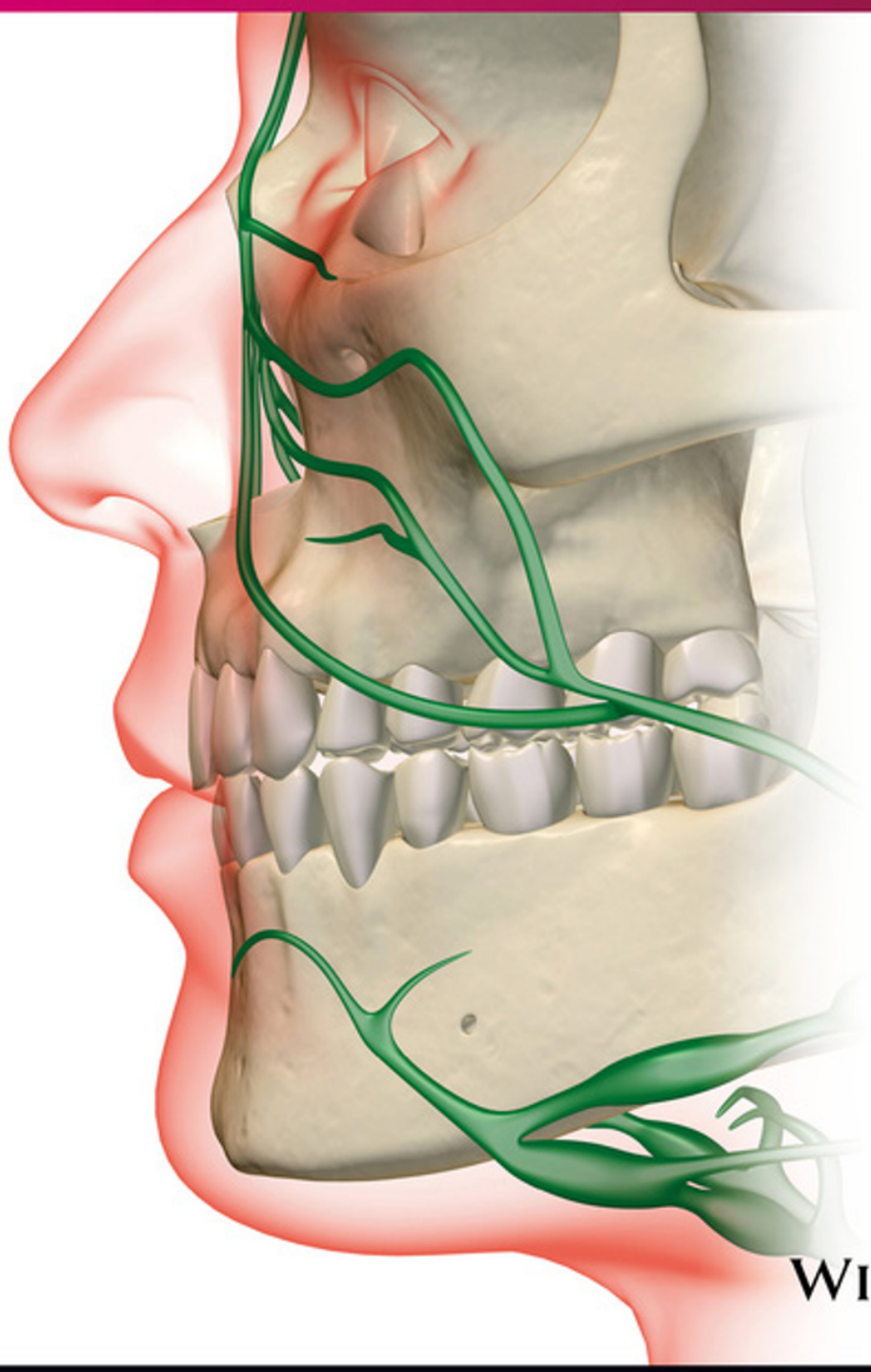
ESSENTIALS

ESSENTIALS OF HUMAN DISEASE IN DENTISTRY

MARK GREENWOOD

SECOND EDITION



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Essentials of Human Disease in Dentistry

Second Edition

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Preface to the first edition

The concept of human disease teaching in dentistry arose out of General Dental Council recommendations in their report 'The First Five Years', published in 2002 and currently under revision. This suggested an integrated approach to the teaching of general medicine and surgery, and the related disciplines. There are slight variations in the subjects incorporated into human disease teaching across UK dental schools, but general medicine and surgery teaching is common to all. Pharmacology, pathology and microbiology are also included in the course at Newcastle University, and the material in this book forms the basis of the theoretical elements of that course.

A dentist should have a firm grounding in all these disciplines to facilitate a broader knowledge and understanding of human disease, which can then be focused on issues of direct relevance to dentistry. This approach enables informed dialogue with colleagues in other healthcare professions, including general medical practitioners.

It is hoped that this book will prove useful to dental undergraduates studying human disease, and that it will also be of use to candidates preparing for the membership examinations of the Royal Colleges of Surgeons.

M Greenwood
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January 2009

Preface to the second edition

This second edition of *Textbook of Human Disease in Dentistry*, now called *Essentials of Human Disease in Dentistry*, aims to build on the strengths of the first edition, but has been updated in several key areas. The underlying principle remains the same – to provide the dental student/dental practitioner with a firm background knowledge of the relevant aspects of general medicine and surgery, pharmacology, pathology and microbiology. New additions to this edition include multiple choice–style questions at the end of each chapter, together with relevant references.

It is hoped that this edition will continue to be of value to undergraduate students of dentistry and those preparing for their postgraduate dental examinations.

M Greenwood
Newcastle upon Tyne, UK
August 2017

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Where illustrations have been imported from other publications, due acknowledgement has been given.

About the companion website

Don't forget to visit the companion website for this book:

www.wiley.com/go/greenwood/human-disease-in-dentistry

The companion website provides all the figures from the book in PowerPoint for download.

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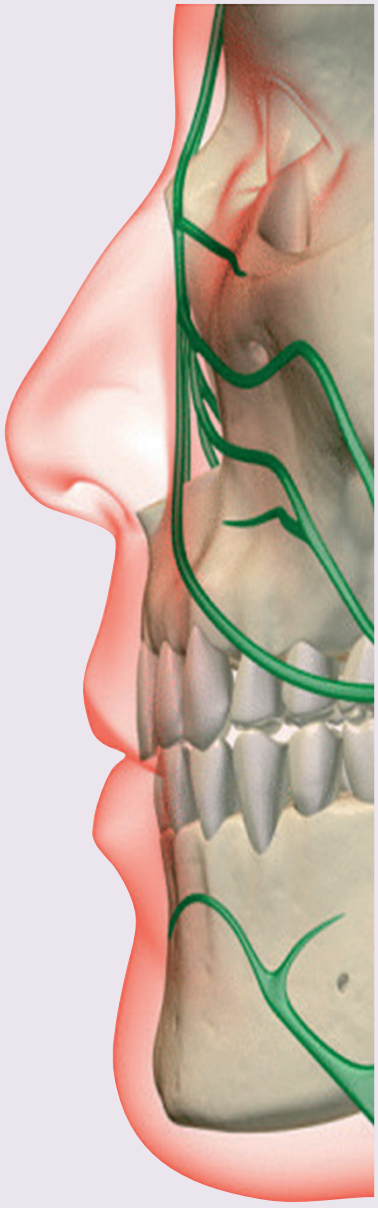
CHAPTER 1

Clinical examination and history taking

M Greenwood



Key topics

- Essential components of a medical history
- Key issues that may arise from the medical history

Learning objectives

- To be familiar with the main components of a medical history.
- To be aware of the medical terms used in taking a medical history, and their meaning.
- To be aware of the normal vital signs.

Essentials of Human Disease in Dentistry, Second Edition. Mark Greenwood.

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Components of a medical history

The medical history aims to:

- Enable the formulation of a differential diagnosis or diagnosis
- Put the patient's disease process into the correct medical and social context.
- Establish a rapport with the patient.

Clinicians engaged in obtaining medical histories should introduce themselves to the patients and give their designations. The taking of the history may then commence and should follow a scheme similar to that shown in Table 1.1.

Presenting complaint

The presenting complaint can be recorded in medical terms, but often is better expressed in the patient's own words. When recording the history in writing, quotation marks should be placed around the patient's words. In a verbal case presentation, it should be stated that the patient's own words are being used. It is important to avoid presumptive diagnoses in the presenting complaint. For example, patients do not *present* with iron deficiency anaemia; they may present with symptoms that arise *from* it. It should be remembered that symptoms are the features of the illness that the patient describes; signs are physical findings obtained by the clinician.

History of the presenting complaint

The history of the presenting complaint should be a chronological but succinct account of the patient's problem. It is important to start at the onset of the problem and describe its progression. Symptoms should be similarly described.

Points to include when asking patients about pain are as follows:

- Site
- Character – for example, tight/band-like (in the chest, suggestive of cardiac origin)
- Does the pain radiate anywhere?
- Onset – sudden or gradual
- Severity (ask the patient to rate on a scale of 1–10, with 10 being the most severe)
- Duration
- Exacerbating/relieving factors (including the use and efficacy of medication)
- Preceding events or associated features
- Has the pain occurred before? / Is it getting better or worse?

Table 1.1 Areas to be covered in a medical history.

Presenting complaint
History of presenting complaint
Past medical history
Allergies
Past dental history
Drugs
Social history
Family history
Psychiatric history

Past medical history

It is worth asking a generic set of opening questions – for example, 'Do you have any heart or chest problems?' Questioning should then focus on specific disorders – for example, asthma, diabetes, epilepsy, hypertension, hepatitis, jaundice or tuberculosis. It is also worth specifically asking about any previous problems with the arrest of haemorrhage. Past problems with intravenous sedation or general anaesthesia should be noted. It is worth asking about any previous history of rheumatic fever, which may have led to cardiac valve damage. In 2008, the National Institute for Health and Care Excellence (NICE) discontinued the regular use of antibiotic prophylaxis for bacteraemia-producing dental procedures in patients with cardiac damage. There were some concerns about this, however, such as the lack of an evidence base for prophylaxis and the fact that Europe and the USA differed in their practices.

Before 2008, a consistent upward trend was apparent in the population-corrected incidence of infective endocarditis in England. Soon after the implementation of the NICE guidelines, the slope of the trend line increased further, although there is no direct evidence that this was due to the discontinuation of antibiotic prophylaxis in dentistry. In 2016, NICE modified the guidance slightly to state that: 'Antibiotic prophylaxis against infective endocarditis is not recommended *routinely* [my emphasis] for people undergoing dental procedures'. This addition emphasises NICE's standard advice on healthcare professionals' responsibilities. Doctors and dentists should offer the most appropriate treatment options, in consultation with their patients and/or their carers or guardians. In doing so, they should take into account the recommendations of NICE guidance and the values and preferences of patients, and also apply their clinical judgement.

To guide decision-making, NICE has provided information regarding which might be considered high-risk and moderate-risk groups for the development of infective endocarditis – see Table 1.2.

It is clearly important that positive findings be recorded. Some important negative findings too are worth recording.

Allergies

Any known allergies should be recorded. This is one aspect of the medical history that should be recorded even if there are no known allergies. Any allergies that are identified should be highlighted in the clinical record.

Table 1.2 Stratification of the risk of infective endocarditis.

High-risk categories

- Patients with a previous history of infective endocarditis
- Patients with any form of prosthetic heart valves (including a transcatheter valves)
- Those in whom prosthetic material was used for cardiac valve repair
- Patients with any type of cyanotic congenital heart disease
- Patients with any type of congenital heart disease repaired with prosthetic material, whether placed surgically or by percutaneous techniques, for the first 6 months after the procedure or lifelong if a residual shunt or valvular regurgitation remains

Moderate-risk categories

- Patients with a previous history of rheumatic fever
- Patients with any other form of native valve disease (including the most commonly identified conditions: bicuspid aortic valve, mitral valve prolapse or calcific aortic stenosis)
- Patients with unrepaired congenital anomalies of the heart valves

Past dental history

In a general history, the dental history should be relatively brief. It can include details of the regularity or otherwise of dental attendance and the use of local anaesthesia or sedation. Any adverse events, including post-extraction haemorrhage, could also be included here.

Drugs

Any medication taken by the patient should be recorded. The use of recreational drugs can be included in this section or in the social history.

'Recreational' drugs

Dentists should have a working knowledge about the implications of patients using recreational drugs, as the use of such drugs is relatively common. Cannabis has a sympathomimetic action that could potentially exacerbate the systemic effects of adrenaline in dental local anaesthetics. Heroin and methadone are both opioid drugs, with methadone being used in drug rehabilitation programmes. Oral methadone has a high sugar content and can lead to rampant caries. Heroin can lead to addicts having a low threshold for pain and can cause thrombocytopaenia, in addition to interfering with drugs that dentists may prescribe. Other details regarding recreational drugs are given in Chapter 19 (titled 'Psychiatric disorders').

Complementary therapies

Complementary therapies are often used by patients. Many patients do not deem it important to tell dental practitioners that they are using such preparations, as they do not feel that it may be of any relevance. It is important to remember, however, that some of the drugs that dental practitioners prescribe can be affected by some complementary therapies. A summary of some of the more common potential interactions is given in Table 1.3.

Table 1.3 Complementary medicines and their interactions with conventional medicines with potential consequences.

Herb	Conventional drug	Potential problem
St. John's wort	Monoamine oxidase inhibitors and serotonin reuptake inhibitors Antidepressants Iron	Mechanism of herbal effect uncertain Insufficient evidence of safety with concomitant use – therefore not advised May limit iron absorption
Karela, ginseng	Insulin, sulfonylureas, biguanides	Altered glucose concentrations
Feverfew, garlic ginseng, ginger	Warfarin	Altered prothrombin time/INR
Echinacea used for >8 weeks	Anabolic steroids, methotrexate, amiodarone, ketoconazole	Hepatotoxicity
Feverfew	Non-steroidal anti-inflammatory drugs (NSAID)	Inhibition of herbal effects
Ginseng	Oestrogens, corticosteroids	Additive effects
Evening primrose oil	Anticonvulsants	Lowered seizure threshold
Kava	Benzodiazepines	Additive sedative effects, coma
Echinacea, zinc (immunostimulants)	Immunosuppressants (such as corticosteroids, cyclosporine)	Antagonistic effects

Implanted cardiac devices

Some ultrasonic scalers and ultrasonic baths produce electromagnetic interference and may therefore be a risk to patients with implanted cardiac devices such as pacemakers and implanted defibrillators. Other such devices include electronic apex locators and electrocautery devices. There is a degree of confusion in the current literature regarding what devices are and are not considered safe to use, and consultation with the appropriate authorities is therefore important.

Social history

This should be a succinct but comprehensive assessment of the patient's social circumstances. It should include the following details:

- Smoking behaviour
- Alcohol consumption – type and quantity – recommended not to exceed 14 units per week (female) and 21 units per week (male)
- Occupation (or previous occupation if retired)
- Home circumstances – a brief description of the residence – for example, a house, flat or sheltered accommodation. Who else lives in the household?

Family history

Any disorders with a genetic origin should be recorded.

Psychiatric history

This will only need to be included in specific cases. More detail is given in Chapter 18 (titled 'Medicine for the elderly').

In hospital practice, after the history comes the systems review. Specific questions are asked to further refine the available knowledge on the patient's overall medical condition. Many schemes are described, and the following scheme has been adapted for the dental clinician.

General questions

As with the history, a series of general questions can help to encompass the wide-ranging possibilities in terms of the underlying medical problems. Questions cover the following topics:

- Appetite
- Weight loss
- Fevers
- The presence of lumps or bumps
- Any rashes or itchy rashes
- Lethargy or fatigue

Cardiovascular system

- Chest pain (a differential diagnosis is given in Chapter 21, titled 'Medical emergencies')
- Dyspnoea – difficult or disordered breathing (beware of co-existing/alternative respiratory causes)
- If dyspnoea on exertion, try and quantify in terms of metres walked or number of stairs climbed before dyspnoea occurs
- Paroxysmal nocturnal dyspnoea (waking up in the night feeling breathless – see Chapter 5, titled 'Cardiovascular disorders')
- Orthopnoea (breathlessness on lying flat – see Chapter 5)
- Ankle oedema – beware of other possible causes of lower limb swelling
- Palpitations (awareness of the beating of the heart)
- Calf claudication (distance walked until pain occurs in the 'calf' muscles of the leg, referred to as the 'claudication distance')

Respiratory system

- The presence of cough, and its duration
- Whether the cough produces sputum
- Haemoptysis (coughing up blood)
- Wheezing

Gastrointestinal system

- Indigestion
- Nausea or vomiting
- Dysphagia (difficulty swallowing)
- Odynophagia (pain on swallowing)
- Haematemesis (vomiting of blood), described as looking like 'coffee grounds'
- Change in bowel habits
- Change in bowel motion – for example, pale stool and dark urine is virtually pathognomonic of obstructive jaundice (see Chapter 7, titled 'Gastrointestinal disorders')
- Melaena is the production of black stool containing blood altered by gastric acid; fresh blood indicates bleeding from further down the gastrointestinal tract

Neurological system

A brief overview is required, in particular:

- Any history of fits or faints
- Disturbance in sensation – particularly in the orofacial region
- Headache or facial pain

Musculoskeletal system

- Gait (overlaps with neurological system)
- Pain/swelling/stiffness of joints
- Impairment of function

Genitourinary system

This is usually of little relevance to the dental practitioner. Repeated urinary tract infections may be relevant insofar as the patient may be undergoing antibiotic treatment – of which the dental practitioner should be aware. For dental patients in general hospital settings, enquiry is useful regarding symptoms of prostatism. Some patients who require significant surgical

procedures may require catheterisation, and an enlarged prostate gland can lead to difficulties with catheter insertion. 'Hesitancy' is the term that is used to describe difficulty in initiating the urine stream, and 'terminal dribbling' is difficulty in stopping. Frequency of urination and nocturia (passing urine at night) should all be included.

Clinical observations in the clothed patient

While it is evident that clinical examination is important, much of the background to a patient's medical condition is gained from the history. Physical examination often serves to confirm what is suspected from the history.

Overall view of the patient

Does the patient look generally well? Is the patient of normal weight, or is he or she cachectic or obese? It is important to note whether the patient is alert or appears to be confused (Table 1.4 lists potential causes of confusion in a patient). As soon as the patient enters the surgery, note should be taken of the gait. Is the patient pale or flushed or of normal complexion? Is he or she breathless?

Not all the preceding observations are necessarily diagnostic of the precise nature of disease. However, if something does not look normal, then it probably is not, and an explanation needs to be found.

In hospitalised patients, it is important that the vital signs be recorded (Table 1.5). This is discussed further in a following section (titled 'Vital signs').

Examination of the hands

In the hands, there are several observable signs that can be of interest to a dental practitioner. The overall appearance of the hands should be noted, together with any abnormalities of the nails, skin and muscles.

Palmar erythema can be seen in pregnancy, rheumatoid arthritis and patients with liver problems. Swollen proximal interphalangeal (PIP) joints suggest rheumatoid arthritis together with ulnar deviation of the hands (Figure 1.1). Swollen distal interphalangeal (DIP) joints suggests osteoarthritis. Gout and the skin condition psoriasis can also cause DIP joint swelling. In psoriasis, there may be the additional feature of finger nail pitting.

Dupuytren's contracture may also be seen. In this condition, the palmar fascia contracts, leading to the little finger (particularly of the right hand) being held passively in a flexed position. There is usually a palpable nodular thickening of the connective tissue overlying the ring and little fingers. The aetiology is often unknown, but can be associated with alcoholism.

Table 1.4 Potential causes of confusion in a patient.

Hypoxia
Infection
Epilepsy
Hypoglycaemia
Drug or alcohol withdrawal
Stroke, myocardial infarction (MI)
Raised intracranial pressure

Table 1.5 The vital signs.

Pulse rate
Blood pressure
Temperature
Respiratory rate

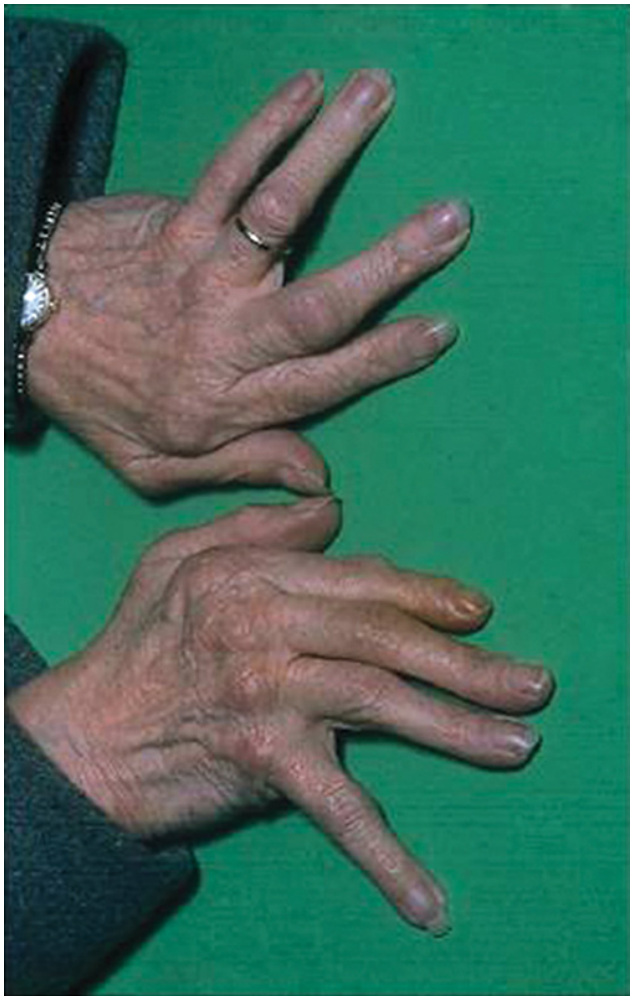


Figure 1.1 Rheumatoid hands. Note the ulnar deviation, which can cause significant limitations in activities of daily living.

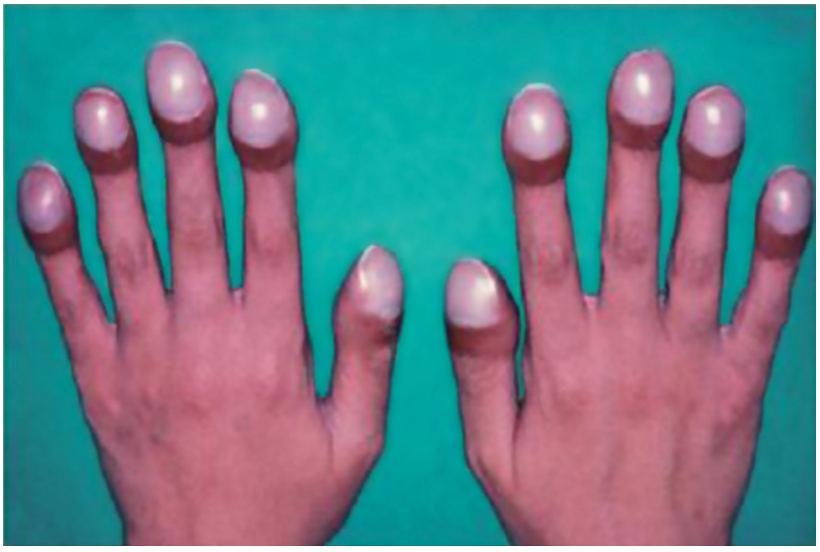


Figure 1.2 Finger clubbing. There is a loss of angle between the nail surface and the skin of the finger, and the nail bed is 'boggy' to pressure.

Clubbing of the fingers should always be looked for and can represent disease processes in diverse systems (Figure 1.2). There is a loss of the angle between the nail and nail bed, and the fingernail has an exaggerated curvature in the longitudinal plane. The area around the nail fold feels boggy to palpation. Potential causes of finger clubbing are given in Table 1.6.

The fingernails may also show splinter haemorrhages that can result from mild trauma, but these may also be a sign of endocarditis (see Chapter 5, titled 'Cardiovascular disorders'). Leukonychia (white fingernails) may be seen in patients with liver disease. Koilonychia (spoon-shaped fingernails) can be seen in patients with chronic iron deficiency anaemia.

Table 1.6 Causes of finger clubbing.

Cardiothoracic causes
- Infective endocarditis
- Cyanotic congenital cardiac disease
- Intrathoracic pus – for example, lung abscess, bronchiectasis
- Bronchial carcinoma
- Fibrosing alveolitis

Gastrointestinal causes
- Inflammatory bowel disease
- Cirrhosis of the liver

Other causes
- Familial
- Secondary to thyrotoxicosis
- Idiopathic

The face

If the patient's complexion is examined, it may display evidence of jaundice. This is rather subjective and unreliable. The best area to look for jaundice is the sclera of the eyes. The clinical and metabolic syndrome seen in chronic kidney disease known as 'uraemia' may also impart a yellowish tinge to the skin. The eyelids may exhibit xanthelasma – deposits in the eyelids, signifying hyperlipidaemia (Figure 1.3). Corneal arcus (Figure 1.4) can be seen in some patients. It is sometimes associated with an increased risk of coronary artery disease. There may also be the malar flush of mitral stenosis or the butterfly rash seen in systemic lupus erythematosus (SLE; see Chapter 11, titled 'Musculoskeletal disorders').

Central cyanosis may be seen by asking the patient to protrude the tongue – a bluish hue is indicative of this. Peripheral cyanosis (seen in the nail beds) is caused by peripheral vasoconstriction, which may be normal, seen in cold conditions or in shock, but may also signify peripheral vascular insufficiency.

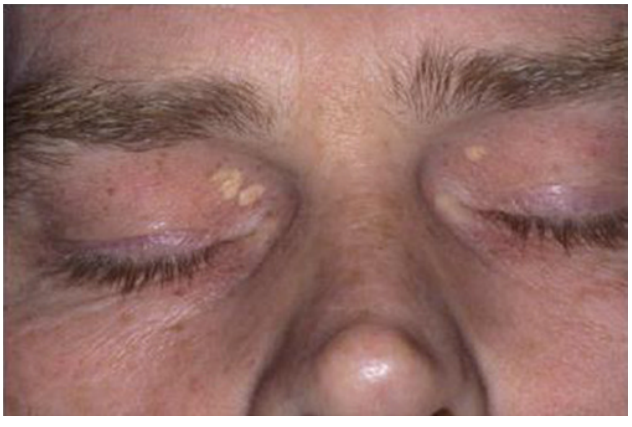


Figure 1.3 Xanthelasma.

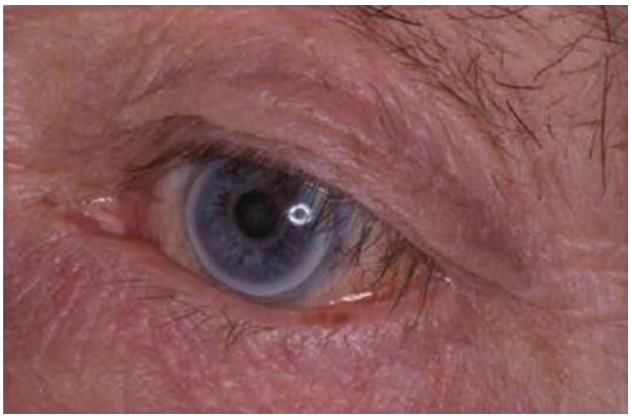


Figure 1.4 A patient with corneal arcus (also sometimes called 'arcus senilis').

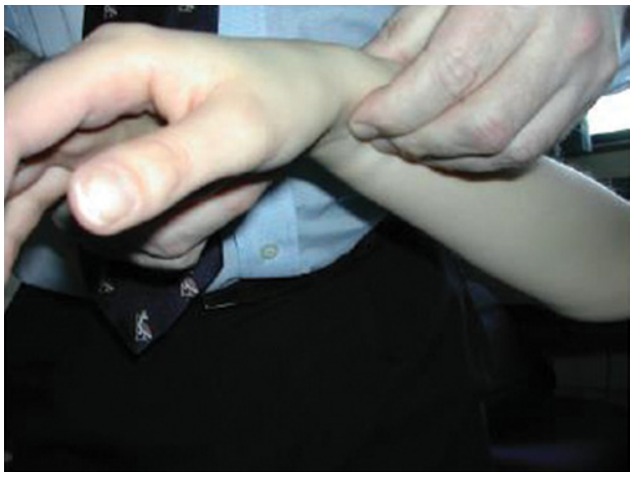


Figure 1.5 Taking the radial pulse. The radial artery is passing roughly along a straight line in this area, and two or three examining fingers can therefore be used for palpation.

Examination of the cardiovascular system in the clothed patient

All clinical examinations should follow the following scheme: inspection, palpation, percussion and auscultation.

Dyspnoea (difficult or disordered breathing) should be noted. It should be borne in mind that there may be a respiratory cause. Is the patient short of breath at rest (SOBAR), or only short of breath on exertion (SOBOE)? If the upper part of the thorax is exposed, there may be evidence of the upper end of a median thoracotomy scar. This will most commonly have facilitated access for a coronary artery bypass graft (CABG) or valve replacement procedure.

In the hands, splinter haemorrhages should be looked for together with finger clubbing and signs of anaemia. Osler's nodes and Janeway lesions may be evident (see Chapter 5, titled 'Cardiovascular disorders').

The radial pulse (thumb side of the wrist) should be taken (Figure 1.5). This is discussed further in a following section (titled 'Vital signs'). Some dental practitioners are proficient in palpating a central pulse in addition to the radial pulse (which is a peripheral pulse). The carotid pulse (a central pulse) is palpated in the neck, along the anterior border of the sternocleidomastoid muscle.

The blood pressure should be taken. The blood pressure cuff is placed around the upper arm, which is placed at rest (see Chapter 5E, titled 'Hypertension').

Jugular venous pressure

Jugular venous pressure (JVP) is a difficult thing to assess. The internal jugular vein acts as a manometer that reflects the right atrial pressure. JVP is measured with the patient sitting at 45° with the head turned slightly to the left. JVP is the vertical height of the column of blood visible in the right internal jugular vein, measured in centimetres from the sternal angle. It is raised if it is >3 cm.

Oedema can be seen in some cardiac patients. Pulmonary oedema reflects left ventricular failure, whereas peripheral oedema reflects right ventricular failure. Left- and right-sided failure together constitutes congestive cardiac failure. Due to gravitational effects, peripheral oedema is seen most commonly in the ankles, but it may be seen in the sacral region in bedridden patients.

Respiratory system

On inspection, the patient may demonstrate breathlessness, cyanosis or finger clubbing (Table 1.6). There may be tar stains on the fingers from smoking – often incorrectly regarded as nicotine stains. In the clothed patient, it may be difficult to assess the thoracic shape, but symmetry should be looked for in respiratory movements, together with use of accessory muscles of respiration. Chest deformities may lead to difficulties in respiration either in isolation or together with spinal deformities. 'Kyphosis' refers to increased forward spinal curvature, and 'scoliosis' refers to increased lateral spinal curvature. On palpation, the trachea should be central in the sternal notch.

Gastrointestinal system

On inspection, the patient may show signs of purpura or spider naevi. Spider naevi can be emptied by pressing on the centre, and they refill from this point. They are only seen in the distribution of the superior vena cava. Leukonychia may be seen (a sign of hypoalbuminaemia). Finger clubbing may also be seen. In cases of marked hepatic dysfunction, a liver flap may be observed – when the hands are held outstretched, they demonstrate a marked flapping movement.

A jaundiced patient may show scratch marks on the skin due to the intense itchiness arising from the bile salts deposited within the skin. Palmar erythema may also be noted, signifying an underlying liver disorder.

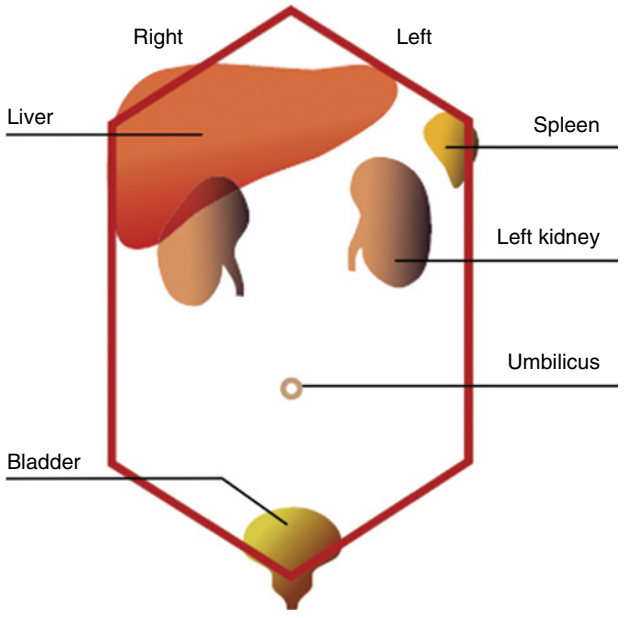


Figure 1.6 A schematic diagram of the abdomen (not to scale).

It is unusual for a dental practitioner to be called upon to examine other systems. A diagram of the abdomen is shown in Figure 1.6.

Vital signs

All hospital patients should have their vital signs measured. Vital signs are summarised in Table 1.5.

In contemporary hospital practice, vital signs are reviewed as part of the National Early Warning Score (NEWS). Any changes (normal score being zero) should prompt a review of the patient.

Pulse

The pulse is usually taken from the radial artery. In very small children and babies, the brachial pulse may be palpated in the antecubital fossa. The pulse should be assessed for its rate (in beats per minute), rhythm and volume. The rhythm of the pulse may be regular or irregular. If the pulse is irregular, this may be in a predictable pattern, in which case it is described as 'regularly irregular'. If the pulse is completely disordered, it is described as 'irregularly irregular'. The most common example of the latter is in patients with atrial fibrillation (see Chapter 5, titled 'Cardiovascular disorders'). It should be ascertained whether the pulse is strong, or weak and 'thready'. A bounding pulse can be a sign of carbon dioxide retention in patients with chronic obstructive pulmonary disease (COPD).

A pulse rate of >100 beats/min is described as 'tachycardia', and a pulse rate of <60 beats/min is described as 'bradycardia' (causes given in Table 1.7). Other abnormalities of the pulse are listed in Table 1.8.

Table 1.7 Causes of tachycardia and bradycardia.

Tachycardia (pulse rate >100 beats/min)
- Physiological – for example, exercise, emotion
- Related to fever
- Secondary to drugs – for example, adrenaline, atropine
- Hyperthyroidism
- Smoking
- Excess caffeine

Bradycardia (pulse rate <60 beats/min)
- Physiological – for example, in athletes
- Immediately post-vaso-vagal attack
- Sick sinus syndrome
- Hypothyroidism

Table 1.8 Commonly seen abnormalities of the radial pulse.

Sinus tachycardia – pulse >100 beats/min
Sinus bradycardia – pulse <60 beats/min
Atrial fibrillation – irregularly irregular pulse
Ventricular extrasystole – 'missed beats'

Blood pressure

The method for measuring blood pressure is given in Chapter 5E (titled 'Hypertension'). The figures quoted are given in millimetres of mercury. The upper figure is the systolic blood pressure (120–140 mmHg), and the lower figure the diastolic blood pressure (60–90 mmHg). Pathological changes in blood pressure are discussed in Chapter 5 (titled 'Cardiovascular disorders').

Temperature

The normal body temperature, measured orally, is 35.5–37.5°C. Many automated digital devices are now available for measuring body temperature, often in the form of a probe inserted into the external auditory meatus. In infants, the thermometer may be inserted into the armpit (axilla).

Respiratory rate

Several disease processes may be manifest by alterations in the respiratory rate and are discussed in the relevant chapters. The normal respiratory rate in a resting adult who is fit and well is 12–18 breaths/min.

Specific lesions

It is useful to have a standard set of parameters to be used in the assessment of lumps and ulcers. These can be applied to any clinical situation with minor modifications if required. These are summarised in Table 1.9 (lumps) and Table 1.10 (ulcers).

Table 1.9 Generic features to be considered in the assessment of lumps.

History
When/how was the lump first noticed?
Are there any symptoms?
Has the lump changed since it was noticed?
Does the lump ever disappear?
Are there any other lumps?
Examination
Site
Size
Shape
Surface – smooth or not – fixed to skin/deep structures
Colour of overlying skin/mucosa
Is it tender?
Edge – indistinct or well defined
Consistency – soft, fluctuant, rubbery or hard
Is it compressible?
Is it pulsatile?
Does it transilluminate when the light from a torch is shone through it?
Enlargement of local lymph nodes?
Consider blood and nerve supply to surrounding area
Is this a localised lump, or part of an associated generalised condition?

Table 1.10 Features to be considered in the assessment of ulcers.

History
Where/how was it noticed?
Symptoms
Changes since noticed
Any previous history of similar ulcers?
Examination
Site
Size
Shape
Base – slough, granulation tissue, deeper anatomy visible
Edge – sloping, suggesting healing
Punched out (square edge)
Undermined edge – for example, TB
Rolled – basal cell cancer (see Chapter 11, titled 'Musculoskeletal disorders')
Everted – squamous cell cancer (Chapter 11)
Depth
Discharge – swab for microbiological analysis
Enlargement of local lymph nodes?
Consider blood and nerve supply to surrounding area
Is this a localised ulcer, or part of an associated generalised condition?

SUMMARY

Most of the assessments of any patient's medical condition is made on the basis of a thorough history.

Examination findings usually serve to confirm suspicions and refine findings.

FURTHER READING

Oxford Handbook of Clinical Medicine. Oxford: Oxford University Press; 2014.

Scully's Medical Problems in Dentistry. London: Churchill Livingstone; 2014.

Antibiotic prophylaxis. Available from: https://www.nice.org/guidance/cg64 (last update 2016).

General Dental Council. Maintaining Standards: Guidance to Dentists on Professional and Personal Conduct. Available from: http://www.gdc-uk.org/Newsandpublications//Publications/ Publications/MaintainingStandards.

Resuscitation Council (UK). Available from: http://www.resusc.org.uk/pages/medental.htm.

MULTIPLE CHOICE QUESTIONS

1. Orthopnoea is a possible symptom of:
   a) Indigestion
   b) Seizures
   c) Productive cough
   d) Left-sided heart failure
   e) Bowel cancer
   Answer = D

2. Which of the following are *not* likely causes of confusion in a patient?
   a) Hypoxia
   b) Infection
   c) Epilepsy
   d) Prescription of a non-steroidal anti-inflammatory drug (NSAID)
   e) Raised intracranial pressure
   Answer = D

3. Koilonychia (spoon-shaped fingernails) is a potential sign of:
   a) Vitamin K deficiency
   b) Albumin deficiency
   c) Chronic iron deficiency anaemia
   d) Infective endocarditis
   e) Patients with liver disease
   Answer = C

4. A facially visible sign of hypercholesterolaemia is:
   a) Malar flush
   b) Xanthelasma
   c) Cyanosis
   d) Jaundice
   e) Ptosis
   Answer = B

5. Which of the following signs is *not* a potential feature of rheumatoid arthritis?
   a) Dupuytren's contracture
   b) Ulnar deviation of the hands
   c) Elbow nodules
   d) Pulmonary fibrosis
   e) Enlarged spleen
   Answer = A

6. The stated alcohol consumption limit per week for females is:
   a) 2 units per week
   b) 6 units per week
   c) 10 units per week
   d) 14 units per week
   e) 20 units per week
   Answer = D

7. Which of the following is *not* a recognised cause of finger clubbing?
   a) Cyanotic congenital heart disease
   b) Bronchial carcinoma
   c) Inflammatory bowel disease
   d) Fibrosing alveolitis
   e) Myocardial infarction
   Answer = E

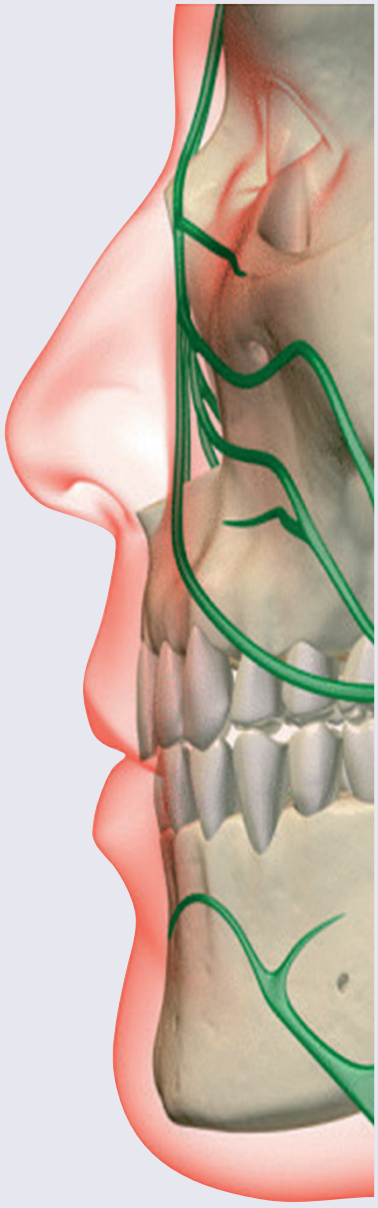
8. The artery used to take the pulse at the wrist in a patient is the:
   a) Brachial artery
   b) Ulnar artery
   c) Radial artery
   d) Popliteal artery
   e) Dorsalis pedis artery
   Answer = C

9. 'Tachycardia' is defined as:
   a) A pulse rate of more than 100 beats per minute
   b) Another word to describe ventricular extrasystole
   c) A pulse rate of more than 90 beats per minute
   d) A pulse rate of more than 110 beats per minute
   e) A pulse rate of more than 120 beats per minute
   Answer = A

10. 'Bradycardia' is defined as:
    a) A pulse rate of less than 100 beats per minute
    b) A pulse rate of less than 90 beats per minute
    c) A pulse rate of less than 80 beats per minute
    d) A pulse rate of less than 70 beats per minute
    e) A pulse rate of less than 60 beats per minute
    Answer = E

CHAPTER 2

Inflammation and anti-inflammatory drugs



CM Robinson and RA Seymour

Key topics

- Overview of the pathology and clinical features of wound healing and inflammation
- Descriptive terms used in the clinicopathology of inflammatory disorders

Learning objectives

- To be familiar with the main pathological processes involved in wound healing and inflammation.
- To be familiar with some of the drugs commonly used in the treatment of inflammatory conditions.

Essentials of Human Disease in Dentistry, Second Edition. Mark Greenwood.

Companion website: www.wiley.com/go/greenwood/human-disease-in-dentistry

Cell and tissue injury – Introduction

Cells are under constant threat of injury as a consequence of changes in their local environment. There are numerous potentially injurious agents that a cell may encounter. The type of mediator depends on the location of the cell within the body. There are agents that cause physical damage to cell integrity – for example, mechanical trauma, thermal injury and chemical damage. Cellular viability is affected by the deleterious effects of microorganisms. Cells are also prone to damage following reductions in oxygen and nutrient supply. Cell injury may be induced by DNA-damaging agents, such as ionising radiation.

Cell injury may be reversible or irreversible. This depends on the type of injurious agent, the duration of the adverse conditions and the ability of the cell to adapt to the changes. If the cell is unable to adapt and survive, there are two distinct pathways leading to cell death – necrosis and apoptosis (programmed cell death). Consequences of tissue injury are shown in Table 2.1 and described in the following text.

Necrosis

Necrosis is the death of groups of cells. It has profound consequences on tissue integrity and function. In some circumstances, for example, in the heart, ischaemic necrosis of the myocardium can result in complete organ failure and death of the individual. Various types of necrosis are described, depending on the microscopic appearances observed within tissues when stained with haematoxylin and eosin (H&E). Haematoxylin stains cell nuclei dark blue, whereas eosin stains the cytoplasm and the connective tissue proteins a reddish pink colour.

Coagulative necrosis

Coagulative necrosis is the most common type of necrosis and can occur in most organs and tissues. Immediately following cell death, the architecture of the tissue is retained. The cell outlines are discernible along with tissue architecture. There is progressive loss of nuclear staining, and there is a loss of cytoplasmic detail, with condensation and breakdown of intracellular proteins. Eventually, all that remains are the 'ghost' outlines of cells embedded in the extracellular matrix that comprises the tissue. Accompanying necrosis is an ensuing inflammatory reaction, which results in progressive dissolution of the damaged tissue with variable attempts at regeneration and repair, depending on the affected tissue.

Table 2.1 Potential consequences of tissue injury.

Inflammation
Coagulative necrosis
Colliquative necrosis
Caseous necrosis
Fibrinoid necrosis
Fat necrosis
Gangrene

Colliquative necrosis

Colliquative necrosis is observed in the brain following cerebral infarction. The brain has little in terms of robust collagenous supporting tissues, and the necrotic neurons and glial tissue break down to form a liquid material (liquefactive degeneration). The latter is progressively removed by microglia (macrophages/histiocytes), leaving a fluid-filled cavity.

Caseous necrosis

Caseous necrosis is characterised by structureless necrotic tissue, which has the textural quality of crumbly cheese. It is typically seen in the context of granulomatous inflammation caused by *Mycobacterium tuberculosis*.

Fibrinoid necrosis

Fibrinoid necrosis is seen in malignant hypertension and diseases characterised by vasculitis. Necrosis of smooth muscle cells in the arterial wall causes plasma to leak into the tunica media with deposition of fibrin. Fibrin takes on a distinct bright red colour when stained with H&E.

Fat necrosis

Damage to adipose tissue and the release of stored intracellular fat elicits an intense acute inflammatory response, which is typically followed by a dense fibrotic repair reaction.

Gangrene

Gangrene is necrosis with accompanying putrefaction (breakdown) of the tissues. Gangrene is typically seen in the lower extremities (legs and toes), and is usually the result of supervening infection of the necrotic tissue with bacteria, particularly *Clostridium*.

Apoptosis

Apoptosis is the process whereby cells can be removed in a controlled manner, without disrupting the integrity of the organ or tissue. Apoptosis is also called 'programmed cell death', which emphasises that it is a cellular process induced and executed by specific biochemical pathways. Apoptosis has a pivotal role in development, and controls organ size and tissue morphogenesis. In the adult, apoptosis counterbalances cellular proliferation, helping to maintain optimal cell numbers and cell types within a particular tissue. Apoptosis is also essential for the establishment of a functional immune system, through deletion of unwanted lymphocyte clones. Apoptosis is considered to play an important role in ageing, and deregulated apoptosis is involved in the pathogenesis of neoplasia.

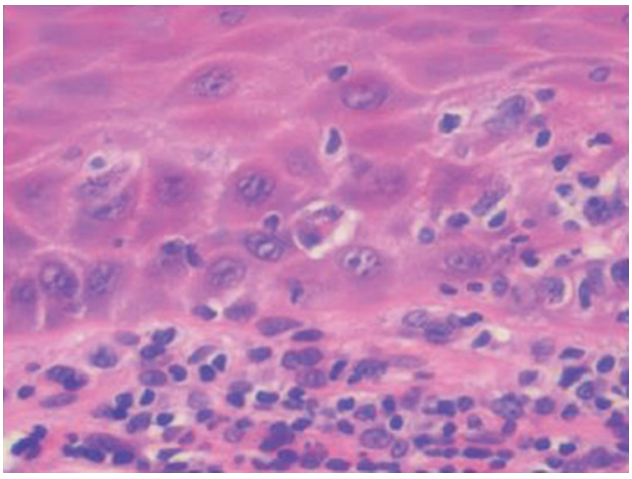


Figure 2.1 The histopathological appearance of an apoptotic keratinocyte (centre of photomicrograph). H&E stain. (See text for details.)

Cells undergoing apoptosis show distinct morphological characteristics when viewed by light microscopy in H&E-stained tissue sections (Figure 2.1). The dying cell shrinks, and there is a loss of cellular adhesion. The chromatin of the nucleus condenses and fragments, producing the appearance of 'nuclear dust'. The dead cell is phagocytosed by adjacent cells or histiocytes. There is no induction of the inflammatory cascade that typically accompanies cell death by necrosis.

Wound healing

Wound healing describes the processes that take place, following tissue injury, which are required to restore or replace damaged tissue. The effectiveness of the healing process is dependent on the ability of the constituent cells to regenerate, reorganise and recreate the original tissue architecture.

Cells in the adult can be classified by their potential to regenerate. Labile cells are continuously being lost and replaced. They include haematopoietic cells of the bone marrow and epithelial cells that constitute the epidermis and line the mucous membranes. Stable cells are not continuously replaced, but can be induced to regenerate in certain conditions; examples include hepatocytes of the liver and the renal tubular cells that make up the kidney. Non-dividing cells cannot be stimulated to proliferate and therefore have no capacity for regeneration; examples include cardiac myocytes and neurons. Labile cells that make up simple tissue structures such as the skin and the mucous membranes are the most effective at restoring tissue architecture following injury (regeneration). Stable cells can be induced to proliferate; however, in the liver and kidney, the complexity of the organ structure precludes successful regeneration and the establishment of physiological function. Damaged tissue composed of non-dividing cells is either removed to leave a tissue defect (e.g. colliquative necrosis following cerebral infarct) or repaired by fibrous tissue to produce a scar (e.g. fibrosis following a myocardial infarct).

Table 2.2 Wound healing.

Soft tissue
• Healing by primary intention
• Healing by secondary intention
Bone
• Haematoma formation in fracture line
• Formation of granulation tissue and osteoclastic activity
• Woven bone forms a fracture callus
• Remodelling of woven bone to form lamellar bone

Skin is used as a model for studying wound healing. Healing of skin is usually described as occurring by primary intention when the wound edges are approximated, and by secondary intention when there is a tissue defect that prevents closure of the wound (Table 2.2).

A surgical incision that has been closed by sutures heals by primary intention. In these circumstances, the apposed wound edges are stuck together by fibrin, which forms a scab at the skin surface. Below the scab, within the damaged epidermis, the basal keratinocytes proliferate and migrate across the narrow defect, and the epithelium completely regenerates within 5–7 days. The fibrin that sticks the incised edges of the dermis together is gradually replaced by cellular fibrovascular tissue. Small capillary buds grow into the wound, providing oxygen and nutrients, and fibroblasts migrate into the area, producing collagen and other extracellular matrix proteins. Gradually, the fibrovascular tissue becomes less vascular and matures to form fibrous scar tissue.

On occasions, it is not possible to appose the edges of a wound, and the tissue defect heals by secondary intention. Initially, the tissue defect is composed of necrotic tissue admixed with clotted blood (haematoma). The necrotic tissue is removed by histiocytes, and the clotted blood is gradually replaced by highly cellular fibrovascular tissue, called 'granulation tissue' (referring to the visual appearance of the tissue in the base of a wound, which is bright red and has a rather granular appearance). It is important to point out here that granulation tissue is distinct from 'granulomatous inflammation', which is discussed in the following text.

Granulation tissue is composed of proliferating endothelial cells that form rudimentary imperforate capillaries, small capillary buds and loops. As the granulation tissue matures, the capillaries become dilated and engorged with blood. There are fibroblasts producing collagen and extracellular matrix proteins that progressively fill the tissue defect. In addition, there are myofibroblasts, which are specialised fibroblasts that contain contractile smooth muscle filaments. Myofibroblasts are thought to play an important role in wound contraction, which facilitates closure of the tissue defect. In some circumstances, this causes marked tissue distortion with attendant cosmetic and functional problems. Towards the skin surface, the epidermal keratinocytes at the margins of the defect divide and migrate below the scab to form a thin sheet of epithelial cells. Gradually, the tissue defect is completely covered by

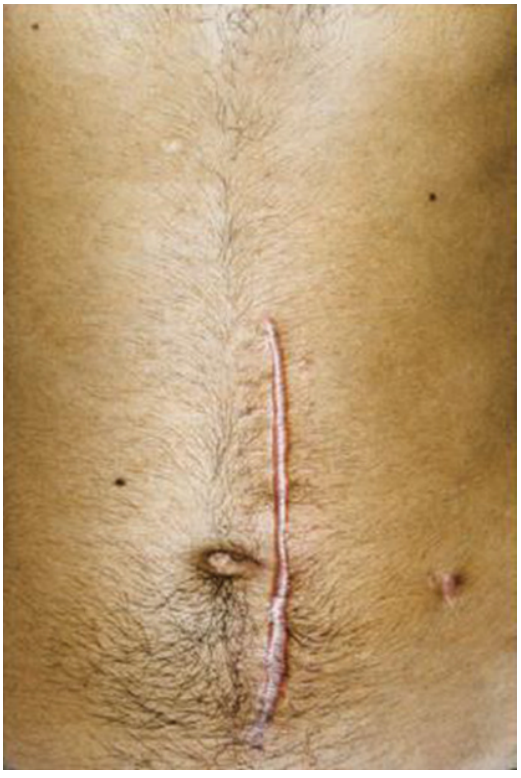


Figure 2.2 A hypertrophic scar. Keloid scars extend beyond the wound margins.

full-thickness epidermis, and the scab is exfoliated. Sometimes, the production of fibrous repair tissue is excessive, and the dermis becomes bulky and lumpy – this is referred to as a 'hypertrophic' or 'keloid' scar (Figure 2.2).

Wound healing proceeds in a similar manner following bone injury (Table 2.2). For example, following the fracture of a limb bone, a haematoma forms at the site of injury and invests dead pieces of soft tissue and devitalised fragments of bone. The soft tissue is removed by histiocytes, and the bone is removed by osteoclasts. Granulation tissue gradually replaces the haematoma, and woven bone is laid down to form a fracture callus. The woven bone of the callus is eventually remodelled to lamellar bone and, consequently, within 6–8 weeks, there is very little evidence of the injury; this is known as 'regeneration'. Healing of long bones is dependent, however, on close apposition of the broken ends of the bone and immobilisation of the fracture site. Failure to ensure the latter may result in failure of bone regeneration and the production of a fibrous union (pseudarthrosis; false joint).

The liver has a complex architecture, with hepatocytes arranged in a lobular configuration around hepatic vessels and bile ducts. Hepatocytes are stable cells that can be induced to proliferate, and small groups of cells are capable of regenerating and recreating the lobular architecture following injury. However, following extensive damage to the liver – for example, owing to long-standing alcohol abuse – there is disorganised nodular regeneration of hepatocytes, as opposed to lobular regeneration, and there is also extensive fibrosis, which results in liver cirrhosis. The kidney is similar, in that the tubular cells are capable of regeneration, but the complex microanatomy of the organ is difficult to recreate, and organ damage usually heals by fibrosis.

Inflammation – Introduction

Inflammation is a protective response, the goal of which is to eliminate the injurious agent and the consequences of tissue damage. Ideally, the inflammatory process facilitates repair of damaged tissue; however, in some circumstances, inflammation can have harmful effects on the tissues and compromise the well-being of the individual.

Inflammation is a complex reaction that occurs in vascularised tissue and comprises changes in blood vessels, which lead to the accumulation of fluid that contains leukocytes, the inflammatory exudate. Inflammation is classified into *acute* and *chronic* phases. Acute inflammation is usually of relatively short duration, lasting minutes, hours or a few days. It is characterised by the accumulation of tissue fluid, plasma proteins and the emigration of leukocytes, principally neutrophils.

Chronic inflammation is of longer duration, and is characterised by the accumulation of specialised immune cells – for example, lymphocytes, plasma cells and macrophages. Long-standing inflammation may cause further tissue damage, which is termed 'bystander damage'. After neutralisation/elimination of the cause of inflammation, there follows attempts at repair. The process of repair is characterised by the proliferation of blood vessels producing richly vascular granulation tissue, and there is usually attendant fibrosis. The inflammatory cascade is orchestrated by chemical mediators triggered by the inflammatory stimulus. The chemical mediators are derived from the plasma, and are released by a variety of cells involved in inflammation.

Conventionally, the process of inflammation is described by the suffix '-itis', preceded by the organ and/or tissues affected (Table 2.3).

Inflammation is caused by:

- Microorganisms: bacteria, viruses, fungi, parasites.
- Physical agents: mechanical trauma, thermal injury, chemical damage, exposure to radiation.
- Tissue necrosis.
- Hypersensitivity reactions.

The clinical signs of inflammation, called the 'cardinal signs', are redness, heat, swelling, pain and loss of function (Table 2.4). Redness is a consequence of increased blood flow to the inflamed tissue, and is called 'hyperaemia'. In peripheral tissues, for example, the skin, the increased blood flow causes the skin surface to feel warmer. In addition, inflammatory chemical mediators contribute to a rise in body temperature, called 'pyrexia'. The development of swelling is mainly a consequence of accumulating tissue fluid, called 'oedema'. Progression of the inflammatory response produces symptoms of pain; there is distortion and stretching of the tissues, and inflammatory chemical mediators

Table 2.3 Inflammation of different body organs.

Organ/tissue	Tissues	Inflammation
Brain	Meninges	Meningitis
Heart	Endocardium	Endocarditis
	Myocardium	Myocarditis
	Pericardium	Pericarditis
Large bowel	Colon	Colitis
	Peritoneum	Peritonitis
Liver	Liver parenchyma	Hepatitis
Lungs	Lung parenchyma	Pneumonitis
	Alveoli	Alveolitis
	Bronchi	Bronchitis
Tooth	Dental pulp	Pulpitis
	Periodontal ligament	Periodontitis

Table 2.4 Cardinal signs of acute inflammation.

Redness – *rubor*
Heat – *calor*
Swelling – *tumor*
Pain – *dolor*
Loss of function – *functio laesa*

sensitise pain receptors in the affected tissues. Loss of function is a consequence of increased pain and swelling.

Pathogenesis of acute inflammation

The acute inflammatory response involves three main processes:

- Vascular response – changes in vessel calibre and blood flow.
- Humoral response – increased vascular permeability and fluid exudation.
- Cellular response – formation of a cellular exudate.

Changes in vessel calibre and blood flow occur at the onset of inflammation. Initially, there is transient vasoconstriction of arterioles that lasts a few seconds, which is followed by prolonged vasodilation and opening of capillary beds, which increases the blood flow to the area (hyperaemia). Physiological fluid exchange within a capillary network is governed by the principles described by Starling, which depends on an intact endothelium.

In inflammation, the capillaries become leaky, and there is escape of protein-rich fluid into the tissues (fluid exudate). Vascular leakage is mainly caused by the formation of gaps between the endothelial cells, and is mediated by a variety of different chemical mediators, which include histamine, bradykinin and leukotrienes. The gaps form by endothelial contraction following remodelling of the intracellular actin cytoskeleton. Vascular permeability is also caused by direct injury to endothelial cells. The loss of protein from the plasma reduces the intravascular osmotic pressure and, coupled with the increase in hydrostatic pressure due to vasodilation, there is a net outflow of fluid into the tissues. Consequently, blood viscosity increases and capillary blood flow becomes slow. These changes precede and facilitate the development of the cellular exudate.

Normally, blood flow through vessels is axial; plasma flows adjacent to the vessel wall, and the cellular component of blood travels as a column in the central part of the vessel lumen, away from the vessel wall. In inflammation, as the blood viscosity increases and the blood flow slows down, leukocytes drop out of axial flow and come in close proximity to the endothelial cells that line the blood vessel; this process is called 'margination'. Following margination, leukocytes, principally neutrophils, adhere to the endothelial cells. Initially, the adhesion is transient and the neutrophils roll along the endothelium, finally coming to rest under the influence of strong intercellular binding.

Over time, the neutrophils almost entirely line the vessel – a process called 'pavementation'. The adherence of leukocytes to the endothelium is mediated by specific cell adhesion molecules (CAMs). Four groups of CAMs are involved: selectins, immunoglobulins, integrins and mucin-like glycoproteins that are under the influence of chemoattractants (bacterial products, components of the complement pathway particularly C5a, leukotrienes and chemokines). The leukocytes insert pseudopodia between the endothelial cells and start the process of emigration into the extravascular compartment. Extravasated neutrophils bind to microorganisms by opsonisation and are capable of phagocytosis and intracellular killing.

Sequelae of acute inflammation

Resolution

Resolution is defined as the complete restoration of normal tissue architecture following inflammation (Table 2.5). Resolution proceeds if there is minimal tissue damage and the tissue has the capacity to regenerate. Resolution is characterised by the restitution of physiological vascular permeability and drainage of excess tissue fluid via the lymphatics. Macrophages play a pivotal role in removing necrotic debris, which facilitates

Table 2.5 Sequelae of acute inflammation.

Resolution
Organisation
Suppuration
Fibrinous inflammation
Serous inflammation
Ulceration

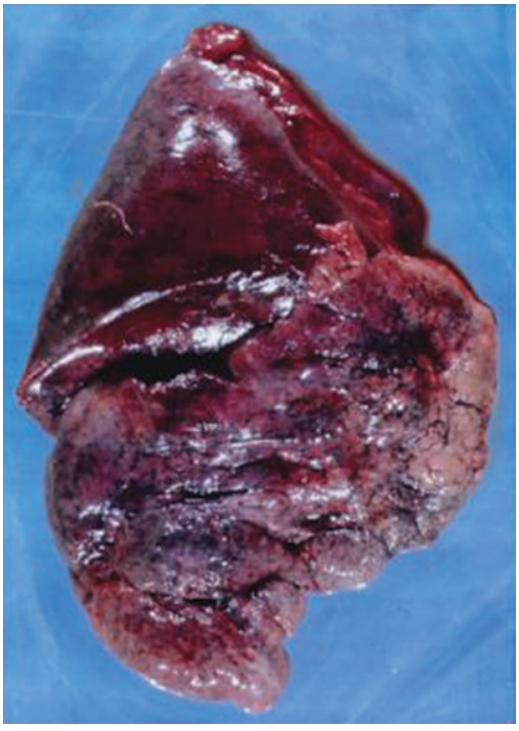


Figure 2.3 Acute lobar pneumonia showing consolidation in the upper lobe.

regeneration of the tissue architecture. The best example of an acute inflammatory condition that resolves completely is acute lobar pneumonia (pneumonitis) (Figure 2.3).

Organisation

In situations where there is extensive tissue damage or there is no capacity for resolution, the affected tissue heals by organisation. Organisation is characterised by the production of granulation tissue. Macrophages clear the dead necrotic material, and new capillary buds grow into the area of inflamed tissue. Migrating and proliferating fibroblasts produce extracellular matrix rich in collagen, causing fibrosis. Healing by organisation often results in distortion of the affected tissues, producing a scar. In some circumstances, scarring may adversely affect organ function – for example, inflammation of the bowel wall with ensuing fibrosis may cause a stricture and obstruction.

Suppuration

Suppuration is the formation of pus, composed of dead and dying neutrophils, bacteria and degenerating cellular debris. Suppuration is usually caused by a persistent bacterial infection. Some species of bacteria are invariably associated with the formation of pus and are called 'pyogenic bacteria' (e.g. *Staphylococcus aureus* and *Streptococcus pyogenes*). Pus is usually contained within

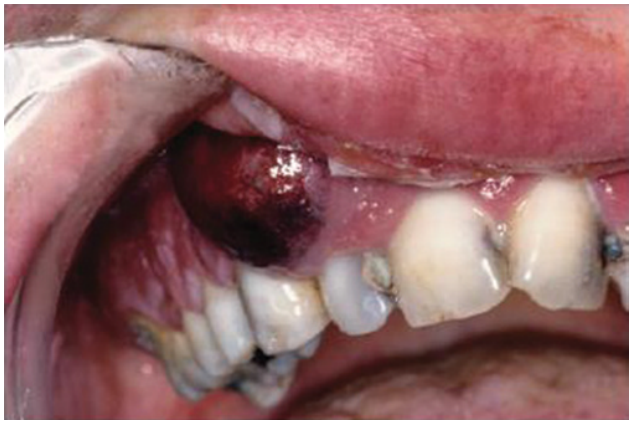


Figure 2.4 An acute dental abscess.

a cavity lined by inflamed granulation tissue and fibrous tissue, called an 'abscess' (Figure 2.4). A hollow body cavity filled with pus is called an 'empyema' (e.g. empyema of the gallbladder).

Fibrinous inflammation

Fibrinous inflammation develops when the inflammatory exudate is rich in fibrin. The fibrin cross-links to form a thick coating. This appearance is typified by the post-mortem description of 'bread and butter' pericarditis, in which the visceral and parietal surfaces of the inflamed pericardium resemble those of two pieces of buttered bread that have been pressed together and then pulled apart.

Serous inflammation

Serous inflammation is characterised by the accumulation of a watery fluid exudate that contains relatively few inflammatory cells. Serous inflammation occurs on the serosal surfaces of the gastrointestinal tract (peritonitis). The watery content of a blister on the skin surface is a consequence of serous inflammation.

Ulceration

An ulcer is a defect of the tissue surface produced by the sloughing of inflamed necrotic tissue. Inflammation of the skin and mucous membranes may typically lead to the development of ulceration (Figure 2.5).

Pathogenesis of chronic inflammation

Chronic inflammation takes time to develop, and is characterised by the accumulation of lymphocytes, plasma cells and macrophages. There is a complex interplay between the various cell types involved in chronic inflammation. The macrophage, derived from the mononuclear phagocyte system, is considered to play a central role in coordinating the chronic inflammatory response. The bone marrow harbours the

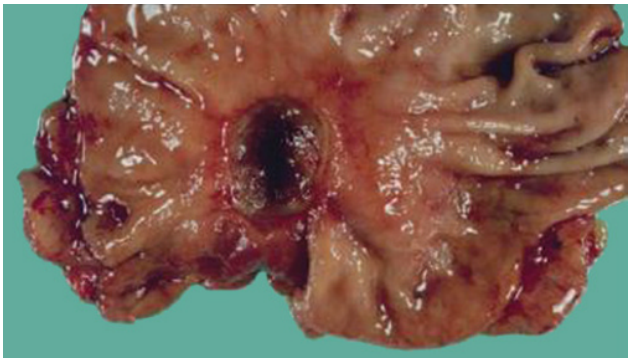


Figure 2.5 A gastric ulcer.

precursor cells, which are released into the blood as monocytes. Monocytes enter the tissues by the same process described for emigrating neutrophils, and they are then termed 'macrophages'. Macrophages scattered throughout the parenchymal connective tissues are termed 'histiocytes'. In some organs and locations, macrophages have different names – liver, 'Kupffer cells'; lungs, 'alveolar macrophages'; central nervous system (CNS), 'microglia'; and lymph nodes, 'sinus histiocytes'. Nevertheless, activated macrophages at all sites have the same role, and are involved in both phagocytosis and the recruitment of other chronic inflammatory cells via the secretion of an array of cytokines, chemotactic factors and growth factors. In addition to the accumulation of specific immune cells, the affected tissues also show attempts at repair, and there is production of granulation tissue and progressive fibrosis (organisation).

Chronic inflammation is usually seen in patients with prolonged exposure to toxic agents, persistent infection or autoimmune disease. Chronic inflammation may follow the acute inflammatory response, particularly if there is suppuration and abscess formation. In these circumstances, failure in draining pus leads to the development of chronic inflammation. For example, in the transition of acute suppurative osteomyelitis to chronic osteomyelitis, fragments of dead bone bathed in pus act as a stimulus for the accumulation of a chronic inflammatory cell infiltrate. In some instances, chronic inflammation develops insidiously, and is not preceded by any significant acute inflammatory response; such cases may be referred to as having primary chronic inflammation.

Primary chronic inflammation

Persistent infection

Microorganisms that resist phagocytosis and intracellular killing induce a chronic inflammatory response. Examples include viral infections and bacterial infections such as *Mycobacterium tuberculosis*.

Foreign body reactions

Foreign body reactions may be induced by either endogenous or exogenous material. Typical examples of endogenous toxins include dead bone in chronic osteomyelitis, degenerate adipose tissue in fat necrosis, and keratin debris from a ruptured epidermoid cyst. Exogenous materials include surgical sutures (stitches), silica particles and asbestos fibres, the latter two causing lung fibrosis.

In the mouth, amalgam debris from restorative procedures can be displaced into soft tissue and taken up by macrophages. This can impart tattooing to the mucosa – an 'amalgam tattoo'.

Autoimmune disease

In this group of diseases, the immune system is inappropriately activated against 'self'-antigens. The generation of autoantibodies and the associated hypersensitivity reactions result in sustained chronic inflammation. An example is autoimmune (Hashimoto's) thyroiditis.

Granulomatous inflammation

Granulomatous inflammation is a distinct type of chronic inflammation characterised by the accumulation of activated macrophages, which superficially have an epithelial-like appearance and are termed 'epithelioid macrophages'. A granuloma is a focal aggregate of epithelioid macrophages that is usually surrounded by a rim of lymphocytes and plasma cells. In addition, some of the macrophages fuse to form giant cells. The giant cells comprise a large amount of cytoplasm with multiple nuclei, sometimes up to 20 per cell. Morphologically distinct types are recognised: cells with haphazardly arranged nuclei are termed 'foreign body giant cells'; cells with nuclei arranged in a horseshoe configuration are termed 'Langerhans giant cells'; and those with a peripheral ring of nuclei and central clear cytoplasm due to lipid accumulation are called 'Touton giant cells'.

The presence of granulomatous inflammation in biopsy material leads to a restricted list of diagnostic possibilities that may be distinguished by additional clinical information or further investigations. Granulomatous disorders can be broadly divided into three groups: those caused by microorganisms (tuberculosis, syphilis, deep mycoses); those associated with foreign body implantation; and, finally, idiopathic diseases (Crohn's disease, sarcoidosis, granulomatosis with polyangiitis, giant cell arteritis) (Table 2.6).

Systemic effects of inflammation

Inflammation may also be accompanied by profound systemic effects. These include pyrexia. In addition, there may be feelings of malaise, anorexia and nausea, with accompanying weight loss. The inflammatory reaction may cause enlargement of regional lymph nodes (lymphadenitis) and, in some instances, enlargement of the spleen (splenomegaly). There are also changes in the

Table 2.6 Causes of granulomatous inflammation.

Diagnosis	Histopathology tests	Clinical tests
Infective causes		
Tuberculosis	ZN stain	Chest X-ray
	Modified ZN stain	Sputum culture
		Tuberculin test
		Heaf test
		Mantoux test
Syphilis	Warthin–Starry stain	Serology – antibodies
		TPIT
		VDRL
		Wassermann reaction
Deep mycoses	PAS and DPAS stain	Check immune status
	Grocott stain	Culture fresh tissue for microbiology
Foreign body implantation		
Foreign body reactions	Birefringent material on cross-polarisation	History of foreign body implantation
	X-ray diffraction studies	
Idiopathic diseases		
Crohn's disease		Barium enema
		Endoscopy
Sarcoidosis		SACE
		Serum calcium
		Liver function tests
		Chest X-ray
		Liver ultrasound
Granulomatosis with polyangiitis (GPA)		cANCA
Giant cell arteritis		ESR/PV
		Angiography

cANCA: cytoplasmic antineutrophil cytoplasmic antibody; DPAS: diastase PAS; ESR: erythrocyte sedimentation rate; PAS: periodic acid–Schiff reagent; PV: plasma viscosity; SACE: serum angiotensin-converting enzyme; TPIT: *Treponema pallidum* immobilisation test; VDRL: venereal disease research laboratory test; ZN: Ziehl–Neelsen.

blood, which can be used as clinical indicators of inflammatory disease – for example, the erythrocyte sedimentation rate and plasma viscosity increase as a consequence of the production of acute phase proteins and immunoglobulins.

Increasing serum levels of C-reactive protein (CRP) is used as an indicator of inflammatory disease. In long-standing chronic inflammation – for example, rheumatoid arthritis – elevated serum amyloid A protein may result in the deposition of amyloid in a variety of organs and tissues (secondary/reactive amyloidosis). There may be increased numbers of circulating leukocytes (leukocytosis). Neutrophilia is characteristic of pyogenic inflammation, whereas eosinophilia is often a consequence of allergic disease or parasitic infection. Lymphocytosis is typically seen in chronic inflammatory diseases. Mononucleosis is associated with Epstein–Barr virus infection (infectious mononucleosis/glandular fever). Anaemia may also be a feature of prolonged inflammatory disease, as a consequence of chronic blood loss or toxic bone marrow suppression.

Anti-inflammatory drugs

Anti-inflammatory drugs block or target various aspects of the inflammatory response. Examples include antihistamines, corticosteroids and non-steroidal anti-inflammatory drugs

(NSAIDs). The latter are dealt with in Chapter 14 (titled 'Pain and anxiety control').

Antihistamines

This is a collective group of drugs that antagonise histamine at receptor sites. They do not alter the formation or release of histamine from tissues or mast cells. Antihistamines are classified according to the histamine (H) receptors that they block (H_1, H_2, H_3). H_1 receptor antagonists are often referred to as the 'classic' antihistamines. H_2 receptor antagonists are used in the management of peptic ulceration, and are considered in Chapter 7 (titled 'Gastrointestinal disorders'). H_3 receptor blockers have been synthesised, but their clinical use and value have yet to be determined.

H_1 receptor antagonists

Examples of this category of antihistamines include chlorphenamine (chlorpheniramine), promethazine and loratadine.

H_1 blockers are competitive antagonists as they interact with H_1 receptors on cell membranes, which results in a decrease in the availability of these receptors for the actions of histamine. Hence, H_1 blockers antagonise the action of histamine on smooth muscles, and thus reduce histamine-induced vasodilation, capillary permeability, and the flare and itch components of the triple response of Lewis. The full description of this physiological response is given in standard texts of physiology. Some H_1 receptor antagonists also have central effects, including sedation and the reduction of nausea and vomiting. These actions are not related to the antagonism of histamine.

Most H_1 receptor antagonists are taken orally; they are well absorbed from the gastrointestinal tract, metabolised in the liver and excreted via the kidneys. Therapeutic effects can be observed 15–30 min after dosage.

Uses

H_1 blockers are widely used in the treatment and prevention of a variety of allergic conditions – for example, rhinitis, hay fever and certain allergic dermatoses such as acute urticaria. Topical preparations may be useful in relieving the itching associated with insect bites. The drugs are also widely used in common cold remedies, usually combined with a decongestant. (While such constituents reduce symptoms, they do not prevent or shorten the duration of the common cold.) The central effects of H_1 blockers make them useful in the prophylaxis of motion sickness and as a sedative, especially in children.

Unwanted effects

Sedation is the main unwanted effect associated with certain H_1 receptor blockers, but the extent and severity of this unwanted effect vary between preparations. Alcohol should be avoided in patients taking antihistamines, as it can enhance the sedative effect. The so-called second generation of antihistamines (cetirizine and loratadine) do not cause sedation, since they are unable to cross the blood–brain barrier.

Topical antihistamine creams are readily available to the public to relieve skin itching and also for insect bites. Such preparations may cause hypersensitivity reactions, and should be avoided in patients with a history of eczema and other allergic-based skin disorders. Their use should be limited to 3 days.

Dental uses of antihistamines

Only H_1 receptor blockers have any dental application. Chlorphenamine 10–20 mg, given by intramuscular or subcutaneous injection, is a useful adjunctive treatment in the management of anaphylaxis (see Chapter 20, titled 'Haematology'). Chlorphenamine must be administered after adrenaline. Promethazine has both sedative and weak atropine-like properties and may be useful as a preoperative sedative agent, particularly in children (see Chapter 14, titled 'Pain and anxiety control').

Corticosteroids

Corticosteroids are naturally occurring substances produced by the adrenal cortex (see Chapter 12, titled 'Dermatology and mucosal lesions'). Synthetic corticosteroids are used extensively in all aspects of clinical medicine as they possess potent anti-inflammatory and immunosuppressive properties. In this section, only the anti-inflammatory properties will be considered. Immunosuppressive actions of corticosteroids are dealt with in Chapter 4 (titled 'Immunological disease').

Anti-inflammatory action of corticosteroids

Corticosteroids inhibit many of the processes associated with inflammation, which include decreased production of prostanoids owing to decreased expression of cyclo-oxygenase-2; decreased generation of cytokines (interleukin (IL)-1 to IL-8 and tumour necrosis factor-α (TNF-α)); reduction in the concentration of complement proteins in the plasma; decreased generation of nitric oxide; and decreased histamine release from mast cells. At the cellular level, corticosteroids reduce polymorphonuclear leukocyte (PMN) chemotaxis and phagocytosis.

These various actions are mediated by corticosteroids binding with glucocorticoid receptors in the cytoplasm of various cells. Such binding then brings about either suppression or induction of various transcription factors, which switch on the genes for the various cytokines listed earlier.

Anti-inflammatory actions of corticosteroids applicable to dentistry

Oral ulceration and oral mucosal lesions

Corticosteroids are widely used in the treatment of recurrent aphthous ulceration and other oral mucosal lesions such as lichen planus, mucous membrane pemphigoid and pemphigus. Many of these conditions are treated by topical applications, and examples of such preparations include hydrocortisone

sodium succinate oromucosal tablets (2.5 mg), beclomethasone spray (50–100 μg) and betamethasone soluble tablets (500 μg) dissolved in water and used as a mouthwash. Applying any topical medication to the oral mucosa is difficult, and often the best results are achieved when there is maximal contact time between the lesion and the medication. For severe cases of oral ulceration, systemic corticosteroids may be necessary, and the drug of choice is prednisolone.

Pulpal inflammation

Corticosteroids can be applied over a carious exposure of the dental pulp to try and reduce pulpal inflammation and pain. One such preparation, Ledermix®, contains triamcinolone and tetracycline (demeclocycline hydrochloride). The efficacy of Ledermix® remains equivocal.

Bell's palsy

This is a unilateral facial paralysis affecting one or more branches of the facial nerve (see Chapter 9, titled 'Neurology and special senses'). Bell's palsy is of unknown aetiology, but may be subsequent to a viral infection. Systemic prednisolone is the treatment of choice, and therapy must be started within 5–6 days of the onset of paralysis. It is usual to start off treatment with prednisolone at a high dose, reducing this over a period of 10 days.

Postoperative pain and swelling after dental surgery

There has been much interest in the use of systemic corticosteroids to reduce pain and swelling after the removal of impacted lower third molars and after orthognathic surgery. For such purposes, a course of corticosteroids is usually short, so unwanted effects are few. Methylprednisolone and betamethasone are the corticosteroids used for this purpose, usually administered intramuscularly just before surgery, or dexamethasone intravenously. The efficacy of corticosteroids for reducing postoperative pain after dental surgical procedures remains uncertain, and such pain may respond better to an NSAID (see Chapter 14, titled 'Pain and anxiety control').

FURTHER READING

Cross S. *Underwood's Pathology: A Clinical Approach*, sixth edition. London: Churchill Livingstone; 2013.

MULTIPLE CHOICE QUESTIONS

1. At post-mortem examination, a patient who died of myocardial infarction would show evidence of:
   a) Fibrinoid necrosis
   b) Gangrene
   c) Colliquative necrosis
   d) Coagulative necrosis
   e) Apoptosis
   Answer = D

2. At post-mortem examination, a patient who died of cerebral infarction would show evidence of:
   a) Gangrene
   b) Colliquative necrosis
   c) Coagulative necrosis
   d) Apoptosis
   e) Fibrinoid necrosis
   Answer = B

3. The skin has the potential to regenerate because:
   a) It has an excellent blood supply
   b) The injury is usually superficial
   c) The majority of cells are stable
   d) Healing is by primary intention
   e) The majority of cells are labile
   Answer = E

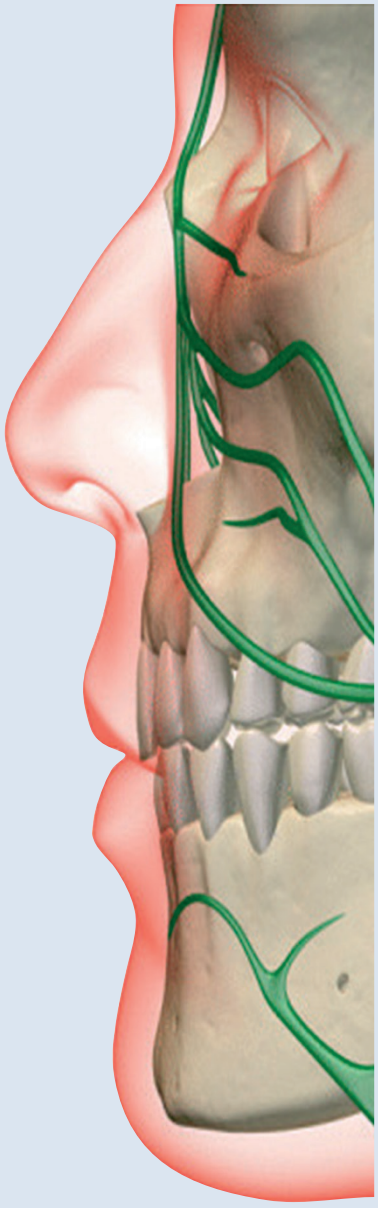
4. Granulation tissue contains:
   a) Pyogenic bacteria
   b) Langerhans giant cells
   c) Epithelioid macrophages
   d) Fibrovascular tissue
   e) Well-formed granulomas
   Answer = D

5. Granulomas contain:
   a) Endothelial cells
   b) Macrophages
   c) Epithelial cells
   d) Myofibroblasts
   e) Fibroblasts
   Answer = B

6. H_1 receptor antagonists are prescribed to patients with:
   a) Peptic ulceration
   b) A previous episode of anaphylaxis
   c) Hay fever
   d) Acute glomerulonephritis
   e) Rheumatic fever
   Answer = C

CHAPTER 3

Principles of infection and infection control



S Waugh, E Ong, S Hogg, JG Meechan, RA Seymour, M Greenwood, C Taylor† and G Toms

Key topics

- An overview of infection and infection control
- Methods of infection control
- Clinical examples of bacterial, viral and fungal infections and their management

Learning objectives

- To be familiar with the common methods of infection transmission and control
- To be aware of some of the common bacterial, viral and fungal infections and outlines of their management

†Deceased

Essentials of Human Disease in Dentistry, Second Edition. Mark Greenwood.

Companion website: www.wiley.com/go/greenwood/human-disease-in-dentistry

3A STERILISATION, DISINFECTION AND ANTISEPTICS

Sterilisation and disinfection

Sterilisation has been defined as the killing or removal of all viable organisms. Concern about transmissible spongiform encephalopathies such as Creutzfeldt–Jakob disease (CJD) and particularly variant-CJD (vCJD) has generated research that has resulted in a much greater understanding of prions, the transmissible agents of the disease. The debate about whether prions are organisms probably reflects similar discussions decades ago regarding the nature of viruses, but the absence of even nucleic acid puts prions in a class apart, at least for now. The fact that prions have been identified as a transmissible agent of disease means that any definition of sterilisation should take them into account. *Sterilisation* is therefore more accurately defined as 'the inactivation or removal of all self-propagating biological entities'.

Disinfection is a less precise concept and has been variously defined, the best definition being that it is 'the reduction in viable organisms to the point where risk of infection is acceptable'.

A related term that is in common use is *antisepsis*, which is usefully defined as 'the disinfection of skin or wounds'.

General principles

The efficacy of a sterilisation or disinfection method is described by the relationship

$$N = k/CT$$

where N is the number of surviving organisms, C is the concentration of the sterilising agent (temperature in the case of heat) and T is the time for which the agent is applied. The constant k depends on many factors, including the species of organism present, its physiological state and many other environmental variables – not least among which is the presence of contaminating organic material such as blood or saliva.

For a given value of C, a graph of Log_{10} viable count versus time can be useful to predict when sterility will be achieved (Figure 3A.1). The slope of the curve is known as the 'death rate', and D is the time taken to achieve a 90% reduction in viable organisms. Survival curves such as the one shown may have a shoulder, a tail or both, signifying that individual cells respond differently to the sterilising agent. In practice, this means that absolute sterility cannot be guaranteed. Therefore, by convention, an instrument is considered sterile if there is less than a one-in-a-million chance of there being one viable organism present.

What should be sterilised?

Ideally, everything in a surgery should be sterile, but this is not practicably possible. The aim is to prevent infection and, importantly, cross-infection. Therefore, anything coming into direct contact with the surgical site should be sterile, and everything else should be disinfected.

Decontamination and pre-cleaning

The presence of contaminating material – especially organic matter such as saliva, blood, faeces and tissue – can significantly degrade the sterilisation or disinfection process by either physically preventing access of the agent or chemical inactivation. In order to ensure proper sterilisation, instruments should therefore be pre-cleaned. If the instruments have been in contact with infectious material, the pre-cleaning should include adequate disinfection to render them safe before they are packaged for sterilisation.

Sterilisation and disinfection methods

Methods of sterilisation and disinfection include dry or moist heat, a wide variety of liquid or gaseous chemicals, β- or γ-emitting ionising radiation and filtration (Table 3A.1). The choice of method depends on the nature of the material being treated, the contaminating organisms and the degree of inactivation required. For example, it is possible to sterilise milk, but this effectively changes its character. On the other hand, it is possible to retain milk's character and reduce its microbial load to a level that increases the shelf-life of milk appreciably by raising its temperature for a period of time (the pasteurisation process).

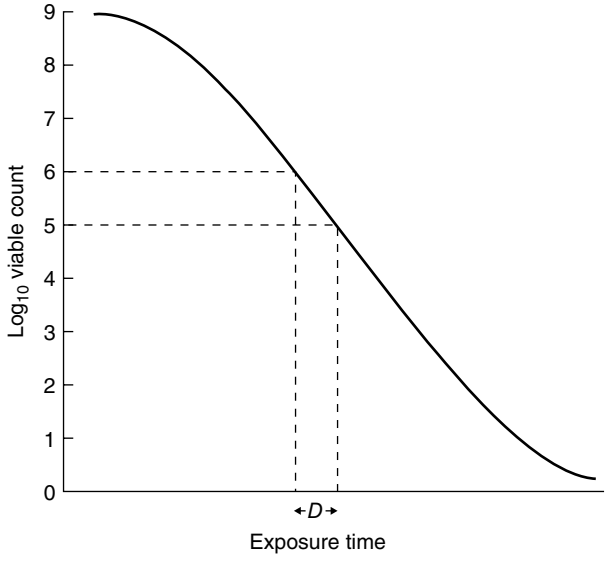


Figure 3A.1 A graphical demonstration of viable organism reduction with time (see text).