent discharge of pus and new bone formation. Pain tends to be mild and intermittent. Sequestra are slowly shed, but may oftenbe felt by probing along a sinus. They give a characteristic rough, grating sensation, and may be felt to be loose. Radiologically a small area of bone destruction may be seen and there may be sclerosis of surrounding bone, together with subperiosteal new bone formation.

Treatment

Chronic osteomyelitis is best treated by decortication of the affected area and insertion of gentamicin-impregnated acrylic beads in the adjacent tissues.

Chronic osteomyelitis in childhood

This entity has been recognized only in recent years. It typically begins at 8-10 years, with intermittent dull aching pain in the posterior mandible. Painful episodes are sometimes accompanied by diffuse swelling in the cheek, but usually respond to antibiotics.

Serial radiographs show migrating areas of moth-eaten destruction of the cancellous and cortical bone throughout the ramus and body of the mandible, eventually followed by complete regeneration with no residual changes.

Despite attempts to establish a bacterial cause, pathogenic bacteria have not been found, but the rapid response to fusidic acid suggests that *Staphylococcus aureus* may be responsible. There is some evidence that many of these patients may have a leucocyte defect which allows the infection to persist. Ord and El-Attar (1987) described three cases of chronic osteomyelitis in children, one of whom responded to extraction of the causative tooth and the others to clindamycin.

Management

Fusidic acid, clindamycin or erythromycin are most likely to be effective, but recurrent symptoms may persist for several years and only resolve in late adolescence. If pain is frequent or persistent, it may be necessary to maintain continuous antibiotic therapy for months or even years, but surgery seems to offer little benefit.

Chronic specific osteomyelitis

Syphilitis, actinomycotic and tuberculous osteomyelitis of the jaws are recognized entities and show the histological features typical of these diseases, but are unlikely to be seen now.

Chronic focal sclerosing osteomyelitis (condensing osteitis)

This is an uncommon bony reaction to exceptionally low-grade periapical inflammation or, alternatively, to an unusually high degree of local tissue resistance to infection.

Patients are typically under 20 and the focus is most commonly related to a mandibular first permanent molar which, though grossly carious and non-vital, is either asymptomatic or causes only mild pain.

Radiographs show a well-circumscribed radiopaque area up to 2-3 cm in diameter below the apex of one or both roots, which typically retain an intact lamina dura. The margins of the lesion can be sharply defined or merge with the surrounding normal bone.

Microscopy shows a dense mass of compact bone with few lacunae, many of which are empty of osteocytes, but prominent resting and reversal lines give it a pagetoid appearance. There are only small amounts of fibrous interstitial tissue infiltrated by small numbers of lymphocytes.

Removal of the infected tooth is followed by slow resolution of the lesion, but an area of sclerotic bone may remain indefinitely.

Chronic osteomyelitis with productive periostitis (non-suppurative osteomyelitis, Garrés osteomyelitis)

This uncommon reaction to periapical or perifollicular infection is characterized by subperiosteal new bone formation.

Only young patients are affected and the lesion is a response to low-grade chronic infection, usually in the mandible and, particularly, the lower first permanent molar. There may be mild pain before the formation of a non-tender, bony hard swelling, usually on the lower border or lateral aspect of the jaw.

Radiographs show a carious tooth with a periapical area of radiolucency or, less commonly, folliculitis round an unerupted tooth. On the cortical surface there is a smooth convex overgrowth of bone. The new bone may show parallel, concentric (onion skin) laminations. The rest of the jaw may appear normal or show radiolucent or osteosclerotic areas due to osteomyelitis.

Microscopy shows the newly formed bone to cosist of primitive bone (osteoid) in fibrous connective tissue, patchily infiltrated by lymphocytes and plasma cells.

Other diseases which resemble proliferative periostitis radiographically include Ewing's sarcoma, osteosarcoma, infantile cortical hyperostosis, fracture callus, ossifying subperiosteal haematoma and peripheral osteoma.

Removal of the infection should lead to gradual remodelling of the jaw.

Diffuse sclerosing osteomyelitis

So-called diffuse sclerosing osteomyelitis was described by Shafer et al (1983) as an unusual proliferative response to low-grade infection, particularly widespread periodontal disease. However, it has the same microscopic appearance as florid osseous dysplasia (gigantiform cementoma) and they are probably not distinct entities (see Chapter 4), though the term may possibly be justified if infection has become superimposed. However, Schneider and Mesa (1990) dispute this view and give reasons for regarding florid osseous dysplasia and chronic sclerosing osteomyelitis as separate entities.

This disease is most frequently seen in middle-aged or elderly Blacks. The mandible, which may be dentate or edentulous, is usually affected and the main symptoms are episodes of mild suppuration with fistula formation and vague pain or an unpleasant taste.

Radiographs show areas of diffuse or nodular sclerosis, resembling the cottonwool radiopacities of Paget's disease, often bilaterally, and sometimes involving both the mandible and the maxilla.

Microscopy shows dense, irregular bone with a pagetoid ('mosaic') pattern of reversal lines. Fibroblastic connective tissue fills the marrow spaces and is patchily infiltrated by variable numbers of chronic inflammatory cells. During acute exacerbations, neutrophils become numerous.

Management

Chronic diffuse sclerosing osteomyelitis needs to be distinguished from Paget's disease, osteopetrosis and late-stage fibrous dysplasia. Removal of any offending teeth and antibiotic therapy are the initial treatment. Often the dense 'cemental' masses form sequestra and when this happens the affected area should be guttered and the dense masses removed. Healing then follows.

Pulse granuloma (chronic periostitis) of the jaw

Pulse (hyaline ring) granuloma is an uncommon lesion which usually affects the edentulous posterior mandible. It can cause recurrent swelling and tenderness. Radiographically, there is typically a radiolucent area with an irregular outline, or erosion of the crest of the alveolar bone, but there is sometimes subperiosteal bony thickening.

Microscopy

Eosinophilic hyaline rings are surrounded by granulation tissue with chronic inflammatory and multinucleated giant cells. The rings may be incomplete but may enclose giant cells, connective tissue and blood vessels. They resemble residues from leguminous vegetable matter by light and electron microscopy. Somewhat similar changes have been produced experimentally by implantation of homogenized cooked pulses: the starch component was gradually digested and the residual cellulose formed rings. These were less grossly thickened than those in human lesions where there appears to be adsorption of plasma proteins and gradual deposition of collagen on the surface. Rarely, starch granules have been seen within the hyaline rings in human material and are present in pulse granulomas sometimes found in the lungs of infants and debilitated adults. The differences between the jaw, lung and experimental lesions may possibly be due to changes induced by long persistence of the foreign material in the tissues.

Excision is curative.

Sclerotic (dense) bone islands (idiopathic osteosclerosis)

Areas of sclerosis in the mandible are sometimes seen by chance in routine, particularly panoramic, radiographs or may be noticed for the first time after a surgical procedure. In the past, these have been interpreted as the result of low-grade infection and have sometimes been removed surgically. They are most frequent in the moral or premolar region and may be related to the apex of a tooth, but separated by the periodontal ligament,

or more deeply in the jaw. Kawai et al (1992) found them in 10% of 1203 Japanese outpatients: this is approximately twice the prevalence of these osteoscleroses in Westerners. These enostoses are normal variations in the bone pattern and microscopically appear, as their name implies, as islands of sclerotic but otherwise normal bone surrounded by normal trabeculae.

Fascial space infections (cervicofacial cellulitis)

Deep fascial space infections, of which the best known example is Ludwig's angina, are characterized by gross inflammatory exudate and oedema, together with fever and toxaemia which may be severe. Before the use of antibiotics the mortality was high and the disease is still life-threatening if treatment is delayed. The clinical variants and their current management have been reviewd by Chow (1992).

These infections have become rare in many parts of Britain, but appear to be considerably more common among Afro-Caribbeans. Such patients are fit, well-nourished young male adults with no apparent predisposing factors other than apical or periodontal abscesses. These patients do not have diagnosable immunological or haematological defects, though many have sickle cell trait. Their oral hygiene is possibly better than that of the general white population.

General clinical features

The characteristic features are diffuse, brawny swelling, pain, fever and malaise. The swelling is tense, tender, with a characteristic board-like firmness. The overlyingskin is taut and shiny. Pain and oedema cause difficulty in opening the mouth and, often, difficulty in swallowing. Constitutional upset is severe with worsening fever, toxaemia and leucocytosis. The regional lymph nodes are swollen and tender.

Once oedema extends towards the glottis, as in Ludwig's angina particularly, or the tongue is forced upwards and backwards in the airway, there is increasing respiratory distress which, if not rapidly relieved, quickly results in asphyxia. Tracheostomy may then be necessary.

Aetiology and pathology

The organisms responsible are mainly odontogenic and include a variety of obligate anaerobes which Chow (1992) found to outnumber aerobes by a factor of 10 to 1 (Table 2.2).

Fasciae covering muscles and other structures are normally in close apposition. If these fascial planes are spread apart, a space is created. Such spaces contain little except loose connective tissue and are almost avascular. If virulent bacteria enter these fascial planes, inflammatory exudate is poured out from nearby vessels, but if it fails to localize the organisms it opens up the fascial space, carrying infection with it. Infection may thus spread through one or more fascial spaces until their natural boundaries are reached.

Table 2.2 Examples of bacteria isolated from perimandibular fascial space infections

Anaerobic Bacteria

Porphyromonas gingivalis
and Bacteroides species
Fusobacteria including
Fusobacterium nucleatum
Peptostreptococci and
peptococci
Eikenella corrodens

Escherichia coli
Klebsiella
Pseudomonas aeruginosa
Staphylococcus epidermidis
and *S. aureus*
Proteus species
Haemophilus influenzae
(children especially)

Aerobic and Facultative Bacteria

Beta-haemolytic streptococci
Viridans streptococci
(S. morbillorum, S. constellatus or *S. sanguis)*

The main cause of cellulitis of the neck is infection arising from the region of the lower molars. Several fascial spaces are accessible from this area and the following factors contribute:

- the apices of the second and, more especially, the third molars are often close to the lingual surface of the mandible

- the mylohyoid attachment inclines downwards as it runs forward; the apices of the third molar are usually, and the second molar are often, below this line

- the posterior border of the mylohyoid is close to the sockets of the third molars; at this point the floor of the mouth consists only of mucous membrane covering part of the submandibular salivary gland.

When a virulent periapical infectin of a lower third molar penetrates the lingual plate of the jaw, it is then at the entrance to several fascial spaces. Anteriorly there are the submandibular and sublingual spaces, while posteriorly are the parapharyngeal and pterygoid spaces. Infection in this area may rarely also spread from an acute pericoronitis, particularly when the deeper tissues are opened to infection by extraction of the tooth during the acute phase. Indresano et al (1992) identified 21 patients, over a 6-year period, with deep space infections attributable to pericoronitis and reached the remarkable conclusion that, in the USA, as many as 15.000 serious or life-threatening infections a year might originate from third molar infections.

Cellulitis can be a complication of acute osteomyelitis of the jaws due to spread of an exceptionally virulent infection, but this is unlikely to be seen now.

In general, perioral cellulitis is only likely to develop when virulent and invasive organisms gain access to the fascial spaces. Since the predisposing causes do not often coincide, cellulitis is uncommon. Cellulitis in the region of the upper jaw is even more uncommon, but may develop in various sites as the result of infected local anaesthetic needles.

Sublingual cellulitis

The *sublingual space* lies between the mucous membrane of the floor of the mouth above, and the mylohyoid below and laterally. Medially, the space is bounded by the geniohyoid and genioglossus muscles, but in front of them the left and right sublingual spaces are continuous. A deep extension of the space lies between the genial muscles. Posteriorly, on either side, the sublingual space is open, communicating round the posterior border of the mylohyoid with the submandibular space below, and with the parapharyngeal space behind. The sublingual space contains the sublingual gland and related arteries and nerves.

Clinical features

The source of infection is usually a mandibular molar, but occasionally infection from a more anterior tooth may penetrate the lingual plate of bone. Sublingual cellulitis is characterized by gross swelling of the floor of the mouth. The mucosa is red or purplish and pushed upwards, level with the occlusal surfaces of the teeth, which indent it. Swallowing is difficult due to oedema of the muscles of the tongue, which becomes swollen and elevated, occasionally so severely as to threatent the airway.

Infection may remain localized in the sublingual space or may spread backwards towards the parapharyngeal, pterygoid or submandibular space.

Submandibular cellulitis

The sbumandibular space contains the submandibular salivary gland and is formed by the splitting of the deep cervical fascia above the hyoid bone. The submandibular space is bounded laterally and below by the superficial layer of the deep cervical fascia which extends from the hyoid bone to the mylohyoid and forms the superior and medial boundary of the space. The intercommunications of the three main fascial spaces in this area are shown by the deep process of the submandibular gland. This curves round the posterior border of the mylohyoid, juts into the entry to the parapharyngeal space and, by curving forward on to the superior surface of the mylohyoid muscle, extends into the sublingual space.

Clinical features

Submandibular cellulitis is typically caused by infection from the second or third molars. Painful brawny swelling is centred on the upper part of the neck, mainly along the lower border of the mandible. Infection may spread into the sublingual or parapharyngeal spaces as already indicated, to give rise to Ludwig's angina.

Ludwig's angina

Ludwig's angina is a severe form of cellulitis which usually arises from the lower second or third molars; it involves the sublingual and submandibular spaces bilaterally almost simultaneously and readily spreads into the parapharyngeal and pterygoid spaces.

The *parapharyngeal space* extends backwards from the lingual aspect of the third molar region, between the superior constrictor of the pharynx medially and the internal pterygoid laterally. Above the mylohyoid line the space is limited anteriorly by the pterygomandibular raphe. Below, the parapharyngeal space is bounded by the muscles arising from the styloid process. The carotid sheath lies within this space.

The *pterygoid space* lies lateral to the pharyngeal space. It is bordered laterally by the mandibular ramus and medially by the medial pterygoid muscle. Above, it communicates with the infratemporal fossa.

Clinical features

Ludwig's angina is characterized by rapid development of sublingual and submandibular cellulitis with painful brawny swelling of the upper part of the neck and the floor of the mouth on both sides. With involvement of the parapharyngeal space, the swelling tracks down the neck, and oedema can quickly spread into the loose connective tissue round the glottis.

Swallowing and opening the mouth become difficult, and the tongue may be pushed up against the soft palate. Oedema of the glottis causes increasing respiratory obstruction. The patient soon becomes seriously ill, with fever, respiratory distress, headache and malaise.

Respiratory obstruction is indicated by noisy breathing and restlessness, going on to violent efforts at respiration using the accessory muscles, and darkening cyanosis. A patient with cellulitis of the neck may die quickly from asphyxia, or later from the effects of spread of infection to the mediastinum via the carotid sheath.

Management

A patient with a brawny swelling of the mouth or neck, fever and malaise must be immediately admitted to hospital. The first essential is to secure the airway. If there is dyspnoea, an endotracheal tube should be inserted withthe help of a fibreoptic bronchoscope. A specimen for culture should be obtained by fine-needle aspiration to avoid contamination by oral bacteria. The mainstay of treatment of cellulitis is vigorous use of antibiotics. Provided that the patient is not allergic, intravenous penicillin (not less than 600 mg given every 6 h) is the traditional treatment, but resistant bacteria are increasingly frequently encountered. To counter anaerobes, metronidazole (800 mg 8-hourly by iv infusion) can be given with penicillin or alone if the patient is allergic to the latter. A case has been made by Finer and Goustas (1992) for the use of ceftazidime, an injectable third-generation cephalosporin as initial treatment for severe infections. It has a wide spectrum of activity particularly against Gram-negative bacteria and is not nephrotoxic or ototoxic. However, metronidazole may also be needed.

The swelling should be incised early to relieve the pressure of exudate, particularly when the swelling is so large as to force the tongue into the airway. Little fluid is produced at first, but continues to dribble away. The neck should be laid open widely, all tissue spaces opened with sinus forceps and multiple corrugated drains inserted. Often through-and-through drainage is required with bilateral drains through the neck into the oral cavity.

General anaesthesia is particularly hazardous in the later stages of Ludwig's angina if the patient has not been intubated. If the patient is dependent on conscious effort to breathe, the airwayis lost immediately as muscle relaxant is given and emergency tracheostomy becomes necessary. This may itself open up further tissue planes to infection. For this reason, surgical drainage should be undertaken early, before respiratory obstruction develops. Should anaesthesia be necessary at this stage, the patient can be given a gaseous induction without muscle relaxants and an attempt made at intubation, preferably using a fibreoptic bronchoscope. The surgeon must stand by ready to perform an emergency tracheostomy.

The tooth from which the infection started should be extracted as soon as the patient's condition allows.

Cavernous sinus thrombosis

Cavernous sinus thrombosis is a life-threatening complication that can rarely arise from an infected upper anterior tooth. Other sources include infected spots or boils on the upper lip or in the anterior nares. Infected thrombi in the anterior facial vein or, less frequently, in the pterygoid plexus of veins communicate with the cavernous sinus via either the ophthalmic veins or via the foramen ovale, respectively.

Clinical features

Gross oedema of the eyelid is associated with pulsatile exophthalmos due to venous obstruction. Venous stasis leads to cyanosis, and the superior orbital fissue syndrome (proptosis, fixed dilated pupil and limited eye movement) rapidly develops. The facial fein is dilated and the conjunctiva is oedematous. There is papilloedema with multiple retinal haemorrhages. The patient is seriously ill with rigors and a high swinging pyrexia. Initially one side is affected, but both sides become quickly affected if treatment is delayed. Blindness complicating cavernous sinus thrombosis secondary to dental infection has been reported by Ogundiya et al (1989), who also reviewed earlier cases.

Management

Administration of antibiotics and drainage of pus are essential. Extraction of the causative tooth may spread the infection and should be delayed until the disease iscontrolled. Corticosteroids are recommended to prevent circulatory collapse secondary to pituitary dysfunction, but the use of anticoagulants is controversial as they may promote spread of infection. There is a 50% mortality and of those who survive half may lose the sight of one or both eyes. Unusually early treatment of a patient reported by Ogundiya et al (1989) allowed restoration of sight.

Necrotizing fasciitis

Necrotizing fasciitis is a rare but potentially lethal infection of subcutaneous tissues and deep fascia, associated with necrosis of the overlying skin due to thrombosis of nutrient vessels. It can arise from a dental infection and affect the face or neck where it can threaten the airway. Severe systemic toxicity is typically associated, but many patients are initially apyrexial. Most patients are young adults but in some, immunosuppression, diabetes mellitus or other deficiency states may be contributory. The infection was originally attributed to beta-haemolytic streptococci. More recently other bacteria, including anaerobes such as Bacteroides species, have been isolated. In about 25% of cases the infection is odontogenic and Rubin and Cozzi (1987) reported fatal necrotizing mediastinitis complicating a dental infection.

Clinically, the rapid spread of tissue destruction is emphasized by Muto et al (1992). Within 24-48 hours the area becomes red, oedematous and painful but soon becomes anaesthetic. The site, whichmay be well- or ill-demarcated, becomes dusky, purplish or black and by the fourth or fifth day necrosis of the skin appears. This necrotic tissue starts to separate within 8-10 days. Cases in Britain have recently been reported by Kaddour and Smelt (1992) and Gaukroger (1992), who have also reviewed earlier reports; all their patients were elderly women.

Management

Diagnosis depends on recognition of both fasciitis and cutaneous necrosis. However, surgical intervention and antimicrobial treatment should start before necrosis develops. A major danger is that in the early stages the infection can be mistaken for cellulitis and reliance placed solely on antibiotics. Release of offensive brownish exudate with gas bubbles is indicative of tissue necross.

The airway should be protected by intubation and adequate hydration maintained. The area should be opened up and the extent of undermining of the skin determined by finger exploration. Drains should be inserted and parenteral antibiotics given as soon as material has been obtained for culture. Initial antimicrobial treatment should start with penicillin or a cephalosporin plus metronidazole, but changed if bacteriological findings dictate. Necrotic muscle and any other tissue should be excised and debridement maintained until the area is clean. If the problem is recognized and treated sufficiently early, little skin may need to be removed, but in many cases grafting is required after subsidence of the infection.

Cancrum oris (noma)

Cancrum oris is a gangrenous infection spreading outwards from the mouth to cause extensive facial destruction and, often, a fatal outcome.

The disease has virtually disappeared from the developed countries, but is still seen in countries particularly parts of Africa, where malnutrition, poor oral hygiene and debilitating diseases are contributory. Two cases were reported by Griffin et al (1983) in children who had been brought from Micronesia.

The disease predominantly affects children under the age of 10 years, and only those with impaired defences dues to protein calorie malnutrition, anaemia or infections such as measles are susceptible.

The microbial cause appears to be the Gram-negative anaerobic fuso-spirochaetal complex of Vincent's infection (traditionally termed *Borrelia (Treponema) vincentii* and a fusiform bacillus which may be *Fusobacterium nucleatum),* probably in combination with other anaerobes such as Bacteroides species.

Cancrum oris starts within the oral cavity as an acute ulcerative gingivitis associated with extensive oedema but extends outwards, rapidly destroying soft tissues and bone. The gangrenous process starts as a painful, small, reddish-purple spot or indurated papule which ulcerates. The ulcer spreads to involve the labiogingival fold, adjacent mucosa and underlying bone. Diffuse oedema of the face, foetor and profuse salivation are associated. As the overlying tissues become ischaemic, the skin turns blue-black. The gangrenous area becomes increasingly sharply demarcated and ultimately sloughs away. The slough is cone shaped, with its apex superficial so that the underlying destruction of hard and soft tissues is more extensive than external appearances suggest. As the slough separates, the bone becomes necrotic; sequestration and exfoliation of teeth follow.

Management

Underlying disease such as malnutrition, malaria, typhoid, tuberculosis and measles must be treated. Parenteral rehydration, together with nasogastric tube feeding, may be needed. Blood transfusions and iron supplements are required when the haemoglobin is below 10 g/L. Without early treatment, the mortality is high.

A combination of penicillin and metronidazole will usually control the local infection. It gradually resolves in survivors, but is severely mutilating.

Soft tissue abscesses

An abscess may form as a result of direct spread from a periapical infection or be the result of localization of a fascial space infection. The cheek and palate are typical sites. The microbial causes are varied and ill-defined.

Buccal abscesses

An abscess affecting the cheek may be either medial or lateral to the buccinator. Infection from the apex of a molar tooth, after breaking through the buccal plate of either jaw, most commonly points on the buccal gingiva but occasionally spreads deep to the buccal sulucs. An abscess may thus form in the vestibule, medial to the buccinator muscle. If the apices of teeth are deep to the level of the attachment of the buccinator, infection can track across, reaching the lateral surface of the muscle (the buccinator space).

Clinically, there is pain, swelling, redness and tenderness of the cheek. There may be a history of acute toothache. The swelling, though not easily defined because of the thickness of the cheek, is more localized than that of cellulitis; systemic effects are slight. In the case

of a vestibular abscess the intraoral swelling is prominent, obliterating the buccal sulcus; the cheek is oedematous and swollen. In the case of a buccinator space infection, the whole cheek is much thickened, red and hot externally. The angle of the mouth is pulled outwards. Later the swelling becomes fluctuant as pus localizes.

Recurrent buccal space abscesses have been described as a rare complication of Crohn's disease by Malins et al (1991).

Palatal abscess

Infection may spread from a lateral incisor because of its backward-sloping root, or from the palatal root of a molar.

Clinically, the swelling is rounded, discrete and tender. It is usually close to the offending tooth, but occasionally infection may spread to the posterior border of the hard palate from a lateral incisor.

Submasseteric abscess

Sometimes infection around a lower third molar tracks backwards lateral to the mandibular ramus and pus localizes deep to the masseter attachment. Such an abscess deep to the thick masseter produces little visible swelling but is accompanied by profound muscle spasm and limitation of opening.

Management of a soft tissue abscess

Antibiotic therapy may be unnecessary if the abscess is small and well localized, as in the case of many vestibular or palatal abscesses. Otherwise 600 mg of penicillin should be given to hasten localization.

The infected tooth should be extracted or the root canal opened using general anaesthesia or regional analgesia well away from the site of infection, and pus must be drained by incision.

Actinomycosis

Actinomycosis is an uncommon, chronic, suppurative infection caused by a filamentous bacterium. It causes multiple abscesses and sinuses, followed by widespread fibrosis. The soft tissue in the region of the angle of the jaw is the most common site.

The causative organism is typically *Actinomyces israelii*, but other bacteria may occasionally be responsible. In culture, pathogenic actinomyces grow slowly on enriched media under anaerobic conditions to form a mass of branching filaments.

Though the infection is caused by organisms present in the normal mouth, it is not clear how it becomes established. Injuries, especially dental extractions or fractures of the jaw, can provide a pathway into the tissues and sometimes precede infection. Nevertheless the organisms are common in the mouth, but actinomycosis rarely follows extractions: most

patients were previously healthy and it is uncommon even in patients with AIDS. The pathogenesis of actinomycosis is therefore unclear.

Clinical features

Men are predominantly affected, typically adults between the ages of 30 and 60 years. The complaint is usually of a chronic soft tissue swelling near the angle of the jaw in the upper neck. There may be a history of dental extractions, especially of lower molars, several weeks previously. The swelling is dusky red or purplish in colour, firm and slightly tender. The skin becomes fixed to the underlying tissues and eventually breaks down as the characteristic sinuses and discharge form. There is often difficulty in opening the mouth, but pain is minimal.

The lymph nodes are not affected, but may occasionally become involved by local spread of the actinomyces or by secondary infection.

Healing leads to scarringand puckering of the skin and, in the absence of treatment, a large fibrotic mass can form, covered by scarred and pigmented skin on which several sinuses open. However, such a picture is largely of historical interest. Currently the more usual clinical features are a persistent subcutaneous collection of pus or a sinus, unresponsive to conventional short courses of antibiotics.

Microscopy

Actinomyces israelii spreads by direct extension through the tissues and provokes chronic inflammation with suppuration. In the tissues, colonies of actinomyces form rounded masses of filaments, at the peripheryof which radially-arrnaged club-shaped thickenings develop. Neutrophils mass round the colonies; pus forms centrally, chronic inflammatory cells surround the focus and an abscess wall of connective tissue is formed.

The abscess eventually points on the skin, discharging pus in which sulphur granules (colonies of actinomyces) may occasionally bevisible. The abscess continues to discharge and the surrounding tissues become fibrotic. Nevertheless, the infection spreads to cause further abscesses. In the absence of effective treatment, the area may eventually become honeycombed with many abscesses and sinuses and widespread fibrosis, but this is unlikely to be seen now. The infection exceptionally rarely develops within the bone of the jaw.

Diagnosis

For bacteriological confirmation of the diagnosis a fresh specimen of pus is needed for culture. Sulphur granules are rarely obvious but may be seen when the pus is rinsed with sterile saline. A positive diagnosis can rarely be made in the absence of sulphur granules. It is also important to tell the laboratory that actinomycosis is suspected to enable the appropriate media to be used and the culture maintained long enough for the organisms to grow.

Frequently small amounts of penicillin have been given earlier. These are insufficient to control the infectin but make bacteriological diagnosis difficult.

Management

The mainstay of treatment is penicillin, erythromycin or tetracycline: 2 g of oral penicillin a day should be given, and continued from 4 to 6 weeks or occasionally longer; pockets of surviving organisms may persist in the depths of the lesion to cause relapse after a short course of treatment. Abscesses should be drained surgicallyas they form. For patients allergic to penicillin, erythromycin is an effective alternative.

Complications

The most dangerous complication is spread of the infection to the lungs or elsewhere, but is rare. Actinomycosis sometimes primarily affects the lungs or ileocaecal region of the gut and in these situations may be fatal.

The deep mycoses

The deep mycoses are rare in Britain, but are most likely to be seen in immunocompromised patients or in those who have come from endemic areas such as South America. Among immunodeficient patients, the chief unlderlying causes are diseases such as lymphoreticular diseases, diabetes mellitus or immunosuppressive treatment. AIDS patients are subject to a great variety of fungal infections (see Table 14.5) which may form the presenting symptom. Nevertheless, there are surprisingly few reports of oral lesions due to the deep mycoses among HIV-positive patients, though superficial candidosis is common.

Clinically, several of the deep mycoses can cause oral lesions at some stage, and often then give rise to a nodular and ulcerated mass, which can be tumour-like in appearance. The orofacial manifestations of the deep mycoses and their treatment have been reviewed by Scully and de Almeida (1992).

As to microscopic diagnosis, the deep mycoses frequently cause granulomatous reactions which may simulate tuberculosis to a greater or lesser degree. The crucial feature, if it can be found, is the characteristic tissue form of the fungus. Culture should be confirmatory, but since a deep mycosis is unlikely to be suspected clinically, fresh material is rarely available. The serology is sometimes informative, but it may be difficult to establish the diagnosis with certainty.

For life-threatening mycoses, intravenous amphotericin, 0.5-1 mg/kg/day is usually the first choice despite its toxicity, but where nephrotoxicity is too great a threat, amphotericin encapsulated in liposomes (1 mg/day increasing to 3 mg/day), fluconazole or itraconazole 200-400 mg/day are frequently effective and less toxic alternatives. Itraconazole is less well absorbed but highly tissue-bound. It has a broader spectrum of activity than fluconazole. Oral flucytosine is well absorbed, is synergistic with amphotericin, but resistance readily develops. However, there have been to few clinical trials to establish definitively the relative efficacy of the different antifungal drugs in specific deep mycoses. Intravenous amphotericin remains the mainstay for life-threatening infections, while fluconazole or itraconazole are mainly used for maintenance therapy.

Even when diagnosis cannot be confirmed by culture or serology, if the patient has been at risk of exposure as a result of residence in an endemic area, and the clinical and microscopic features are consistent with those of a mycosis, antifungal chemotherapy with a drug such as fluconazole may be justified. Response to such treatment will in turn help to confirm the diagnosis, and is likely to save the patient from further spread of the infection.

Histoplasmosis

Histoplasma capsulatum can cause localized or generalized disease, but is subclinical in perhaps 95% of cases.

Histoplasmosis is seen in the endemic areas of the Americas, Africa, South East Asia and Australia and can be secondary to immunodeficiency states, but is not naturally present in Britain. The main clinical types of infection are pulmonary, which may heal without symptoms, or disseminated and fatal. Oral lesions may develop in 30-50% of cases of disseminated disease. Virtually any part of the mouth can then be affected, but the lesions are not distinctive. Nodular, granulomatous, proliferative and ulcerative oral lesions of histoplasmosis are readily mistaken clinically for neoplasms. Extensive and painful tissue destruction can develop and palatal perforation is well recognized.

Microscopy

The lesions simulate tuberculosis to a variable degree, with granuloma formation and focal collections of epithelioid cells, together with Lamghans-type giant cells, and there may be caseous necrosis. Alternatively, there may be diffuse sheets of inflammatory cells. The yeast forms, 2-4 microm in diameter, can sometimes be demonstrated, particularly in PAS or silver-stained sections, in epithelioid or giant cells, but are more likely to be numerous, in the absence of granulations formation.

Antifungal treatment with intravenous amphotericin is essential to control pulmonary infection and prevent dissemination but itraconazole may also be effective.

Mucormycosis (phycomycosis, zygomycosis)

Mucormycosis is an invasive infection caused by any of the Phycomycetales, particularly Absidia, Mucor and Rhyzopus. These common saprophytic moulds, which grow on decaying organic material, had long been thought to be entirely harmless. Mucor species have rarely been reported among the normal human flora.

Aetiology and pathology

The spores are probably inhaled, but infection mainly affects those with underlying disease, particularly poorly controlled diabetes mellitus or acute leukaemia, or those having immunosuppressive treatment.

The main forms of mucormycosis are pulmonary and rhinocerebral. Rhinocerebral mucormycosis typically starts in the maxillary antrum, particularly in young adult, poorly controlled diabetics. Invasion of surrounding tissues can cause necrotizing ulceration of the

palate with a blackish slough and exposure of bone. Local pain and tenderness over the sinus and low fever are associated with nodular thickening of the antral lining and sometimes radiographic evidence of patchy destruction of the walls of several paranasal sinuses. There may also be nasal congestion or bloody discharge.

More important is spread to the orbit causing blurred vision, proptosis and limitation of movement of the eye. Spread to the brain is indicated by clouding of consciousness, cranial nerve plasies, loss of vision, coma and death, often within 2 weeks of the clinical signs.

Microscopy

Once infection has become established, the hyphae can be recognized in the tissues by their characteristically irregular width (3-20 microm) and by a crushed ribbon appearance. The hyphae are typically non-septate and show righ-angled branching. They may be seen in haematoxylin and eosin stained sections, but more clearly when PAS or silver staines are used. The infection characteristically involves blood vessels with thromboses and haemorrhages, an inflammatory response and tissue necrosis.

Diagnosis

When oral lesions are the first complaint, biopsy should enable the fungus and its characteristic pathological effects to be recognized, and allow relatively early diagnosis. If the only feature is sinusitis, biopsy is also important, but rapid diagnosis may be possible by examination of a wet smear of crushed fresh tissue stained with methylene blue. Such investigation is particularly important in a diabetic who appears to be developing ketotic coma unresponsive to insulin and other appropriate measures. Early loss of vision may help to differentiate rhinocerebral phycomycosis from pyogenic cavernous sinus thrombosis. No reliable method of immunological diagnosis is available.

Surgical debridement and antifungal treatment, usually with amphotericin, together with control of any diabetes are essential. Despite such treatment the mortality is high, especially in patients with leukaemia.

Aspergillosis

Aspergillus species (particularly *A. fumigatus)* are now a cause of opportunistic infections, rivalling candidosis in frequency as a complication of long-term antimicrobial or immunosuppressive treatment. Aspergillosis only rarely affects otherwise healthy patients.

Aspergillosis can have widely different manifestations. They include systemic aspergillosis and either pulmonary or disseminated infection in the immunosuppressed, allergic pneumonitis (an asthma-like disease) or rhinocerebral asperigillosis, or harmless aspergillomas (fungus balls) in the maxillary antrum. Zinreich et al (1988) report the value of MRI to detect calcium and other metallic deposits characteristic of aspergillus infection of the sinuses.

Oronasal (rhinocerebral) aspergillosis

Rhinocerebral aspergillosis is a rare variant. It is usually caused by a *A. flavus*, and particularly affects poorly controlled diabetics, though Martinez et al (1992) have described invasive maxillary aspergillosis after a dental extraction in a previously healthy patient. Pain, swelling of the face and nasal discharge may be early signs. Like rhinocerebral mucormycosis, aspergillosis tends to spread through the orbit to the brain, but spread is via tissue spaces rather than blood vessels, and is slower than in mucormycosis. Occasionally, infection extends through the palate to produce a necrotic brown or blackish ulcer. Painful, bleeding oral lesions have also been reported as a rare feature of disseminated aspergillosis.

Diagnosis is by recognition of the dichotomous hyphae in the tissues by microscopy, but the characteristic mop-like spore-bearing structures are rarely seen. Culture is therefore also essential and serology may be informative. Treatment is by surgical excision of infected tissue and intravenous amphotericing. Itraconazole is a possible alternative.

An aspergillomatous fungus ball is a rare cause of opacity of the antrum in a healthy person. The mass appears brown and dry and the hyphae are recognizable only by microscopy, though culture is confirmatory if fresh material is available. Following removal of the fungal mass, no treatment is necessary, provided that the patient remains healthy.

Cryptococcosis

The spores of *Cryptococcosis neoformans* are frequently spread by bird droppings, but infection is often subclinical. Cryptococcosis can develop in normal persons but is usually secondary to immunosuppressive treatment, lymphomas or diabetes mellitus. In the USA, Diamond (1991) reported a prevalence of cryptococcosis in 5-15% of AIDS patients and it is the most frequent initial opportunistic infection.

Clinical features

The main forms of cryptococcosis are chronic meningitis, or pulmonary or disseminated infection. Oral lesions of cryptococcosis are reported to be uncommon and mainly a complication of widespread disease. In AIDS there may be fungaemia but an indefinite febrile illness.

An oral lesion has no distinctive clinical features, but appears as a granular swelling, a large necrotic ulcer or sometimes smaller ulcers.

Microscopy

Cryptococcosis cause granuloma formation with histocytes, giant cells and lymphocytes, which may surround areas of necrosis. The organism is a spherical or ovoid spore surrounded by a characteristic halo formed by the large gelatinous capsule. It may be seen within giant cells or histiocytes or free in the tissues. It is helped by its unique ability among fungi to form melanin; Masson Fontana staining shows darkly staining budding yeasts.

Diagnosis can be confirmed by culture and positive latex agglutination or ELISA tests for capsular antigen.

Treatment with intravenous amphotericin together with flucytosine or fluconazole is successful in most cases, with a 90% survival rate. In AIDS patients, relapse is so common that continuous suppressive treatment with fluconazole or itraconazole must be given.

Blastomycosis (North American blastomycosis)

Males aged between 40 and 60 years are mainly affected with pulmonary or cutaneous disease. Lesions of the oral or nasal mucosa may be present in 25% of patients. Occasionally, oral lesions may be the first sign leading to the diagnosis, but are non-specific in character. They may be ulcerated or resemble actinomycosis; the regional lymph nodes are usually enlarged.

Microscopy

Blastomyces dermatidis causes a chronic granulomatous reaction, usually with numerous macrophages and giant cells, but a tendency to suppuration. Within these lesions, the tissue phase of the organism may sometimes be seen as a large thick-walled yeast with single buds attached by a broad base.

Blastomycosis usually responds rapidly and completely to intravenous amphotericin and drainage of any abscesses, but fluconazole or itraconazole may be effective for less virulent infections.

Paracoccidioidomycosis (South American blastomycosis)

Infection by *Paracoccidioides brasiliensis* is endemic in and virtually confined to South America. Infection can be mucocutaneous, pulmonary or disseminated. Adult males are mainly affected, and frequently have oral lesions which, though often secondary to pulmonary or disseminated disease, are a common early sign. The fungus probably enters through gross or microscopic wounds, which may include periodontal tissues and extraction wounds. The lesions are frequently nodular and ulcerative, can affect any part of the mouth and sometimes extend on to adjacent skin. The ulcers may have a mulberry-like appearance with pinpoint haemorrhages (de Almerida et al, 1991) and the regional lymph nodes may be involved. Proliferative or papillomatous lesions resembling those on the skin can also develop in the mouth but have rarely been reported.

Microscopy

Mucosal lesions are usually granulomatous, but with an acute inflammatory infiltrate and abscess formation. The tissue phase of the organism is a spherical yeast cell considerably larger than that of *Blastomyces dermatidis;* mutiple budding produces appearances described as Mickey Mouse or pilot wheel cells. These may lie free in the inflammatory infiltrate or within giant cells, but may not be readily found.

Paracoccidioidomycosis responds to amphotericin but itraconazole may also be effective.

Systemic infections by oral bacteria

The mouth is inhabited by a great variety of microbes, but has high levels of local immunity. As a result, bony wounds caused by multiple extractions or oral surgery usually heal without incident despite the innumerable pathogens present in periodontal pockets. The virulence of these bacteria is shown by the fact that human bites cause considerably more severe infections than animal bites. Moreover, oral bacteria escaping into the bloodstream of immunocompromised patients can cause severe metastatic infections or septicaemias, which can be fatal. Even *Leptotrichia buccalis*, long thought to be a harmless component of dental plaque, can cause septicaemia in immunodepressed patients.

A special example of a systemic infection of dental origin is infective endocarditis, which can follow dental operations, particularly extractions, and cause irreparable damage to heart valves or other organs.

Oral sources of bacteraemias

It is difficult to appreciate the sheer number of bacteria inhabiting the gingival margins when oral hygiene is poor, or the even vaster numbers present in periodontal pockets. By contrast, few bacteria inhabit the oral mucosa, and most are being constantly washed away by the saliva.

Sections of human teeth *in situ* show bacterial plaque in two dimensions, but *in vivo* plaque in a typical periodontal pocket consists of a solid mass of bacteria which usually forms a collar round the whole circumference of every tooth. As a result of the inflammation induced by these bacteria, they are in close contact with dilated, thin-walled blood vessels. Movement of the teeth during chewing, or more violently during extractions, repeatedly compresses and stretches or ruptures these vessels, so that bacteria can in effect be pumped into the bloodstream. Extractions appear, therefore, to be the precipitating factor in over 95% of cases of dentally related cases of infective endocarditis.

Chronic periapical lesions, by contrast, contain few bacteria, and it is difficult to obtain bacteria from them. Bacteria escaping from a necrotic pulp are immediately mopped up by inflammatory cells. Such few bacteria as are present are also well-isolated by the thick wall of granulation tissue that forms the bulk of the lesion. However, some physicians still regard periapical radiolucencies as 'dental abscesses' and a threat to patients' health. The 1920s idea of so-called focal sepsis has been difficult to eradicate from medical mythology.

Acute apical abscesses may contain many bacteria, but the numbers are still small in comparison with those filling periodontal pockets and unlike the latter usually only affect a single tooth and are unlikely to be an important source of systemic infection.

The chief effects of bacteraemias of dental origin in susceptible patients are:

- infective endocarditis

- lung and brain abscesses

- metastatic infections or septicaemias in immunodeficient patients.

Infective endocarditis

Little needs to be said here, other than that patients with congenital or acquired heart lesions are particularly at risk, and that the highest incidence of and mortality from this disease is in the elderly.

Only dental operations traumatizing the gingival tissues (extractions, scaling and mucogingival surgery) carry a significant risk of inducing infective endocarditis, because of the large numbers of bacteria that can be forced into the bloodstream from this region. Nevertheless, only 10-15% of cases of endocarditis follow dental operations. Many other dental procedures (even toothbrushing) can cause bacteraemias, as can other medical procedures, such as endoscopy or intubation, but bacteraemia is *not* synonymous with infective endocarditis, and such minor bacterial showers do not justify antibiotic prophylaxis.

Root canal treatment hardly ever leads to endocarditis in clinical practice and antibiotic prophylaxis is not recommended for it.

Lung and brain abscesses

Some of these abscesses are due to oral anaerobic bacteria which are probably aspirated during sleep to cause a lung abscess and a secondary brain abscess. Isolated brain abscesses caused by oral bacteria are recognized but difficult to explain.

Immunodeficiency status

In severe immunodeficiency states, such as in organ transplant patients or those with lymphoreticular diseases, bacteraemias of oral origin can sometimes cause metastatic infections or septicaemias. Many of these are spontaneous and probably induced by chewing; there is little evidence of dental operations precipitating bacteraemias in these patients, including those with AIDS.

However, if antibiotic cover for dental operations is felt to be desirable, there neither is nor can be a definitive prophylactic regimen, as the causes are varied and unpredictable. A combination of amoxycillin 3 g plus metronidazole 400 mg by mouth, 1 hour before operations, may possibly offer some protection and can be repeated 6 hours later, if thought desirable.

Prosthetic joint replacements

These are susceptible to experimental blood-borne infections, but only when inocula are so heavy as to kill 50% of the animals. It is misleading to compare these experimental infections with the human situation. Despite the tens of thousands of such operatins that have been carried out over the past 30 or more years in many countries, there have been virtually no authenticated cases where late prosthetic infection has been convincingly linked to dental treatment. The risks from antibiotic prophylaxis for dental procedures outweighs the benefits. Nevertheless, if an orthopaedic surgeon is adamant about the need for cover (as for infective endocarditis), it may be prudent to agree for the peace of mind of all concerned.