Contents

Preface

With its tenth edition, this textbook celebrates its 60th anniversary. When the first edition appeared in 1962 the practice of dentistry was very different. The book covered practical surgery and topics such as facial fractures that dental students were expected to know, and possibly use, immediately on qualification. Surgery was a significant part of general practitioner's workload, biopsy was routinely performed and oral conditions were managed without medical support. Constant introduction of new drugs and concerns about interactions in dentistry made pharmacological and general medical knowledge essential.

Advances in restorative care, implants, the ageing of population, and increased demand for cosmetic treatment have contracted dentistry back to management of teeth and periodontium to the extent that some dentists now practice on the edges of the cosmetic industry. The expansion of postgraduate specialties has brought many of the topics in this book into specialist, rather than general, practice. Nevertheless, the undergraduate dental students need to be familiar with many of the conditions included. As noted in the learning guide, the average general practice will have many patients with oral diseases that need to be managed and many of the conditions are seen in primary care, even if only infrequently.

This edition has evolved to meet the changed needs of its readers. Previous editions were written for undergraduates in dentistry, with the emphasis on explanation and fostering understanding of oral disease. However, the last two editions have been used more by postgraduates, who need a reference book with less explanation and more facts. Factual content and additional references have been added to increase the breadth and depth of coverage for this audience. It has been updated in accordance with the 2023 WHO Classifications of Head and Neck Tumours and the 2020 International Classification of Orofacial Pain. More diseases have been added, both well-established entities and new ones, such as Covid-19 and Mpox. A new chapter on cosmetic procedures has been added. However, it retains its key focus on oral and facial disease, the medical aspects of dentistry and differential diagnosis. References to onward reading have been carefully selected to avoid propagation of the misinformation available on the internet. My hope is that whoever reads the book will find it interesting and informative.

My thanks are to Alex Mortimer, Fariha Nadeem and the production staff at Elsevier for maintaining the excellent production standards of previous editions.

I am grateful to colleagues who have helped me by suggesting changes, reading chapters, and providing material, particularly Prof Francis Hughes for Periodontology, Dr Stacey Clough for Special Care Dentistry, and Dr Jackie Brown for Radiology. Most of all, my thanks go to my wonderful wife Wendy for her unconditional support and for maintaining her sense of humour during the year I spent in front of my computer writing this new edition.

References

References to further reading are inserted throughout, immediately adjacent to the relevant text. To make searching for web URLs straightforward, links to the relevant websites can be found at http://sites.elsevier.com/cawsonsessentials. Various types of reference are provided, all designed to be immediately available through the internet. In the electronic version of this book they are direct links:

PubMed ID: These are shown with a few words of description and a number in the format PMID: 25556809. Entering the text PMID and number into an Internet search engine should take the reader direct to the reference. Alternatively, it can be entered direct into the PubMed search box at the top of the main page at the PubMed website at http://www.ncbi.nlm.nih.gov/pubmed/ and this has the advantage of immediately showing the abstract and links to the full text of the article. References have been selected to be open access full text publications where possible, but it may be necessary to log in to publishers' websites or access through an institution library to obtain the full text. Use the references in these papers to direct onward reading.

PubMed Central ID: These are shown similarly, with a few words of description and a number in the format PMCID: PMC4334280. The majority of PubMed Central ID numbers have been changed to PubMed IDs in this edition. If an open access PubMed Central version is available, there will be a link direct to it on the PubMed webpage. Otherwise PMC reference numbers can be resolved in the same way as above. If searching on the PubMed website for a PMC number, do not forget to select PMC in the window to the left of the search box.

ISBN numbers: These are ISBN13 codes to books in the format ISBN-13: 978-0723435938. The numbers can be entered either into a search engine, although a search in the website of an online bookseller or your university library will take you directly to the book title and a copy. Where possible, books available in electronic format have been selected.

Web Uniform Resource Locators URLs or web addresses. These may be entered directly into the address bar of a web browser. Some are long and complex and case sensitive. To avoid this, some are given just as the home page of an organisation with instructions on text words to enter into the search box. These should find the relevant resource more reliably that a complex URL that may change.

DOI: Digital Object Identifiers can be resolved at the DOI website https://www.doi.org/

Principles of investigation, diagnosis and treatment

1

The principles of patient investigation and diagnosis are summarised in Box 1.1.

TAKING A HISTORY

Taking a history and making a diagnosis are not completely generic skills that can be learned and then applied to any patient. Gaining rapport, listening and questioning skills are common to all complaints, but to ask targeted incisive questions requires the ability to construct a good differential diagnosis. Effective history-taking is therefore founded in clinical and pathological knowledge.

Rapport is critical for gaining trust and eliciting the most useful information, but gaining rapport can be difficult because almost all patients are nervous to a degree, some are inarticulate and others are confused. History-taking needs to be tailored to the individual patient.

Initial questions should allow patients to speak at some length and to gain confidence. It is usually best to start with an 'open' question (Tables 1.1 and 1.2). Medical jargon should be avoided, because even regular hospital attenders who appear to understand medical terminology may use it wrongly and misunderstand. When a patient uses technical jargon, it is wise to check what they mean by it. Leading questions, which suggest a particular answer, should be avoided because patients may feel compelled to agree with the clinician.

It is sometimes difficult to avoid interrupting patients when trying to structure the history for the written record. Structure can only be given after the patient has had time to give the information. Constant note-taking while patients are speaking is undesirable. Notes should be a summary of relevant information only.

Questioning technique is most critical when eliciting any relevant social or psychological history or dealing with embarrassing medical conditions. It may be appropriate to delay asking such questions until after rapport has been gained. Some patients do not consider medical questions to be the concern of the dentist and it is important to be able to give reasons for such questions.

During history-taking, the mental and emotional state of the patient should be assessed. This may have a bearing on some diseases and will also suggest what the patient expects to gain from the consultation and treatment. If the patient's expectations are unreasonable, it is important to try to modify them during the consultation, otherwise no reassurance or treatment may be satisfactory (Box 1.2).

Box 1.1 Principles of investigation and diagnosis

A detailed medical and dental history

- Clinical examination
  - Extraoral
  - Intraoral
- Investigations selected for specific purposes
  - Testing vitality of teeth
  - Radiography or other imaging techniques
  - Biopsy for histopathology (including immunofluorescence, immunocytochemistry, molecular biological tests)
  - Specimens for microbial culture
  - Haematological or biochemical tests

Table 1.1 Types of questions

Type of question	Example
Open	Tell me about the pain.
Closed	What does the pain feel like?
Leading	Does the pain feel like an electric shock?

Demographic details

The age, sex, ethnic group and occupation of the patient should be noted routinely; even though apparently trivial, such information is occasionally critical. Increasing age predisposes to malignant neoplasms, autoimmune disease tends to have onset in middle-aged female patients and aphthous stomatitis is often diagnosed in the young. Identifying and recording a patient's heritage or ethnic group can be misconstrued, but it

Table 1.2 Advantages and disadvantages of types of questions

Types of question	Advantages	Disadvantages
Open	Allows patients to use their own words and summarise their view of the problem Allows patients partly to direct the history-taking, gives them confidence and quickly generates rapport	Clinicians must listen carefully and avoid interruptions to extract the relevant information Patients tend to decide what information is relevant
Closed	Elicits specific information quickly Useful to fill gaps in the information given in response to open questions Prevents vague patients from rambling away from the complaint	Patients may infer that the clinician is not really interested in their problem if only closed questions are asked Important information may be lost if not specifically requested Restricts the patient's opportunities to talk

Box 1.2 Essential principles of history-taking

- Introduce yourself and greet the patient by name
- Be culturally aware
- Act courteously and respectfully, maintain professional detachment
- Put patients at their ease, be empathic
- Start with an open question
- Mix open and closed questions
- Avoid leading questions
- Avoid medical and dental jargon and idiomatic expressions
- Listen 'actively'
- Explain the need for specific questions if asked
- Divide the consultation into manageable sections for the patient
- Summarise your findings back to the patient for confirmation of meaning
- Assess the patient's mental health state
- Assess the patient's expectations from treatment

Box 1.3 History of the present complaint

- Record the description of the complaint *in the patient's own words*
- Elicit the exact meaning of those words
- Record the duration and the time course of any changes in symptoms or signs
- Include any relevant facts in the patient's medical history
- Note any temporal relationship between them and the present complaint
- Consider any previous treatments and their effectiveness
- Check previous investigations to avoid their unnecessary repetition

Table 1.3 Features required in a pain history

Characteristic	Informative features
Character	Ache, tenderness, dull pain, throbbing, stabbing, electric shock. These terms are of limited use, but information on the constancy of pain is useful
Severity	Mild – responds to mild analgesics (e.g., aspirin/paracetamol) Moderate – unresponsive to mild analgesics Severe – disturbs sleep
Duration	Time since onset. Duration of pain or attacks
Nature	Continuous, periodic or paroxysmal If not continuous, is pain present between attacks?
Initiating factors	Any potential initiating factors Association with dental treatment, or lack of it, is especially important in eliminating dental causes
Exacerbating and relieving factors	Record all and note especially hot and cold sensitivity or pain on eating as they suggest a dental cause
Localisation	The patient should map out the distribution of pain if possible. Is it well or poorly defined? Does it affect an area supplied by a particular nerve or artery? Is the distribution of the pain consistent with sensory nerve anatomy?
Referred pain	Try to determine whether the pain could be referred
Other neurological features	If the pain suggests a neuralgia, is it accompanied by sensory deficit or paraesthesia and are any motor alterations present?

cannot be avoided for fear of being considered racist. Many diseases have a restricted ethnic distribution that aids diagnosis, such as Paget's disease of bone* or florid cemento-osseous dysplasia.

History of the present complaint

Frequently, a complaint, such as toothache, suggests the diagnosis. In most cases, a detailed history (Box 1.3) is required and sometimes, as in aphthous ulceration, a provisional diagnosis can be made on the history alone.

If earlier treatment has been ineffective, any previous diagnosis must be reconsidered. Many patients' lives have been shortened by having malignant tumours treated with repeated courses of antibiotics.

Pain is completely subjective and, when physical signs are absent, special care must be taken to detail all its features (Table 1.3). Especially important are features suggesting a dental cause. Pain from a fractured tooth or cusp, dental hypersensitivity or pain on occlusion is easily misdiagnosed.

Causes of pain are discussed in detail in Chapter 39.

Medical history

A medical history is important because it aids the diagnosis of oral manifestations of systemic disease. It also ensures that medical conditions and medications that affect dental or surgical treatment are identified. Such conditions are increasingly frequent in aging populations worldwide.

To ensure that nothing significant is forgotten, a printed questionnaire for patients to complete is valuable and saves time. It also helps to avoid medicolegal problems by providing a written record that the patient's medical background has been considered. Some patients may find it easier to fill in a questionnaire than answer questions. However, a questionnaire alone does not constitute a medical history, and the information must be checked verbally, augmented as necessary and confirmed with the clinician's signature. It is important to

* This book continues to use medical eponyms. Although some would prefer to see all medical eponyms banished, many remain in widespread use. It is generally accepted that the person associated with the condition or anatomical structure was rarely the first person to describe it, but they often produced the most comprehensive description or added significant understanding of the pathogenesis. The original suggestion that eponyms should be discontinued in medical literature (PMID: 46972) did indicate that eponyms should continue if "time-honoured designations unless there is good reason for change".

Unfortunately alternative names are often no better than the eponym and some diseases, such as Parkinson's disease have no good alternative. Eponyms also introduce an interesting element of history into medicine and dentistry.

Table 1.4 Questions to be included in a medical history and their relevance*

Question	Subsidiary or follow-up questions	Important features of relevance – not all can be included
Are you taking any medicines, medications or tablets at present?	Including over-the-counter drugs and complementary medicine such as herbal remedies or recreational drugs	Potential interactions with treatment for oral conditions Potential oral adverse effects of drugs, of which there are many Steroid use and risk of steroid collapse, infections in immunosuppression Some herbal preparations interact with sedation drugs
	Include medication taken in the past	Patients may forget past courses of drugs with important effects such as bisphosphonates (risk of osteonecrosis), or gold injections (risk of lichenoid reaction) and others
Have you ever been in hospital for any illnesses or operations?	Any problems with the operation or the anaesthetic?	Hospitalisation usually indicates severe health problems; this general question should reveal information on malignant disease, chemotherapy, radiotherapy and immunosuppression
	… routine recovery, not readmitted, no allergies? How long were you in hospital?	Indicate previous reactions to anaesthetics and possibly bleeding problems or other medical complications
Do you carry any medication cards or MedicAlert, Medi-Tag, Mediband or similar devices?		Provide details of medications, doses and effect, usually anticoagulants, steroids, allergies and significant medical conditions Note that some of these alerts may carry patient-reported diagnoses as well as medically confirmed diagnoses
Do you have, or have you had, any problems with your heart?	Elicit type, particularly valvular disease	Indicates risk of angina, myocardial infarct or other cardiac emergency in the dental surgery Potential anaesthetic problem Possible predisposition to infective endocarditis, depending on defect
Have you ever had rheumatic fever?	Do you have any heart damage as a result?	Possible predisposition to infective endocarditis
Do you have, or have you had, hepatitis or jaundice?	Known or likely type of hepatitis, if unknown clues may be in where and how it was contracted and the clinical course Questions to exclude non-infectious causes of jaundice such as haemolytic anaemias, gall stones, liver failure, alcohol, etc.	Infection control risk for hepatitis B and C Liver damage can cause coagulation defect, and the metabolic defect can contraindicate prescription of some drugs
Have you ever had epilepsy or other fits or faints?	Assess severity of epilepsy, type of seizure, frequency, duration and eliciting factors	Risk of epileptic attack or status epilepticus in the dental surgery Adverse effects of antiepileptic drugs such as phenytoin
	Degree of drug control and date and severity of last seizure	Likelihood and possible severity of future seizure(s)
	If other type of seizure or fit, what cause?	Fits of unknown cause may relate to head and neck neurological complaints and indicate a CNS cause Risk of vasovagal attack in dental surgery
Do you have diabetes?	How is it managed? With insulin, other drugs or diet? How well controlled? Ever requiring hospital admission?	Risk of hypoglycaemic collapse in insulin dependent diabetics, and, less likely, hyperglycaemia Diabetes predisposes to infection, particularly candidal but also bacterial and periodontal disease Dry mouth may result from dehydration
	How is blood glucose monitored? Normal levels and range	
Do you have high blood pressure?	Taking the blood pressure may be required and is a recommendation for dentists in some countries. Hypertension is often asymptomatic and dentists have a role in detecting and referring patients with poorly controlled or undetected hypertension.	May indicate risk of stroke, angina or myocardial infarction in the dental surgery Oral adverse reactions of antihypertensive drugs include dry mouth, gingival hyperplasia, lichenoid reactions, burning mouth and taste loss Risk of interaction with some vasoconstrictors in local anaesthetic Anaesthetic risk Patients may faint from hypotension after rising from a supine position for dental treatment
Have you ever been anaemic?	Do you know the reason?	Anaemia predisposes to numerous oral conditions including aphthous stomatitis, candidosis, glossitis and burning mouth
	Do you or anyone in your family have thalassaemia? For patients of African heritage, do you or anyone in your family have sickle cell anaemia?	Anaesthetic risk for sickle cell anaemia and thalassaemia. Thalassaemia is now so geographically widespread that limiting questioning to people of Mediterranean heritage is too specific

Continued

Table 1.4 Questions to be included in a medical history and their relevance*—cont'd

Question	Subsidiary or follow-up questions	Important features of relevance – not all can be included
Do you have any allergies …	Ask specifically about penicillin and other drugs including local anaesthetic	Reveals atopic patients prone to allergy
… to medicines? … to metals, foods, plasters, etc.?	Ask whether the patient has ever taken penicillin	Allergies to medication potentially prescribed by the dental surgeon, including related drugs Latex allergy and cross-reacting food allergies Identify potential triggers of attack relevant to dentistry
… or asthma, hay fever, rashes, etc.?		Rashes may be cutaneous counterparts of oral disease Potential adverse effects of steroid inhalers used for asthma
Have you ever had any problems stopping bleeding after a cut or surgery?	Does anyone else in your family have problems with bleeding? Have problems followed tooth extraction? Have you ever taken Warfarin or any medicines to 'thin' your blood?	Risk of haemorrhage following extraction, surgery or possibly local anaesthetic If familial, raises possibility of haemophilia and other inherited bleeding conditions Contraindicates prescription of drugs that prolong bleeding such as aspirin Anticoagulants interact with drugs prescribed for oral conditions and prolong bleeding after surgery
Have you ever come into contact with someone with human immunodeficiency virus (HIV) infection or acquired immunodeficiency syndrome (AIDS)? … or any other sexually transmitted infection?	An open question to allow patients to proffer relevant information in this sensitive area. Not usually followed up unless the patient offers that they are or may be HIV positive, in which case minimum information required is the name of the relevant physician and permission to contact them for details of the condition If positive ask about viral load, CD4 count and medication	Infection control risk following blood exposure Oral manifestations of immunosuppression Risk of significant medical complications that may present to the dental surgeon Oral adverse effects of anti-HIV medication and drug interactions Patients at risk should be encouraged to have an HIV test Gives an indication of degree of immunosuppression and infection risk
Do you smoke? Or use smokeless tobacco or betel quid …	Type and amount smoked, expressed in pack years (number of 20-cigarette packs per day multiplied by number of years of smoking). 25 g or 1 oz loose tobacco is equivalent to 50 cigarettes.	Predisposes to oral, nose and sinus and aerodigestive tract carcinoma Predisposes to atheroma, hypertension and cardiac disease Associated with oral red and white lesions and potentially malignant disorders Amenable to cessation advice in the dental setting
… or marijuana, cannabis or other drugs?		Cannabis carries additional health risks over smoking, possibly including oral carcinoma
Do you drink alcohol?	Units consumed per week and type of alcohol	Synergistic effect with smoking for oral potentially malignant disorders and oral cancer
For female patients, is there any chance you might be pregnant …	Stage of pregnancy	Risk from X-ray exposure Pregnancy modulates healing and is association with remission in aphthous stomatitis and predisposes to pyogenic granuloma and gingivitis
… or are trying to become pregnant?		Contraindicates prescription of many drugs
Are you otherwise generally fit and well?		An open question to allow patients to provide information that may not be covered by more specific questions
For parents of child patients – is your child receiving any other therapy or special support?	Type and reason Developmental milestones achieved? Any additional support at school?	A broad question to identify behavioural and developmental conditions that may affect provision of treatment
Do any diseases run in your family?		May reveal haemophilia and other bleeding disorders and a host of other genetic diseases and syndromes
Is there anything else about your health you would like to tell me?		May reveal general malaise, fevers, weight loss, psychiatric problems and reveal attitudes to health and disease not elicited by other questions
Do you experience any mental health conditions?		The stigma attached to mental health and learning difficulty problems requires a subtle approach if this is suspected but nothing has been elicited by previous questioning.

*There is deliberate 'redundancy' in medical history questioning, that is, a point of significance may be covered by questioning from more than one perspective to ensure nothing significant is missed. Thus, even if a patient claims that their heart is healthy, rheumatic fever should be asked about specifically and jaundice and hepatitis both explored independently. Patients may well not recognise medical names and react to one question but not another.

This table groups conditions that are related, but some favour following a systems-based approach, a surgical sieve, various mnemonics or a medical history questionnaire. Clinicians should become adept at using whatever system they prefer and use the same system all the time to avoid inadvertent omissions.

A standardized European medical health questionnaire is available (***PMID:*** 18299219). This links to and expands on the American Society of Anaesthesiologists (ASA) Physical Status Classification System. This questionnaire is comprehensive but, like the ASA system, is focused on detecting potential medical complications of dental treatment rather than eliciting medical history for diagnosis of oral disease.

assess whether the patient's reading ability and understanding are sufficient to provide valid answers to the questionnaire.

Medical history questionnaires vary widely in style and the questions asked. All dental surgeons should be able to take a history without the guidance of a questionnaire. The questionnaire itself is less important than understanding exactly why the questions are being asked and what follow-up questions are relevant (see Table 1.4). However, some structure is required to ensure no items are missed, and questionnaires perform a useful function in this regard.

If the patient's history suggests, or examination reveals, any condition beyond the scope of the dentist's experience or clinical knowledge, referral for a specialist medical examination may be necessary.

Medical warning cards may indicate that the patient is, for example, a haemophiliac, on long-term corticosteroid therapy or is allergic to penicillin. It is also worthwhile to leave a final section open for patients to supply any other information that they think might be relevant.

A detailed drug history is essential. Drugs can have oral effects or complicate dental management in important ways (Ch. 16 and Ch. 43).

In the relevant ethnic groups, enquiry should be made about the many potentially carcinogenic habits such as betel quid (pan), khat, hookah or smokeless tobacco use (Ch. 20).

Holistic patient assessment PMID: 24923937

Theory of diagnostic reasoning for dentists PMID: 21094715

Medical history US perspective PMID: 9344272

The European standardized medical risk-related history questionnaire PMID: 18299219

Web URL 1.1 UK good practice guideline for clinical examination and records URL: https://cgdent.uk/clinical-examination-and-record-keeping/ (requires FGDP login)

The dental history

A dental history and examination are obviously essential for the diagnosis of dental pain or to exclude teeth as cause of symptoms in the head and neck region.

Symptoms of toothache are normally recognised as such by patients but are very variable and may masquerade as a variety of conditions from the trivial to the sinister (Box 1.4). The relationship between symptoms and any dental treatment, or lack of it, should be noted.

The family and social history

Whenever a symptom or sign suggests an inherited disorder, such as haemophilia, the family history should be elicited. Ideally, this is recorded as a pedigree diagram noting the proband (presenting case) and all family members for at least three generations. Even when no familial disease is suspected, questions about other family members often lead naturally into questions about home circumstances, relatives and social history which can be revealing if, for example, psychosocial factors are suspected.

Web URL 1.2 Drawing a pedigree chart URL: https://www.genomicseducation.hee.nhs.uk/taking-and-drawing-a-family-history/

Consent

It is imperative to obtain patients' consent for any procedure, including examination. At the very least, any procedures to be used should be explained to the patient and verbal consent obtained. If no more than this is done, the patients' verbal consent should be noted in their records. However, it is better to obtain written consent, and this is now often required for any minor procedure in some countries. Many hospitals now require clinicians to give precise descriptions of treatment plans, however routine, and to obtain written consent. Written treatment plans are also required in dental practice in the UK.

Patients have a right to refuse treatment. Any such refusals may sometimes be due to failure of the clinician to explain the need for a particular procedure, or failure to soothe the patient's fears about possible complications. Some of these fears may be irrational, but all fears are real to the patient. In such cases, even prolonged explanations and persuasion may be unsuccessful, and a patient's signature in the notes may then be required as evidence of their wish not to consent.

When a biopsy is necessary, the patient will consent to the surgical procedure but must also be made aware that their tissue may be retained in the pathology department for many years in case future reference to it is needed. When the biopsy is also to be used for DNA analysis, the patient must be made aware of this, and when there are implications for other family members' health, the consent process may be complex.

In the case of more major surgery, a consent form may need to take into account a general anaesthetic, the nature of the operation and significant complications or risks. This will require knowledge of the pathology of the disease. For example, in the case of an ameloblastoma, it would be necessary to point out the risk of recurrence after a conservative removal versus the complications of a larger excision.

For consent to be legally valid, patients must be given sufficient information about the proposed treatment for them to make their own decision and the clinician must check that the information has been understood. This is formalised in the concept of 'informed consent', although being informed is only one factor required to make consent valid under UK law (Table 1.5). The UK law on consent is complex and often enshrined in case law rather than Acts of Parliament. The Mental Capacity Act 2005 and The Human Tissue Act 2004 both govern some aspects, but consent

Box 1.4 Toothache and its mimics

- Toothache
  - Pulpitis
  - Periapical periodontitis
  - Fractured cusp/tooth
  - Dentine hypersensitivity
- Mimics of toothache
  - Prodromal Herpes zoster infection
  - Postherpetic neuralgia
  - Trigeminal neuralgia
  - Neuropathic pain after trauma or central nervous system disease
  - Maxillary sinusitis
  - Temporal arteritis
  - Migrainous neuralgia
  - Otitis media
  - Referred pain of angina pectoris
  - Referred pain of temporomandibular joint myofascial pain dysfunction
  - Atypical odontalgia / facial pain

Table 1.5	Requirements for consent
Capacity	Not impaired for any reason May differ procedure to procedure Understands information given Able to weigh information to make a decision
Voluntary	Given freely Without pressure or undue influence
Informed	Understands nature and purpose of procedure Aware of the operator's training and competence No relevant information is withheld Told of 'material' or 'significant' risks or unavoidable risks, even if small Informed of alternatives to the proposed treatment Aware of the risks of not having the treatment Aware of how any tissue removed will be treated and stored
Clinician	Informed and trained Able to judge capacity
Timing	Consent is a process, not a single event, and must be checked and revisited Consent remains in force until withdrawn Consent should be given within a reasonable timeframe of the procedure Material changes in any element must be explained
Recorded	The process of obtaining consent must be recorded Written consent is required for significant procedures and risks

evolves constantly, and readers need to be aware of the regulations and professional advice (the latter often more stringent) in force where they practice. When a written consent is required, a standardised form should be used to ensure compliance with local requirements.

Particular difficulties in oral medicine and surgery arise with the prescription of drugs because reactions are varied but infrequent. Usually, patients do not clearly distinguish risk and harm and tend to make decisions about treatments based on the magnitude of potential harm. It is difficult to explain to a patient that anaphylactic reactions in persons not known to be allergic to penicillin are exceedingly rare but, nevertheless, potentially fatal.

Patients reading the extensive information leaflets provided with prescription drugs are frequently concerned about the risks of even safe drugs such as aspirin. Since it is estimated that 200 million tablets of it are consumed every year, the chances of a reaction are almost infinitesimally small. The amount of information to be given to the patient is that which would be expected by 'the prudent patient'. However, patients differ, some reading drug information leaflets avidly, whereas others dispose of them unread. The dentist must balance the information given against the patient's expectation. For surgical interventions the patient must be told all 'material facts', specifically including any dangers of the procedure to that particular patient.

Consent is not normally taken from patients for prescription of medications. However, the same principles apply because significant adverse effects can be caused by drugs for dental treatment. It is important to maintain vigilance to reduce risk, for instance by recording allergies and checking before prescribing. Sometimes patients at risk of severe adverse effects can be identified. For example, in the case of azathioprine, patients deficient in the enzyme thiopurine methyltransferase (TPMT) can be excluded from treatment because of their risk of bone marrow toxicity. Fortunately such examples are rare but risks from drugs are unpredictable in type and severity.

It is essential to point out any precautions necessary when taking a particular drug and warn patients to return as soon as they think that there has been an adverse reaction. Adverse reactions should be reported in the UK through the yellow card system.

Web URL 1.3 UK consent (includes separate Scotland advice):

URL: https://www.dentalprotection.org/uk/articles/consent-advice-booklet

CLINICAL EXAMINATION

Extraoral

First, look at the patient, before looking into the patient's mouth. Anaemia, thyroid disease, long-term corticosteroid treatment, parotid swellings or significantly enlarged cervical nodes are just a few conditions that can affect the facial appearance.

Palpate the parotid glands, temporomandibular joints (for clicks, crepitus or deviation), cervical and submandibular lymph nodes and thyroid gland. Lymphadenopathy (Ch. 32) is a common manifestation of infection but may also signify a malignant disease – the cervical lymph nodes are often the first affected by lymphomas. Note the character (site, shape, size, surface texture and consistency) of any enlargement. Always examine the neck from behind the patient and palpate through slack, not taut, skin. Guide the patient's head forward and to one side with one hand to loosen the skin and platysma muscle and move the sternomastoid muscle, below which some nodes lie. Use the flat tips of the fingers with sufficient pressure to feel through overlying tissues. Proper examination of the neck is not possible with the patient supine; the patient should be sitting upright or leaning slightly backward.

Press on the maxilla and frontal bone over the sinuses to elicit tenderness if sinusitis is suspected.

Oral examination

Examination of the oral cavity can be performed adequately only with good light, mirrors and compressed air or other means of drying the teeth. If viscid saliva prevents visualisation of the tissues and teeth, a rinse with a traditional dentists' mouthwash will help. This contains sodium bicarbonate, and the alkaline pH changes the charge on the salivary mucins and makes them more soluble.

Soft tissues

The soft tissues of the mouth should usually be inspected first. Examination should be systematic to include all areas of the mouth. Care should be taken that mirrors or retractors do not obscure lesions. To ensure complete examination of the lateral tongue and posterior floor of mouth, the tongue must be held forward in gauze and gently reflected from side to side.

Abnormal-looking areas of mucosa should be palpated for scarring or induration indicating previous ulceration, inflammation or malignancy. Examination should include deeper tissues accessible to palpation from their oral aspect, including the submandibular glands.

If abnormalities extend close to the gingiva, the gingival crevice or pockets should be probed for any communication. Mucosal nodules, especially those on the gingiva or alveolar mucosa that suggest sinus openings, should be probed to identify any sinus or fistula. Check the openings of the salivary ducts while expressing saliva by gentle pressure. Check that saliva flows freely and equally from all glands and is clear in colour. Do not mistake normal anatomical variations (Table 1.6) for disease.

After examination of the oral mucosa, try to visualise the oropharynx and tonsils.

Retrocuspid papilla PMID: 1065843

Foliate papilla ISBN-13: 978-0723438120

Leukoedema: Review: PMID: 1460680

Teeth

When undertaking a consultation for a complaint apparently unrelated to teeth, dental examination must still be thorough, both for the patient's sake and for medicolegal reasons. As a minimum, the standing teeth with a summary of their periodontal health, caries and restorative state and any tooth wear should be recorded. When dental pain is a possibility, full charting, assessment of mobility and percussion of teeth are necessary and further investigations will probably be required.

Table 1.6 Some anatomical variants and normal structures often misdiagnosed as abnormalities

Structure	Description
Fordyce's spots	Sebaceous glands lying superficially in the mucosa are visible as white-coloured or cream-coloured spots up to 0.5 mm across. Usually on labial mucosa and buccal mucosa. Occasionally prominent and very numerous (Figs 18.1 and 18.2). Increase in prominence with age
Lingual tonsils	Enlarge with viral infection and occasionally noted by patients. Sometimes large or ectopic and then mistaken for disease (Figs 1.1 and 1.2)
Circumvallate papillae	Readily identifiable but sometimes prominent and misinterpreted by patients or healthcare workers
Retrocuspid papilla	Firm pink nodule 0.5–4 mm diameter on the attached gingiva lingual to the lower canine and lateral incisor, usually bilateral but sometimes unilateral. Prominent in children but regresses with age
Dorsal tongue fur	Furring of the dorsal tongue mucosa is very variable and is heavier when the diet is soft. Even light furring may be regarded as pathological by many patients. When pigmented black by bacteria and with overgrowth of the filiform papillae, the condition is called black hairy tongue (Ch. 17)
Leukoedema	A milky white translucent whitening of the oral mucosa that disappears or fades on stretching. More common Black people (Ch. 18)
Tori	Exostoses in the midline of the palate or in the lingual alveolus in the premolar region are termed tori (Ch. 12). They are present by young adulthood and also arise at other sites, particularly on the maxilla over premolar and canine roots.

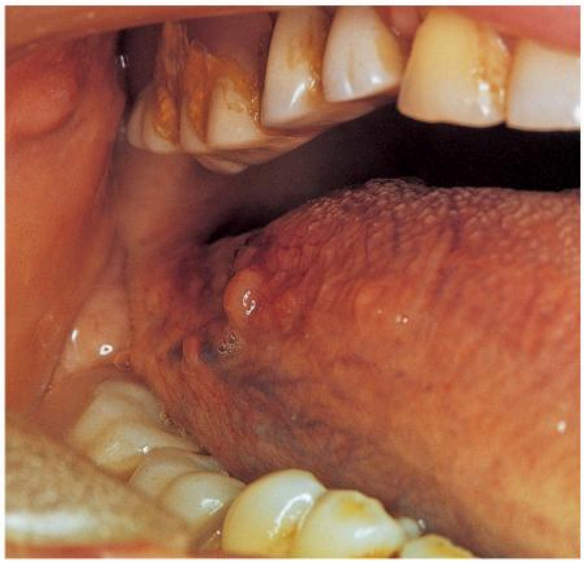


Fig. 1.1 Large foliate papilla or lingual tonsil that may be mistaken for a lesion on the side of the tongue.

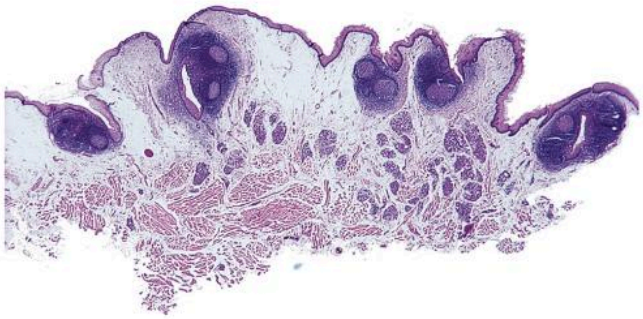


Fig. 1.2 Section showing the nodular surface, small tonsillar crypts and lymphoid follicles in a foliate papilla.

The vitality of teeth must be checked if they appear to be discoloured or causing symptoms. It is also essential to determine the vitality of teeth in the region of cysts and other radiolucent lesions in the jaws at presentation. The information may be essential for diagnosis and cannot be determined after treatment.

To be absolutely certain, several methods may have to be used. Checking hot and cold sensitivity and electric pulp testing are relatively easily performed (Box 1.5). Unfortunately, it may not be apparent that a pulp test result is misleading. Care must always be taken to avoid causes of false-positive or false-negative results (Table 1.7). Poorly localised pulp pain from teeth of dubious vitality can be difficult to ascribe to an individual tooth. In such circumstances, a diagnostic local anaesthetic injection on a suspect tooth may stop the pain and indicate its source.

Pulp test accuracy PMID: 26789282

MEDICAL EXAMINATION

In practice, it is usual for dental investigations to be performed first, but the dentist should be capable of performing simple

Box 1.5 Precautions for electric pulp testing

- Remember these are sensibility tests of nerve continuity and patient reaction, not direct tests of vitality
- Isolate individual teeth with a small portion of rubber dam if necessary
- No one method is completely reliable; supplement electric methods with hot and cold tests to be certain
- Ensure the correct method is being followed, depending on whether the tester is bipolar or unipolar
- Use an electrically conducting jelly or other agent to ensure good electrical contact
- Always record electric pulp test values in the notes – a progressive change in reading over time may indicate declining vitality
- A definite failure to react or clear vitality are more useful outcomes than the numerical reading on the control
- If results remain uncertain, cut a test cavity or remove suspect restorations without local anaesthetic
- Compare reading with those from control teeth – usually contralateral teeth of the same type
- Use Doppler flowmetry to determine blood flow when pulpal nerve function is compromised, for instance following trauma

Table 1.7 Possible causes of misleading electric pulp test results

Problem	Causes to consider
Pulp by-passed by electric current	Electrical contact with next tooth through touching amalgam restorations, orthodontic appliance or saliva Electrical contact with gingival margin through amalgam restoration or saliva film
False positive	Stimulus can be conducted by fluid in necrotic pulp chamber and felt by stimulating nerves in the periodontal ligament
Electrical insulation of the pulp	Large composite or non-conducting restorations
Falsely low reading	Incompletely formed root apex Teeth being moved orthodontically Operator's gloves can partially insulate the electrical circuit of some testers
Partially vital pulps	Multiple canals
No check on validity of results	No normal teeth for comparison
Patient fails to report accurately	Failure to differentiate pulpal from soft tissue or periodontal ligament sensation

medical examinations of the head and neck. Examination of the skin of the face, hair, scalp and neck may reveal unexpected foci of infection to account for cervical lymphadenopathy or even malignant neoplasms. The eye can readily be inspected for conjunctivitis or signs of mucous membrane pemphigoid, anaemia or jaundice. Examination of the hands may also reveal relevant information (Table 1.8). Dentists should be able to examine cranial nerve function, but more extensive medical examination by dentists is usually performed only in hospitals.

Table 1.8 Useful diagnostic information from examination of the hands

Site	Signs
Flexor surface of wrist	Rash (or history of rash) consisting of purplish papules suggests lichen planus, especially if itchy
Finger morphology	Clubbing may be associated with some chronic respiratory and cardiac conditions (including infective endocarditis), lung cancer, lung abscesses, cardiac disease and other remote malignant neoplasms Joint changes may suggest rheumatoid arthritis (joint swelling, ulnar drift) or osteoarthritis (Heberden's nodes)
Abnormal nails	Koilonychia suggests longstanding anaemia. Hypoplastic nails may be associated with several inherited disorders of epithelium with oral significance including ectodermal dysplasia and dyskeratosis congenita
Skin of fingers	May be thin, shiny and white in Raynaud's phenomenon (periodic ischaemia resulting from exposure to cold – often associated with autoimmune conditions particularly systemic sclerosis (Fig. 1.3) or Sjögren's syndrome) Note any tobacco staining. Is the degree commensurate with the patient's reported tobacco use?
Palmar-plantar keratosis	Associated with several syndromes including Papillon–Lefèvre syndrome (including early-onset periodontitis)

CLINICAL DIFFERENTIAL DIAGNOSIS

The diagnosis and appropriate treatment may be obvious from the history and examination. More frequently, there are several possible diagnoses, and compiling a differential diagnosis becomes a critical part of the overall diagnostic process. At this stage the clinician must integrate their knowledge of likely diseases and their range of presentations with the findings from one specific patient, thinking broadly but keeping focused. If a good differential diagnosis is compiled, then the process of selecting investigations and narrowing down to the final diagnosis will usually be straightforward. Conversely, if the correct diagnosis is not included in the differential diagnosis, it may never be discovered. Mistakes often follow clinicians simply forgetting to consider a possible diagnosis, and a written differential diagnosis helps even experienced clinicians to organise their thoughts.

A well-crafted differential diagnosis lists possible diagnoses in order of probability, based on their prevalence and the likelihood of causing a specific combination of symptoms

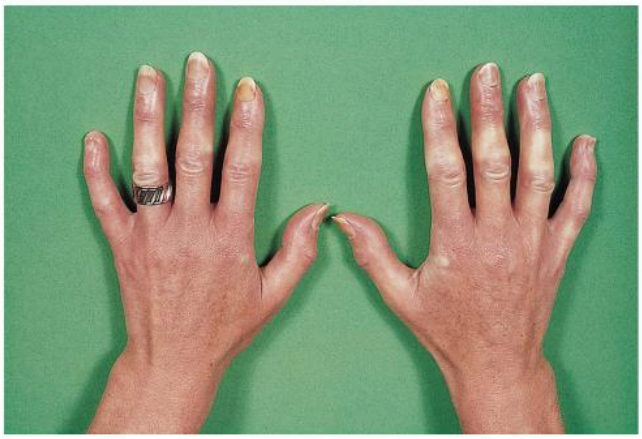


Fig. 1.3 Hands with taut, shiny, pale skin on the tapering fingers, a long-term effect of Raynaud's phenomenon, in this case associated with systemic sclerosis.

and signs. Even if only one diagnosis seems appropriate, it is worthwhile to note the next most likely possibility and any other causes which can be excluded. This ensures that all appropriate investigations are remembered and reduces the possibility of the patient having to return for further investigations. When the patient's complaint or presentation is relatively nonspecific, do not list every possible cause. Too long a list is difficult to convert into a focused investigation strategy, and it may be best to use generic terms such as 'benign neoplasm' or 'odontogenic tumour' to keep the initial list manageable.

When the list includes conditions with significant implications for the patient, such as a malignant neoplasm, it is conventional to put them at the top of the list even though their likelihood may be low. This ensures important diagnoses are not forgotten and that they are investigated and excluded first, before moving on to more likely, but less serious, conditions.

INVESTIGATIONS

Innumerable types of investigation are possible. It may be difficult to refrain from asking for every conceivable investigation so as not to miss something unsuspected and to avoid medicolegal complications. Although it may be tempting to explore every possibility, however remote, this approach may prove counterproductive in that it can produce a plethora of reports that confuse rather than inform. The more investigations performed, the more likely one will produce a spurious result.

The differential diagnosis forms the basis on which investigations are selected and keeping focused on the list ensures that only appropriate investigations are requested. Every investigation must be selected to answer a specific question, and none should be regarded as a 'routine test'. Some investigations carry risks that may need to be balanced against the probability of a useful result, notably those involving X-rays.

In all healthcare systems, investigations are expensive, some exceedingly so, and some can only be performed in specialised centres. It is the duty of every clinician to keep the cost-to-benefit ratio of investigations in mind and order only those that will confirm the differential diagnosis or exclude options from it. Often investigations that specifically exclude diseases are the most valuable.

A few diseases, such as mumps, may be diagnosed on the basis of a single test, but others, such as Sjögren's syndrome*, may require many tests and some difficult interpretation to make the diagnosis.

Any test will occasionally produce an erroneous result. Sometimes this is the result of inappropriate samples or delay in specimen transport. However, for many blood tests, a result may be flagged as 'out of normal range' because the value is in the highest or lowest 5% of the population. This is not necessarily an abnormal result. Unexpected or inexplicable test results are often best repeated before accepting the result, provided the test is easily performed.

Screening and diagnostic tests

This book is primarily concerned with diagnosis, but the difference between screening and diagnostic tests must be appreciated.

To be useful in diagnosis, a test result, whether positive or negative, must indicate a specific disease or condition. This is measured by the parameters of the sensitivity, specificity, positive predictive value and negative predictive value of the test. The definitions of these parameters are shown in Table 1.9.

Sensitivity describes whether a test can correctly identify a condition, and the specificity determines whether it can correctly exclude a condition. However, no test is completely accurate, and there are always false-positive and false-negative (incorrect) results. You can also see from the definitions that the sensitivity and specificity are only measures that relate to a population in which the correct disease status is already known. That is not helpful when using the test in real life, and the value of the test is better described by the positive and negative predictive values. The ideal test would have a high positive and a high negative predictive value.

A further complication is introduced by considering the value of tests when they are performed in different circumstances. Suppose a test is not very accurate, but the disease being tested for is very common. Under these circumstances, the test will perform well enough to be useful because a few false-positive results will be outweighed by the value in detecting the many patients with the disease. However, if the disease were very rare, the majority of the results would be false positive and the test would be useless.

The value of the test therefore depends on how it is used. If a clinician performs many tests on all patients, the positive predictive values will not be as high as if the test were used in a more focused manner. This explains why tests must be used to answer specific questions and not thrown randomly at difficult diagnostic dilemmas.

*This book continues to use an apostrophe after many eponyms. It has been suggested that this should be abolished (PMID: 46972) because "the author neither had nor owned the disorder". This idea has been promoted by those who think that the change gives patients 'ownership' of their disease. However, the suggestion is based on a lack of knowledge of grammar. The *'s* is not a possessive case, as often said, but a synthetic genitive indicating association rather than ownership. Its meaning is the same as in New Year's Eve, replacing the sense of the word *of*. The genitive case in English is complex and can have many meanings apart from ownership. This usage is known as the classifying or descriptive function. Often the *'s* is essential to the meaning. Moon molars sounds as if they are named because their pitted surface looks like the moon, an understandable misconception, while Moon's molars clearly associates the first description of this manifestation of congenital syphilis to Henry Moon, a dental surgeon at Guy's Hospital in London. This book is called Cawson's Essentials, not because it belonged to Professor Cawson, but because he wrote it. Not using an apostrophe is more common in US usage than elsewhere.
For a detailed discussion see, Dirckx, JH. The synthetic genitive in medical eponyms: Is it doomed to extinction? Panace@. 2001;2(5):15-24.

Table 1.9 Sensitivity, specificity, positive predictive value and negative predictive value

Parameter	Definition
Sensitivity	The proportion of patients known to have the disease who test positive
Specificity	The proportion of patients known to NOT have the disease who test NEGATIVE
Positive predictive value	The proportion of all positive results that are true positives (correct results)
Negative predictive value	The proportion of all negative results that are true negatives (correct results)

Diagnostic tests are required to have high predictive values, and the more significant the diagnosis, the higher the predictive value must be. Conversely, screening tests are used in population screening and are only intended to identify individuals who might have a disease. Screening tests need to be economical and easily performed in great numbers, and a lower predictive value is acceptable. Patients who test positive for the screening test will then be referred for more accurate diagnostic tests.

Tests used for diagnosis in oral disease generally have high predictive values. Dentists need to be aware that many less-than-ethical companies sell tests to general dental practitioners for the diagnosis of diseases such as caries, periodontal disease, oral cancer and oral premalignant diseases. It is not always clear whether these are screening or diagnostic tests. In some countries these tests are marketed direct to patients. When evaluating whether using such a test is likely to be effective and its use ethical, it would be strongly advisable to find out what the predictive values of the test would be when used in your own patient population.

Imaging

The most informative imaging techniques in the head and neck are radiography and cone beam computerised tomography (CBCT), medical computerised tomography (CT), magnetic resonance imaging (MRI) and ultrasound. Their advantages and disadvantages are shown in Table 1.10.

Plain radiography is widely available, and simple additional techniques can add value (Box 1.6). Even simple manoeuvres, such as introducing a gutta percha point or probe into a sinus to trace its origins, may provide critical information. It is also advisable to request a formal radiologist's report on radiographic films whenever the radiographic features appear unusual or beyond the experience of the clinician.

Imaging and diagnosis ISBN-13: 978-0702045998

Histopathology

Value and limitations

Removal of a biopsy specimen for histopathological examination is the mainstay of diagnosis for diseases of the mucosa, soft tissues and bone. In the few conditions in which a biopsy is not helpful, it may still be valuable to exclude other possible causes.

As with all other investigations, biopsy must address a specific question. For instance, recurrent minor aphthae lack specific microscopic features and biopsy is rarely justified. Conversely, a major aphtha may mimic a carcinoma that only microscopy will exclude.

Histological examination is not a 'test' in the same way as a blood investigation. The pathologist will issue a report that describes the macroscopic and histological features seen in the specimen and provide an interpretation, usually specific, sometimes less so (Box 1.7). The interpretation will be based on the clinical information transmitted to the pathologist on the request form, and often this is critical to the reported diagnosis. Pathology reports, and not just the 'bottom line' diagnosis, need to be read and understood because they may contain important caveats about the confidence with which a diagnosis is made or suggestions for further investigations.

Biopsy

Biopsy is the removal and examination of a part or the whole of a lesion.* There are several different biopsy techniques (Box 1.8).

The most important technique is surgical biopsy. Leaving aside medical contraindications, the only important contraindications to biopsy are when the site of disease contains important structures, such as the facial nerve in the parotid gland, or when the biopsy risks seeding a tumour more widely in the tissues. The most common parotid neoplasm (pleomorphic adenoma) has an unusual tendency to spread and recur at a biopsy site because of its gelatinous nature. In such instances, alternatives would be to perform a fine needle aspiration or excise the entire lesion with a margin of surrounding normal tissue and confirm the suspected diagnosis afterwards.

Selecting the biopsy site

If the wrong site is selected for biopsy, the chance of a definitive diagnosis is reduced. Choice of site is often a compromise between ease of access, methods available and removing the ideal tissue sample.

Identifying the ideal tissue should take precedence and requires the clinician to understand the disease process at a microscopic level so that the tissue most likely to show diagnostic features is selected. For large tumours, a central sample is often easiest, but it is often critical to include the margin to assess the growth pattern and possible peripheral invasion. For mucosal disease, ulcers must be avoided because they are inflamed and have no epithelium. For potentially malignant diseases, red and speckled areas are the most important, followed by white areas. For immunobullous disease, the perilesional tissue is best because it is less friable and will not disintegrate on biopsy. However, samples for immunofluorescence should be taken away from the lesion, usually from clinically normal buccal mucosa, because they are used to identify bound autoantibody and not the histopathology of the active disease.

It is often stated that a biopsy should include normal tissue at the margin. However, this is widely misunderstood. The pathologist does not require adjacent tissue for comparison; he or she will be very familiar with the normal histological variation in the mouth. However, there may be better reasons for choosing to include normal tissue in the sample. Cancers and some other lesions can be friable and disintegrate on biopsy so that having some normal tissue at one end helps support the sample and holds the suture more firmly. If a malignant process is suspected, the margin is where invasion of surrounding tissue will be seen. When performing an excision biopsy, a small collar of normal tissue may prevent recurrence of some lesions. When removing a sample of a white lesion, including the edge will aid diagnosis of mild

*Biopsy is derived from the Greek words meaning 'to see in life'. Thus, a biopsy specimen is taken from a living patient. Its opposite is necropsy: 'to see in death'; a post-mortem or autopsy.

degrees of dysplasia. However, always try to take the largest sample of lesional tissue and only include normal tissue for a specific reason.

Large lesions and those with areas that look or feel different may well require several biopsies to sample them adequately. Those in which the epithelial thickness is markedly increased, such as verrucous carcinoma and verrucous leukoplakias, may need a sample several millimetres thick. The specimen must extend down to and include the underlying connective tissue to assess whether or not invasion is present.

It can be seen that selecting the correct site can be a challenging intellectual exercise requiring a good differential diagnosis and knowledge of the basic histopathology of the likely disease – just one reason why dental students should know some basic histopathology.

Surgical biopsy methods

Surgical removal of tissue to determine the diagnosis may be undertaken with a scalpel, biopsy punch, cutting laser, electrocautery or a wide cutting needle ('core biopsy'; Trucut biopsy). In general, a scalpel biopsy is almost always preferred for intraoral sampling. The tissue is removed cleanly without damage, and the incision can be shaped to heal by primary intention. Silk sutures are soft and comfortable in the mouth, and an appointment for removal a few days later

Table 1.10 Imaging techniques for lesions of the head and neck

Technique	Advantages	Limitations
Conventional radiography	Widely available and inexpensive Simple, many common lesions may be identified with a high degree of accuracy Panoramic radiographs can show unsuspected lesions	Small X-ray dose unavoidable Difficult to interpret in some areas of the jaws because of the complex anatomy Little information about soft tissue lesions
Computerised tomography (CT)	Good definition of soft tissue structures in any plane Useful for areas of complex anatomy such as maxilla or base of skull Definition further improved by use of contrast media	Expensive Available only in hospitals Frightening for patients. Scanner tunnel can provoke claustrophobia Shadows of dental restorations can obscure part of the image Larger X-ray dose than plain radiographs
Cone beam CT	Low-cost high-resolution CT ideal for the head and neck, oral surgery, implantology and endodontics	As CT but lower dose and higher resolution Has quickly become a routine radiological investigation for head and neck diagnosis Image density not directly proportional to bone density Relatively poor soft tissue resolution
Radiography or CT with contrast medium	Valuable for outlining extent of duct systems, hollow structures such as cysts or blood vessels (angiography), etc.	Requires more expertise than plain radiography
Magnetic resonance imaging (MRI)	Produces clear tomograms in any plane without superimposition Particularly good for soft tissue lesions, better than CT No X-ray dose Clear definition of bones and teeth	Expensive and limited availability Frighteningly noisy. May be refused by claustrophobic patient (as for CT) Slow, sometimes scans take more than 1 hour Possible risk to the foetus (unconfirmed)
Ultrasound	No X-ray dose Shows soft tissue masses and cysts well Useful for salivary gland cysts, Sjögren's syndrome, stones, and for thyroid and neck lesions May be combined with Doppler flow analysis to measure blood flow through a lesion	Limited resolution, requires expertise in interpretation A dynamic technique interpreted live and difficult to record effectively in pictures Overlying bone obscures soft tissue lesions
Scintigraphy	Uses a radioactive isotope to visualise particular types of cells With technetium 99^m provides an assessment of function in each salivary gland Can be used if sialography not possible Other isotopes are used for detection of bone metastases	Equipment not always available Small radiation dose but isotope rapidly cleared
Positron emission tomography (PET scanning)	Short-life radioactive isotope used to identify biochemical activity, usually glycolysis, to identify putative tumour size, location or metastasis Good for identifying unsuspected metastases Helps identify neoplasms when post-surgical artefact or inflammation obscure them on CT or MRI Also available as a combined PET-CT and PET-MRI scan, but with reduced CT or MRI resolution	Expensive Intake of radioactive substance Risk of detecting unsuspected abnormalities of minimal or no significance that then require further investigation

Box 1.6 Requirements for useful oral radiographic information

- Always take bitewings when dental pain is suspected. Small carious lesions may be missed in periapical films and poorly localised pain may originate in the opposing arch
- When imaging bony swellings with plain films, always take two views at right angles
- Panoramic tomograms often cannot provide high definition of bony lesions. Only a cross-section of the lesion is in the focal trough and if the bone is greatly expanded, only a small portion will be in focus. To detect internal structure in bony lesions, plain films such as oblique lateral views of the mandible or oblique occlusal films are better. For better localisation where complex anatomical features are superimposed, cone beam computed tomography may be more useful
- Cone beam imaging provides excellent bone imaging but has poor soft tissue contrast
- Radiography of soft tissues is occasionally useful, for instance to detect a foreign body or calcification in lymph nodes

Box 1.7 Possible reasons for failures in histological diagnosis

- Specimen poorly fixed or damaged during removal (e.g., Figs 1.4 and 1.5)
- Specimen unrepresentative of the lesion or too small
- Plane of histological section does not include critical features
- The disease does not have diagnostic histological features, e.g., aphthous ulcers
- The histological features have several possible causes, e.g., granulomatous inflammation
- The histological features are difficult to interpret, e.g., malignant tumours may be so poorly differentiated that their type cannot be determined
- Inflammation may mask the correct diagnosis

Box 1.8 Types of biopsy

- Surgical biopsy (incisional or excisional)
  - Fixed specimen for routine diagnosis
  - Frozen sections for rapid diagnosis
  - Fresh tissue for immunofluorescence, microbiological culture or molecular analysis
- Fine needle aspiration biopsy
- Wide needle/core biopsy

provides an opportunity to review healing and discuss the diagnosis. Resorbable sutures may be used to avoid a second appointment but are spiky and less comfortable and often persist for many days in the mouth.

Removal of tissue using laser or electrocautery is useful to prevent bleeding, and the coagulated surface requires no sutures. These techniques are most useful to remove excess tissue or excise nodular lesions of the gingiva or mucosa. However, even when properly adjusted, the heat or electrical current will pass through the tissue and denature it, rendering a proportion of the sample unsuitable for diagnosis.

Fig. 1.4 An artefactual polyp produced by grasping normal mucosa with forceps to steady it during biopsy.

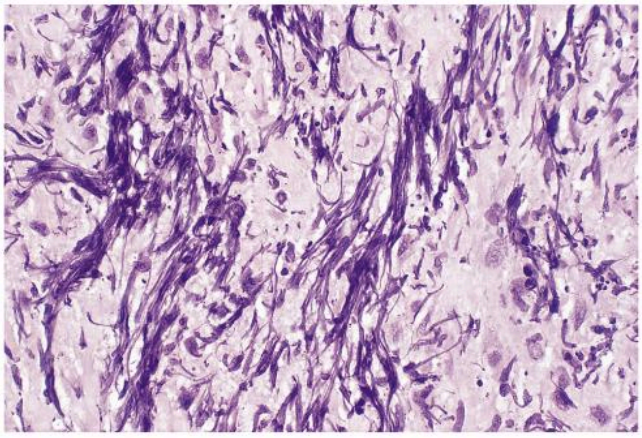


Fig. 1.5 Stringy artefact. This appearance is due to breakage of cells and their nuclei when the specimen is stretched or crushed. It is particularly common in lymphoma and some types of carcinoma.

Electrocautery is particularly prone to damage epithelium over a wide area and should never be used for a biopsy to assess dysplasia or other epithelial diseases but is ideal for removal of suspected fibroepithelial polyps.

Cutting needles or core biopsies are useful to remove a core of tissue, usually 1 mm or so in diameter, from deeper structures such as lymph nodes in the neck (Box 1.9).

A biopsy punch is a circular cutting blade designed to excise a circle of skin. These work well on skin because, when the blade penetrates to the subcutaneous fat, a cylinder of skin is mobilised and can be lifted upwards and sliced off. However, punches are badly suited to oral biopsy. The circular blade will only cut taut tissue so that flexible mucosa has to be stretched before cutting. After cutting the sample springs back to its original size, and may then be too small, less than half the punch diameter. The round wound does not lend itself to healing by primary intention or easy closure with sutures. Punch biopsy is often recommended on firm tissue such as the palate and for salivary neoplasms on the palate. At these sites, it is easy to orientate the punch perpendicular to the tissue. Even here it can fail if the deep core of tissue remains fixed to the patient and only a disc of overlying

Box 1.9 Core or needle biopsy

- Needle up to 2 mm diameter is used to remove a core of tissue
- Specimen processed as for a surgical biopsy
- Larger sample than fine needle aspiration (FNA), preserves tissue architecture in the specimen
- Definitive diagnosis more likely than with FNA
- Risk of seeding some types of neoplasms into the tissues
- Risk of damaging adjacent anatomical structures, causing haemorrhage or nerve damage
- Useful for inaccessible tumours, e.g., in the pharynx or lymph nodes
- Less used in the head and neck now that FNA is more widely available, but may be the next step if FNA fails

mucosa comes away. Elsewhere a scalpel biopsy is almost always preferred. Despite this, punch biopsy has become popular with dentists because of its speed and simplicity. It is better to take a biopsy with a technique you are happy with than to avoid it, but biopsy punches must be used intelligently.

Surgical biopsy may be incisional or excisional. Incisional biopsy is the removal of part of the lesion for diagnosis only. In excisional biopsy, the whole lesion is removed. The latter is usually performed to confirm a confident clinical diagnosis or when a lesion is too small to require diagnosis and removal in separate steps.

Oral biopsy is a simple procedure that should be within the capability of any dentist. Avoiding or referring for a biopsy in the mistaken belief that the procedure is too unpleasant for general practice is unwarranted. Surveys show that patients rarely complain or suffer adverse consequences from mucosal biopsy, often take no analgesia afterward and much prefer to have their disease properly investigated. Occasionally, sedation or general anaesthesia is required for children or specific patients, and referral is necessary.

The pathology request form should contain all the clinical information used to reach the clinical diagnosis. The purpose is to ensure an accurate diagnosis and not (as some clinicians seem to think) to see whether the pathologist can guess it without the relevant information. If appropriate, give the vitality of teeth associated with the lesion.

The essential principles of biopsy are summarised in Box 1.10.

Patient view: PMID: 11235976

Frozen sections

Frozen section is a laboratory technique that allows a stained slide to be examined within 10 minutes of taking the specimen (Box 1.11). The tissue is sent fresh to the laboratory to be frozen by immersion in liquid nitrogen (–196°C) or dry ice (–78°C), very cold to ensure freezing is near instantaneous and does not allow time for ice crystals to form in the tissue (which would expand and break open the cells). A section is then cut on a refrigerated microtome and stained. The equipment for frozen sections is often in the theatre suite to speed the process even further.

Frozen sections can only be justified if the rapidity of the result will make an immediate difference to the operation in progress because the technique is less slightly accurate than routine histopathology. This low risk of misdiagnosis means that frozen section is used more frequently to assess whether excision margins are free of a cancer during an operation rather than to make a preoperative diagnosis. If a rapid diagnosis is required in other circumstances, techniques such as fine needle aspiration biopsy or a routine specimen with special rapid laboratory processing are usually preferable.

Box 1.10 Essential biopsy principles

- Choose the most diagnostic or suspicious area, e.g., red area when potential malignancy is suspected in the oral mucosa
- Avoid ulcers, sloughs or necrotic areas
- Give regional or local anaesthetic – do not inject into the lesion
- Include normal tissue margin if the lesion itself may be friable or malignancy is suspected
- Specimen should preferably be at least 10 x 6 mm and 3 mm deep for mucosal disease, larger for large lesions, smaller on mucoperiosteum
- For mucosal disease, specimen edges should be vertical, not bevelled
- Design the sample shape and incision for easy primary closure
- Before incising, pass a suture through the specimen to control it and prevent it being swallowed or aspirated by the suction
- For large lesions, several areas may need to be sampled
- Include every fragment removed for histological examination
- Never open, incise or divide the specimen, always send it intact
- Suture and control any post-operative bleeding
- Label specimen bottle with patient's name and clinical details
- Warn patient of possible soreness afterward. Give or recommend an analgesic
- Check the histological diagnosis is consistent with the clinical diagnosis and investigations
- Discuss with pathologist or repeat biopsy if diagnosis is unclear or not understood

Box 1.11 Advantages and limitations of frozen sections

- Can establish, during an operation, whether or not a tumour is malignant and whether excision needs to be extended
- Can confirm, during an operation, that excision margins are free of tumour
- Microscopic appearances differ from those in fixed tissue
- Freezing artefacts due to poor technique can distort the cellular picture
- Definitive diagnosis sometimes impossible
- Only to be used when the result will alter the immediate surgical plan

Fine needle aspiration biopsy

Removing very small numbers of cells by aspiration using a fine needle (FNA), even if not completely conclusive, is

often sufficient to distinguish benign from malignant neoplasms, to initiate treatment or to indicate a need for further investigations. FNA should be used as an early step in the diagnosis of salivary neoplasms, lymph nodes in the neck, thyroid lumps and other deep tissues. Among the diagnoses that can be confidently made on FNA are many types of salivary neoplasm, tuberculosis and high-grade lymphomas (Box 1.12).

Brush biopsy and exfoliative cytology

This technique uses a round stiff-bristle brush to collect cells from the surface and subsurface layers of an epithelial lesion by vigorous abrasion and is discussed more fully in Chapter 20. It is an excellent method for taking small samples for experimental analysis, as a screening test or for patient follow-up but has not yet achieved an evidence base for oral diagnosis. The sample removed can be analysed in a variety of ways.

Exfoliative cytology is examination of cells scraped from the surface of a lesion but samples only surface cells and provides no information on deeper layers. It is now rarely used in the mouth, brush biopsy (Box 1.13) having superseded it.

Box 1.12 Principles and uses of fine needle aspiration biopsy

- A narrow (21-gauge) needle is inserted into the lesion and cells aspirated and smeared on a slide
- Rapid and usually effective aid to diagnosis of swellings in lymph nodes and parotid tumours especially
- Cells can be fixed, stained and examined within minutes
- Valuable when surgical biopsy could spread tumour cells (e.g., pleomorphic adenomas)
- For deep lesions, ultrasound or radiological guidance may be used to ensure that the needle enters the lesion
- No significant complications
- Small size of the needle avoids damage to vital structures in the head and neck
- Cells may be pelleted and processed for sections to allow immunocytochemistry and other specialised stains
- Some sample may be sent for microbiological culture
- Small specimen may be unrepresentative; several 'needle passes' often taken
- Definitive diagnosis not always possible (though a differential diagnosis may be very helpful to plan treatment or further investigations)

Box 1.13 Uses and limitations of brush biopsy

- Quick, easy
- Samples all levels in the epithelium, but no deeper
- Local anaesthetic not required
- Useful research technique
- Value depends on the analytical method applied to the sample
- Unreliable for diagnosing cancer. Frequent false-positive and false-negative results

Laboratory procedures

Although a clinician does not need to understand the details of laboratory procedures, it is necessary to understand the principles to enable the optimal results to be obtained. Failure to prepare or send the specimen appropriately can prevent diagnosis and necessitate an additional biopsy.

Fixation

Fixation is a key process. Fixation denatures the molecules in the tissue, killing the cells and preventing their enzymes from degrading the tissue, so stabilising it against autolysis.

The surgeon must immerse the specimen in ten times the specimen volume of 10% formal saline immediately on removal. Do not delay. In the absence of proper fixative, it is better to delay the biopsy and obtain the correct solution. Specimens placed in alcohols, saline or other materials commonly available in dental surgeries are frequently useless for diagnosis (Box 1.14). Do not confuse 10% formal saline (formol saline) with normal saline. Formal saline is formaldehyde dissolved in saline and kills and fixes tissue to prevent autolysis. Normal saline is isotonic saline, not a fixative.

Special types of fixative are required for electron microscopy and for urgent specimens. Whenever microbiological culture is required, the specimen should be sent fresh to the laboratory or a separate specimen taken because fixation will kill any micro-organisms.

All fixatives take time to diffuse through the tissue and fix it, many hours for large surgical resections.

Tissue processing

The fixed tissue is dehydrated by immersion in a series of solvents and impregnated with paraffin wax. The wax block is mounted on a slicing machine called a microtome and sections, usually 4 μm thick, are cut and mounted on glass microscope slides for staining. It takes 24–48 hours to fix, process, section and stain a specimen before the pathologist can report on it. In many laboratories the stained section is digitised and the pathologist can examine the tissue on a computer screen rather than a microscope, allowing measurements and facilitating automated counting and artificial intelligence diagnostic aids.

Box 1.14 Essential points about specimen fixation

- Fixation is a critical step to prevent autolysis and degradation of the microscopic structure of the specimen
- The usual, routine fixative is 10% formal saline (formaldehyde solution in saline or, ideally, in a neutral pH saline buffer)
- Fixation must be complete before the specimen can be processed
- Fixative must diffuse throughout the specimen–fixation is a slow process
- Small surgical specimens fix overnight, but large specimens take 24 hours or longer
- Chemical reaction with the tissue causes the fixative to become weaker as fixation proceeds. Therefore, specimens should generally be put in at least ten times their own volume of fixative
- Never fix specimens for microbiological culture or immunofluorescence; take these fresh to the laboratory immediately on removal or use special transport media

Table 1.11 Examples of haematoxylin and eosin staining of various tissues

Eosin (acidic, red)	Haematoxylin (basic, blue)
Cytoplasm of most cells*	Nuclei (DNA and RNA)
Keratin	Mucopolysaccharide-rich ground substance
Muscle cytoplasm	Reversal lines in decalcified bone
Bone (decalcified only)	
Collagen	

*The cytoplasm of some cells (such as oncocytes in some salivary gland tumours) is intensely eosinophilic. In others such as plasma cells it is basophilic or intermediate (amphophilic).

Some common stains used for microscopy

The combination of haematoxylin and eosin (H&E) is the most common routine histological stain. Haematoxylin is a blue-black basic dye; eosin is a red acid dye. Their typical staining patterns are shown in Table 1.11.

Periodic acid–Schiff (PAS) stain is probably the second most frequently used stain. It stains sugar residues in carbohydrates and glycosaminoglycans pink. This is useful to identify salivary and other mucins, glycogen and candidal hyphae in sections. Alcian blue is a turquoise stain for proteoglycans with negatively charged sugars, such as the sialic acid containing salivary mucins. Salivary mucins therefore stain with both PAS and Alcian blue, whereas ground substance in connective tissue stains only with Alcian blue.

Decalcified and ground (undecalcified) sections

Specimens containing bone and teeth need to be softened by decalcifying in acid to allow a thin section to be cut. This delays the diagnosis by days or weeks according to the size of the specimen and technique used.

Decalcification must be avoided if examination of dental enamel is required, for instance to aid diagnosis of amelogenesis imperfecta, because the heavily mineralised enamel is almost completely dissolved away. In such cases, a ground section is prepared by sawing and grinding using special saws and abrasives.

Immunofluorescent and immunohistochemical staining

Immunostaining methods make use of the highly specific binding between antibodies and antigens to stain specific molecules in the tissues.

Antibodies that bind to specific antigens of interest can be purchased. They are produced either by immunising animals with the purified target molecule and then separating the resulting antibodies from serum, or generated *in vitro* (monoclonal antibodies). The staining process is shown in Figs 1.6–1.8. The antibody binds extremely specifically to the target molecule, and the combination is made visible, either by binding a fluorescent molecule that can be seen in an ultraviolet microscope or an enzyme such as peroxidase that can react with a soluble substrate to form a visible red or brown deposit. Immunofluorescence is the more sensitive technique but is usually performed only on frozen sections.

Immunostaining has revolutionised histological diagnosis. Antibodies are available to stain many cell components and are widely used to identify epithelium (by staining cytokeratin molecules), lymphocyte subtypes (by staining T cell and B cell membrane antigens), viruses (by staining their surface antigens) and cell proliferation (by staining molecules involved in the cell cycle). In most laboratories, immunostaining is a relatively low-cost automated process.

It is important to know when immunostaining is required because fixation or decalcification may denature the antigens in the tissue and so prevent the antibody binding. Specimens for immunofluorescence must not be fixed in formalin but immediately be sent to the laboratory or sent in special transport medium.

The main circumstances in which diagnosis depends on immunostaining are shown in Table 1.12.

Molecular biological tests

Molecular diagnostic tests have revolutionised medical diagnosis, particularly in screening for and identifying genetic abnormalities and for rapid identification of tumours, bacteria and viruses. Techniques are evolving rapidly, and only principles will be illustrated. DNA sequencing and techniques for detecting messenger RNA expression are now rapid and inexpensive, and many medical tests based on single-sequence targets are being replaced by targeted sequencing of multiple specific genes or even whole-genome sequencing.

These methods are not yet widespread in dentistry but are available in most large hospitals and increasingly used for cancer diagnosis. When confronted with a difficult diagnosis, it is sensible to discuss the case with the pathologist or microbiologist before biopsy, to ensure that appropriate samples are available for these specialised tests.

In addition to its role in diagnosis, molecular analysis is increasingly used to select appropriate treatments. Examples include drugs targeting specific chromosomal fusions in salivary and soft tissue tumours and treatments targeting individual mutations, such as the *BRAF* p.V600E mutation found in ameloblastoma.

Polymerase chain reaction and quantitative polymerase chain reaction analysis

When a known DNA or RNA sequence is associated with a specific disease, it can be detected by polymerase chain reaction (PCR). In this test, the clinical sample is solubilized, and the nucleic acids within it hybridised with probes complementary to the target sequence. If, and only if, the target sequence is present, PCR will copy the nucleic acid repeatedly until enough is synthesised to be detected, either in an electrophoresis gel (Fig. 1.9) or by another laboratory method. PCR is rapid and can be automated on robotic analysers.

Common applications of PCR are detecting pathogens or mutations in genes. Identification of mycobacteria is a good example of the value of this type of test. Previously, identification of mycobacterial infection required approximately 6 weeks to culture the sample. PCR can be performed in 48 hours, is more sensitive and differentiates different types of mycobacteria with a high degree of precision. PCR is also used to detect the causative mutation of fibrous dysplasia and to detect micrometastases in sentinel node biopsy.

PCR is extremely sensitive. It can detect a single copy of a nucleic acid sequence in a sample, but this high sensitivity makes it prone to false-positive results. Quantitative PCR (qPCR) is an automated process that detects the PCR product while the amplification is in progress and uses the rate of amplification to measure how many copies of the target

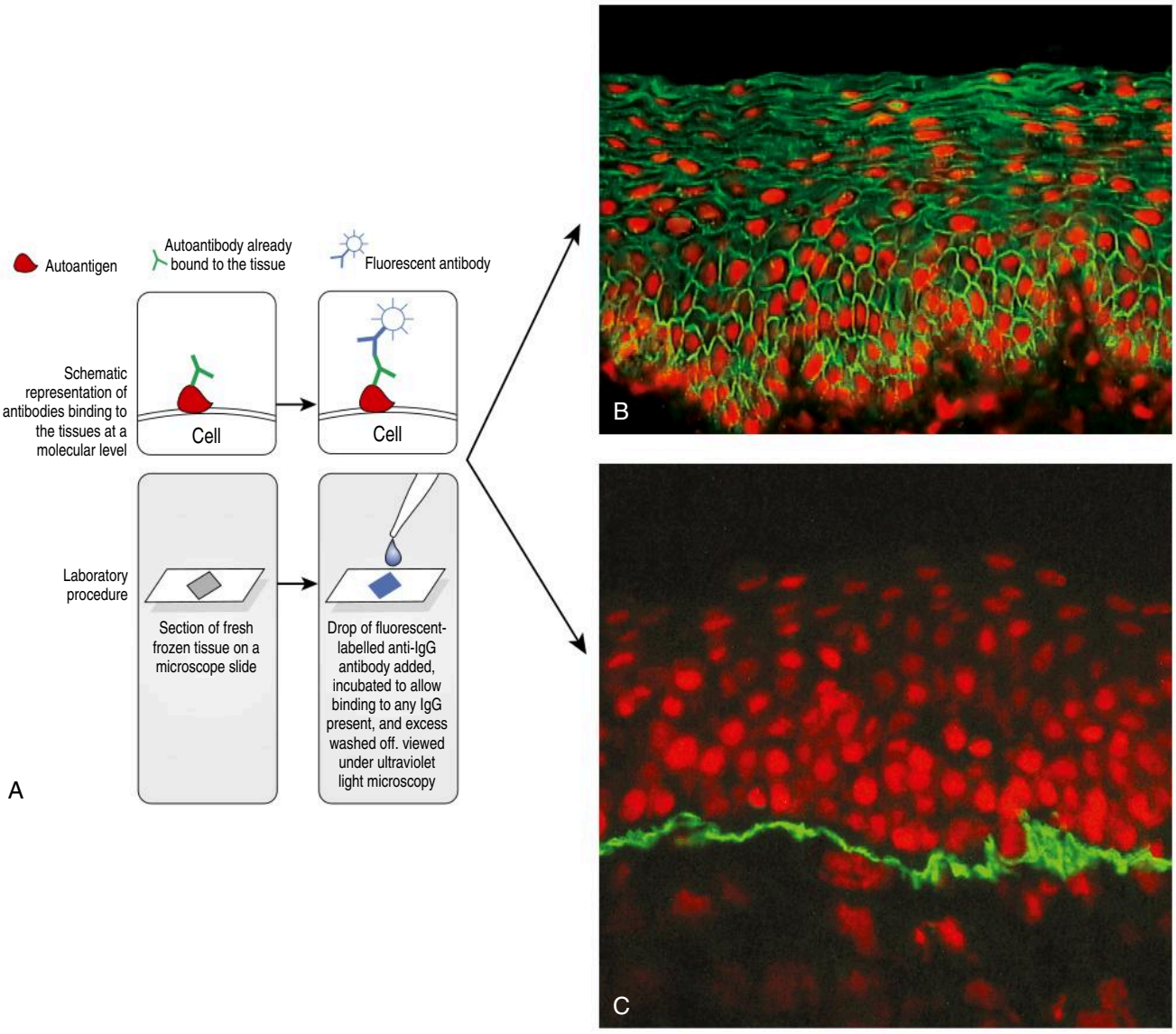


Fig. 1.6 Method and application of direct immunofluorescence. (A) Example: diagnosis of pemphigus and pemphigoid. Aim: to detect the site of the immunoglobulin (IgG) autoantibody already bound to the tissues in a biopsy. All tissues contain a small amount of immunoglobulin from serum, but this is not bound and so is washed away in the process. Green fluorescence indicates site of antibody binding; red fluorescence is a stain for cell nuclei to make the tissue structure more easily interpreted. (B) In pemphigus, green fluorescence reveals IgG autoantibody bound around the surface of the prickle cells in the epithelium (see Fig. 16.28). (C) In pemphigoid, green fluorescence reveals IgG autoantibody bound along the basement membrane (see Fig. 16.33). *(Courtesy Dr B Bhogal.)*

sequence were originally present in the sample. This allows threshold values for a true positive result to be defined and adds a further level of confidence in the result.

The high sensitivity may not always be advantageous. During the COVID-19 pandemic, PCR tests were widely used as the most sensitive test, but gave a positive result from tiny quantities of viral RNA and RNA fragments after recovery from disease, long after the patient was no longer infectious.

In situ hybridisation and fluorescent in situ hybridisation analysis

Known DNA and RNA sequences can also be detected by in situ hybridisation (ISH) or fluorescent in situ hybridisation (FISH). As in PCR, the sequence of interest is detected by hybridising with a complementary probe, but the hybridisation is performed on tissue sections instead of on solubilised tissue. As in PCR, the probe will only bind if the target sequence is present. Once bound, the probe can be rendered visible by a fluorescent marker or enzyme reaction in the same way that bound antibodies are visualised in immunohistochemistry. In situ hybridisation is less sensitive than PCR but has the advantage that the location of the target sequence can be seen in the tissue, so that it can be confirmed it is in the expected place, nucleus or cytoplasm, and in the correct tissue. This adds an additional level of confidence that the test is detecting the correct target and makes it popular for tumour diagnosis. PCR, being performed on solubilised tissue, cannot demonstrate this.

In situ hybridisation is an automated staining process in many laboratories and often used to detect viruses in tissues. Epstein Barr virus and HPV type 16 genes integrated in oropharyngeal carcinoma are common applications in dentistry.

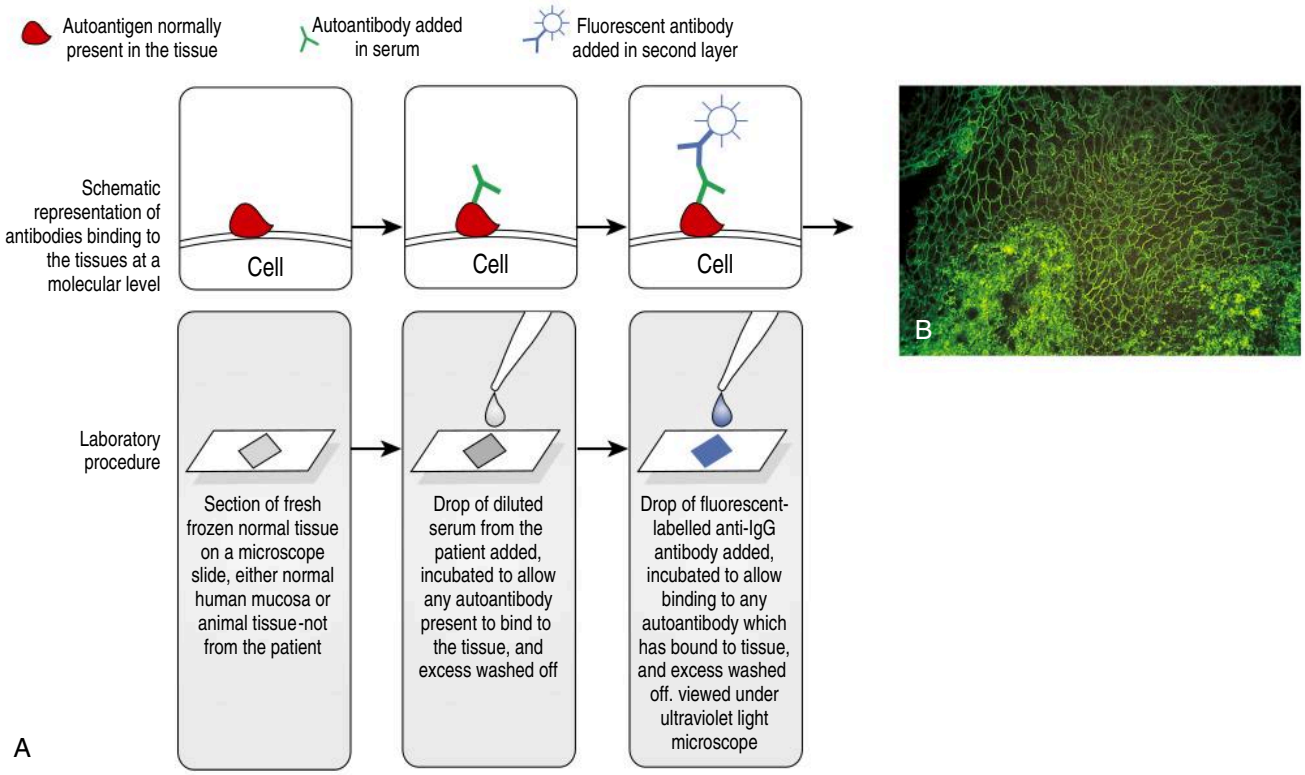


Fig. 1.7 Method and application of indirect immunofluorescence. (A) Example: diagnosis and control of treatment for pemphigus. Aim: to detect circulating autoantibody in the serum of patients with pemphigus. (B) If present, serum autoantibody binds around the surface of the prickle cells in the epithelium and is revealed by the binding to it of the green fluorescent antibody. Non-binding irrelevant immunoglobulins wash away. In this example the nuclei are not counterstained red.

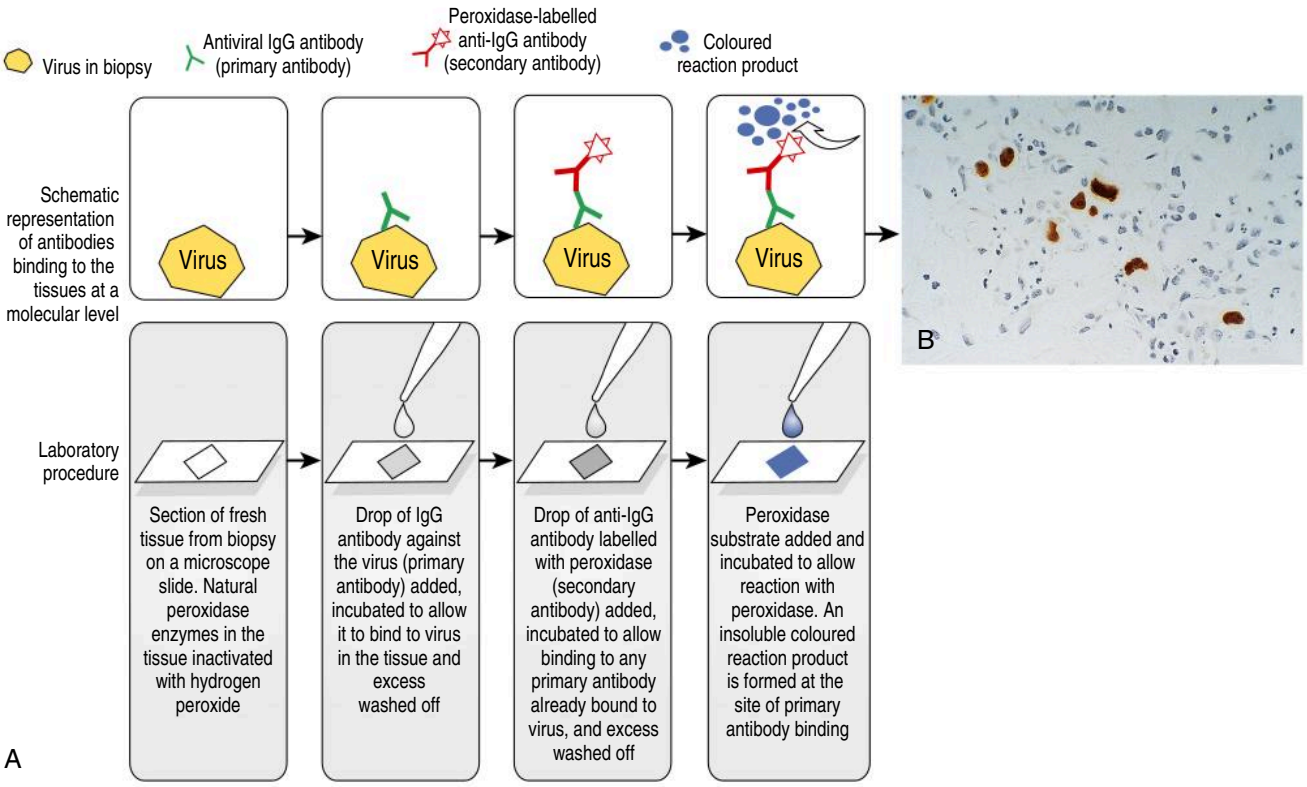


Fig. 1.8 Method and application of immunocytochemistry. (A) Example: diagnosis of viral infection. Aim: to detect viral antigens in infected cells. (B) In this example, brown reaction product identifies cells infected with cytomegalovirus.

Table 1.12 Important uses of immunostaining techniques

Disease	Molecule detected	Significance
Infections	Specific pathogens	Epstein Barr virus in epithelial cells in oral hairy leukoplakia, *Treponema pallidum* in ulcers indicates syphilis
Pemphigus	Autoantibody bound to epithelial desmosomes (desmoglein 3)	Indicates pemphigus
Pemphigoid	Autoantibody and/or complement C3 bound to basement membrane	Indicates pemphigoid
Myeloma or B-cell lymphoma	Monoclonal production of kappa or lambda light chains of immunoglobulin	Monoclonal production (production of only one isotype of light chain) indicates a neoplastic process. Production of both types indicates a polyclonal infiltrate that is inflammatory in nature
Lymphomas	Cell surface markers specific for different types of T and B cells	Indicates whether a lymphoma is of B- or T-cell origin and its type, essential for treatment
Undifferentiated tumours	Intermediate filaments (components of the cytoskeleton)	Presence of cytokeratins indicates an epithelial neoplasm, vimentin a mesenchymal neoplasm and desmin or myogenin a muscle neoplasm

NB Positive reactions, in themselves, are not necessarily diagnostic of disease and must be interpreted in the light of other histological and clinical findings.

It is also the method of choice to detect the fusion genes that result from chromosomal translocations, which are often specific to individual types of salivary neoplasms (Ch. 23). The break points in the chromosomes are known, and two probes labelled with different colour fluorescence markers are designed to bind on each side of the break point. In a normal cell the probes bind close together, one on each side of the potential break point, and can be seen down a microscope as four spots of colour in each nucleus (because there are two copies of each gene in a normal cell). Both colours are visible close together. If one of the gene copies is rearranged (the gene is broken), one pair of markers binding to the normal chromosome will show the normal pattern. The fluorescent markers on each side of the broken gene no longer bind close together and are seen as two widely separated spots of colour in the nucleus.

The application of in situ hybridisation is shown in Figs 1.10 and 1.11.

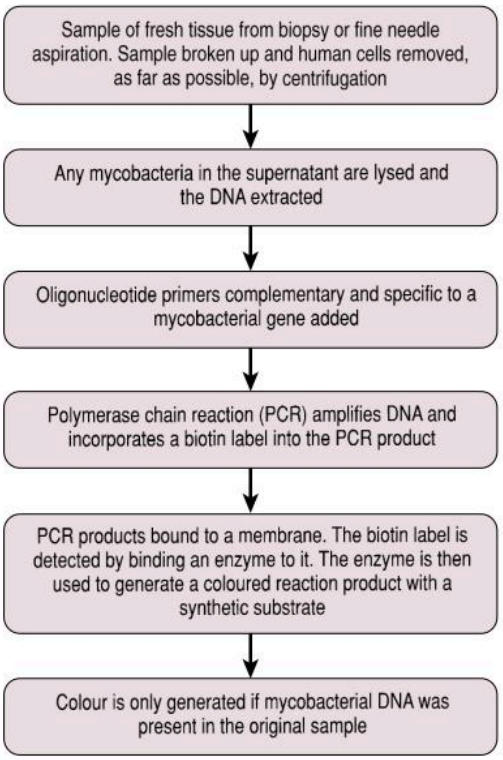


Fig. 1.9 Example application for the technique of polymerase chain reaction for identification of mycobacterial infection.

Haematology, clinical chemistry and serology

Blood investigations are clearly essential for the diagnosis of diseases such as leukaemias, myelomas or leukopenias which have oral manifestations, or for defects of haemostasis that can greatly affect management. Blood investigations are also helpful in the diagnosis of other conditions such as some infections and sore tongues or recurrent aphthae that are sometimes associated with anaemia.

As noted earlier, tests should address specific questions (Table 1.13). The request form should always be completed with sufficient clinical detail to allow the haematologist or clinical chemist to check that the appropriate tests have been ordered and to allow the interpretation of the results. It is important to include details of any drug treatment on blood test request forms. Always put the blood into the appropriate tube because some anticoagulants are incompatible with certain tests. A haematologist will not be impressed by a request for assessment of clotting function on a specimen of coagulated blood.

Microbiology

Despite the most common oral diseases being infectious, traditional microbiological culture of organisms is surprisingly rarely of practical diagnostic value in dentistry (Table 1.14, Box 1.15). Direct Gram-stained smears will quickly confirm the diagnosis of thrush or acute ulcerative gingivitis, and H&E-stained smears can show the distorted, virally infected epithelial cells in herpetic infections more easily than microbiological tests for the organisms themselves.

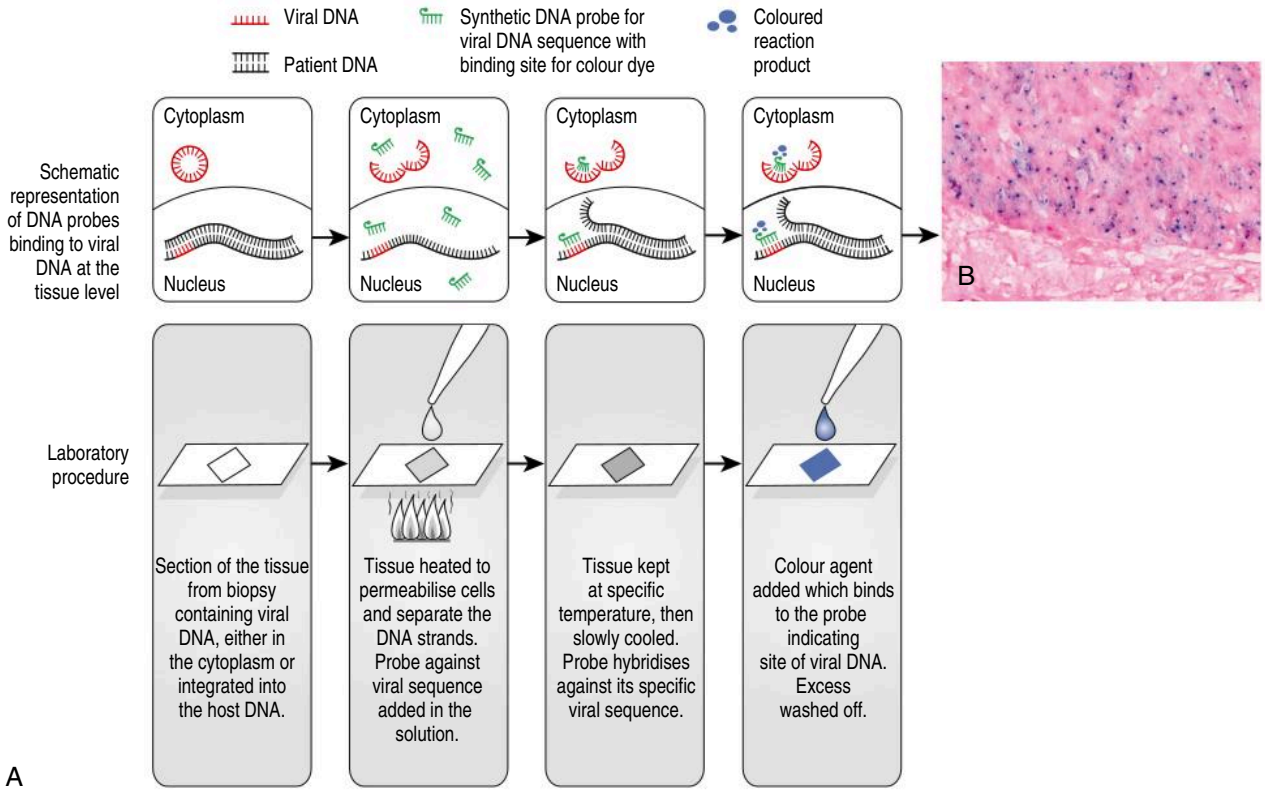


Fig. 1.10 (A) Method and application of in situ hybridisation to detect viral DNA in tissues. (B) In this carcinoma, blue colour reaction product indicates the site of human papillomavirus DNA.

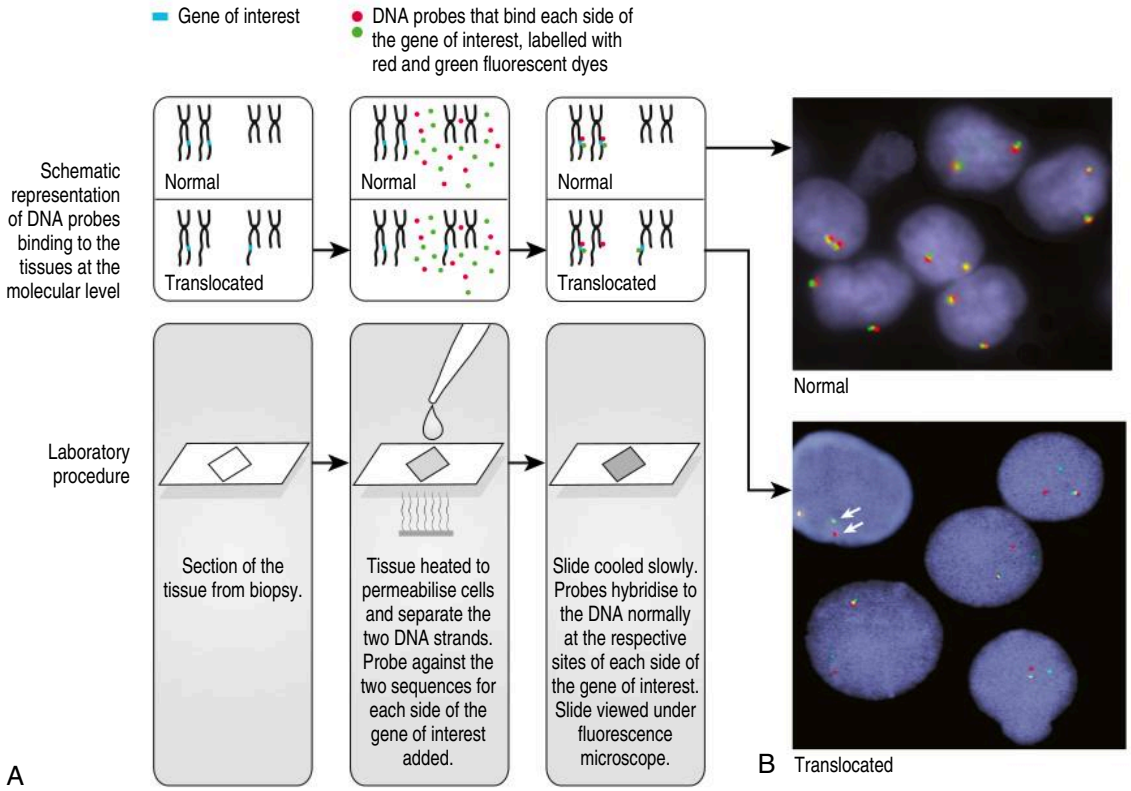


Fig. 1.11 (A) Method and application of in situ hybridisation to detect a chromosomal translocation using 'break apart' probes. (B) In this salivary carcinoma, the *myb* gene (blue) is translocated to another chromosome. In the normal cell the red and green probes are seen to bind to the DNA close together, each side of the *myb* gene. In the cell with the translocation, one copy of the gene is normal, but the other shows 'break apart' of the red and green probes, indicating a translocation involving a break point between the binding sites of the two probes within or close to the gene of interest. For the *myb* gene, this indicates that the carcinoma is an adenoid cystic carcinoma. When the red and green fluorescent spots are very close, the red and green colours merge to produce yellow. The background blue is a DNA-binding dye to show the nuclei.

Table 1.13 Types of blood test useful in oral diagnosis (see also Appendix 1.1)

Test	Main uses
'Full blood picture' usually includes erythrocyte number, size and haemoglobin indices and differential white cell count	Anaemia and the effects of sideropaenia and vitamin B_{12} deficiency associated with several common oral disorders. Leukaemias
Blood film	Leukaemias, infectious mononucleosis, anaemias
Erythrocyte sedimentation rate	Raised in systemic inflammatory and autoimmune disorders Particularly important in giant cell arteritis and Wegener's granulomatosis
Serum iron and total iron-binding capacity	Iron deficiency associated with several common oral disorders
Serum ferritin	A more sensitive indicator of body stores of iron than serum iron and total iron-binding capacity but not available in all laboratories
Red cell folate level	Folic acid deficiency is sometimes associated with recurrent aphthous ulceration and recurrent candidosis
Vitamin B_{12} level	Vitamin B_{12} deficiency is sometimes associated with recurrent aphthous ulceration and recurrent candidosis
Autoantibodies (e.g., rheumatoid factor, antinuclear factor, DNA-binding antibodies, SS-A, SS-B)	Raised in autoimmune diseases. Specific autoantibody levels suggest certain diseases
Viral antibody titres (e.g., Herpes simplex, Varicella zoster, mumps virus)	A rising titre of specific antibody indicates active infection by the virus
Paul–Bunnell or monospot test	Infectious mononucleosis
Syphilis serology	Syphilis
Complement component levels	Occasionally useful in diagnosis of systemic lupus erythematosus or familial angio-oedema
Serum angiotensin-converting enzyme	Sarcoidosis
Serum calcium, phosphate and parathormone levels	Paget's disease and hyperparathyroidism
Human immunodeficiency virus (HIV) test	HIV infection
Skeletal serum alkaline phosphatase	Raised in conditions with increased bone turnover, e.g., Paget's disease and hyperparathyroidism Lowered in hypophosphatasia
Serum IgG4 level	Often raised in IgG4-related disease, but predictive value is not high

Table 1.14 Microbiological tests useful in oral diagnosis

Test	Main uses
Culture and antibiotic sensitivity	Detect unusual pathogens, e.g., actinomyces in soft tissue infection Antibiotic sensitivity for all infections, particularly osteomyelitis and acute facial soft tissue infection
Smear for candida	Candidosis
Viral culture or antigen screen	Viral culture identifies many viruses but requires considerable time Screening for viral antigen by ELISA or similar immunological methods is faster but detects a more limited range of viruses

A key microbiological investigation is culture and sensitivity of pus organisms. Whenever pus is obtained from a soft tissue or bone infection, it should be sent for culture and determination of antibiotic sensitivity of the causative microbes. Those of osteomyelitis, cellulitis, acute parotitis or other severe infections need to be identified if appropriate antimicrobial treatment is to be given. However, treatment has usually to be started empirically without waiting for the result, which takes a few days; the sensitivity test may dictate a change of treatment later.

Soft tissue infections of the head and neck are often treated without microbiological diagnosis. This is partly because the flora is complex and mixed with many anaerobes and organisms that are difficult to culture. The anaerobes do not survive ordinary sample-taking procedures. Culture results are usually a poor reflection of the actual flora unless specialised anaerobic sampling and culture are performed. When antibiotic treatment fails, advice should be sought from a microbiologist as to whether this type of sampling may help.

Viral identification is rarely required for oral diseases because many oral viral infections are clinically typical and indicate the causative virus. A smear alone may show the nuclear changes of herpetic infection in epithelial cells from the margins of mucosal ulcers. A more sensitive and almost as rapid result may be obtained by sending a swab for virus detection using ELISA (enzyme-linked immunosorbent assay) or PCR analysis.

Key reminders for microbiological investigations are in Box 1.15.

Box 1.15 Reminders for microbiological investigation

- Always take a sample of pus for culture and antibiotic sensitivity from bone and soft tissue infections *before* giving an antibiotic
- Always take the temperature of any patient with a swollen face, enlarged lymph nodes, malaise or other symptom or sign that might indicate infection
- Culture of *Candida* from the mouth does not necessarily indicate infection because this is a commensal organism. Demonstration of hyphae in a scraping of epithelial cells indicates active infection.

Other clinical tests

Urine tests are valuable for the diagnosis of diabetes (suggested by repeated candidal or periodontal infection), kidney damage which can have resulted from autoimmune disorders such as granulomatosis with polyangiitis (Wegener's granulomatosis) and for the detection of Bence-Jones protein in myeloma.

Taking the patient's temperature is an easily forgotten investigation. The temperature should be noted whenever bone or soft tissue infections are suspected. It helps distinguish facial inflammatory oedema from cellulitis and indicates systemic effects of infections and the need for more aggressive therapy.

Interpreting investigations and making a diagnosis and treatment plan

Check that the results of each investigation are compatible with the proposed diagnosis. If a result appears at odds with other information, take into account the normal variation, perhaps with age or diurnal variation, and consider the possibility of false-positive and false-negative results. A common cause of unusual blood test results is a delay in transporting blood samples to the laboratory.

Further advice and specialised tests may be appropriate, but more extensive investigations, those carrying risks or radiation dose, are best organised through other medical specialties. In referrals, it is important to state whether the dentist is requesting the medical specialist to exclude a condition and refer the patient back, or to take over the investigation. If the latter, it is essential that dental causes have been completely eliminated as the cause of the problem.

Finally, ensure that the patient's notes include a complete record of the consultation and investigation results. This must be correctly dated, legible, limited to relevant facts and include a clear complaint history, list of clinical findings, test results and plan of treatment organised in a suitable form for quick reappraisal. It must be signed by the clinician and, in addition, the name should be printed below. It should be possible for another person to continue to investigate or treat the patient without difficulty on the basis of the clinical record.

Photography or computerised video imaging is a very valuable adjunct to the clinical record. Pictures are especially useful in monitoring lesions that vary in the course of a long follow-up, for instance, white patches. It is useful to include teeth or a scale in the frame to allow accurate assessment of small changes in size. Photographs may also be helpful in explaining to patients about their condition and to show the effects of treatment, but consent for the intended uses of the photographs must be obtained first, and digital image files must be stored securely in the same way as other patient-identifiable digital files.

Appendix 1.1

Normal haematological values

Red cells

Haemoglobin (adults)	Males 130–170 g/L	Females 115–165 g/L
Haematocrit (packed cell volume – PCV)	Males 0.40–0.54%	Females 0.36–0.47%
Mean cell volume (MCV)	80–100 fL	
Mean cell haemoglobin concentration (MCHC)	300–370 g/L	
Mean cell haemoglobin	27–32 pg	
Red cell count	Males 4.5–6.5 $\times 10^{12}$/L	Females 3.8–5.8 $\times 10^{12}$/L
Erythrocyte sedimentation rate (ESR)	Males 1–10 mm/h	Females 3–15 mm/h

White cells

Total count	3.6–11 $\times 10^9$/L
Neutrophils	1.8–7.5 $\times 10^9$/L
Lymphocytes	1–4 $\times 10^9$/L
Monocytes	0.2–0.8 $\times 10^9$/L
Eosinophils	0.1–0.4 $\times 10^9$/L

Platelets 140–400 $\times 10^9$/L

Note. These reference ranges are for adults and are calculated assuming a normal distribution of results and excluding the upper and lower 2.5% of the range as abnormal. Therefore, approximately 5% of healthy persons have values outside the figures quoted above. These are average values and vary slightly between laboratories, and you should always check normal values with the testing laboratory. Reference ranges for some tests may vary between different ethnic groups.

Disorders of tooth development 2

Development of an ideal dentition depends on many factors (Box 2.1).

Significant structural defects of teeth are much less common than irregularities of alignment of the teeth and abnormal relationship of the arches. The main groups of disorders affecting development of the dentition are summarised in Table 2.1 and Summary chart 2.1 and Summary chart 2.2.

ABNORMALITIES IN THE NUMBER OF TEETH

Anodontia

Total failure of development of a complete dentition (anodontia) is exceedingly rare. If the permanent dentition fails to form, the deciduous dentition is retained for many years. If the teeth survive caries, attrition will eventually destroy the crowns. Lack of alveolar bone growth may make implant placement difficult.

Isolated oligodontia

Oligodontia, often referred to as hypodontia, means few teeth. Failure of development of one or two teeth is relatively common and often hereditary. The teeth most frequently missing are third molars, second premolars or maxillary second incisors (Fig. 2.1), the last teeth in each series. Absence of third molars can be a disadvantage if first or second molars, or both, have been lost; otherwise, orthodontic problems of alignment and space loss are the only effects.

Absence of lateral incisors can sometimes be conspicuous because the large, pointed canines erupt in the front of the mouth beside the central incisors. It is often impossible to prevent loss of space, even if the patient is seen early. It is also difficult and time consuming to make space by orthodontic means to replace the laterals, so combined procedures with prosthodontic replacement are often used. Disguising the shape of the canines is destructive of the tooth, usually unconvincing cosmetically and produces a poor contact.

Box 2.1 Requirements for development of an ideal dentition

- Formation of a full complement of teeth
- Normal structural development of the dental tissues
- Eruption of each group of teeth at the appropriate time into an adequate space
- Normal development of jaw size and relationship
- Eruption of teeth into correct relationship to occlude with their opposite numbers
- Maintenance of tooth position by normal soft tissue size and pressure

Oligodontia without a syndromic association or systemic disease can be caused by alterations in over 15 genes, most commonly *WNT10*, *AXIN2* or *LRP6* in the WNT signalling pathway and *MSX1* in the transforming growth factor beta pathway. These are the same genes that are often altered in the syndromes with oligodontia.

General review PMID: 24124058

Genetic causes PMID: 25910507 and 29969831

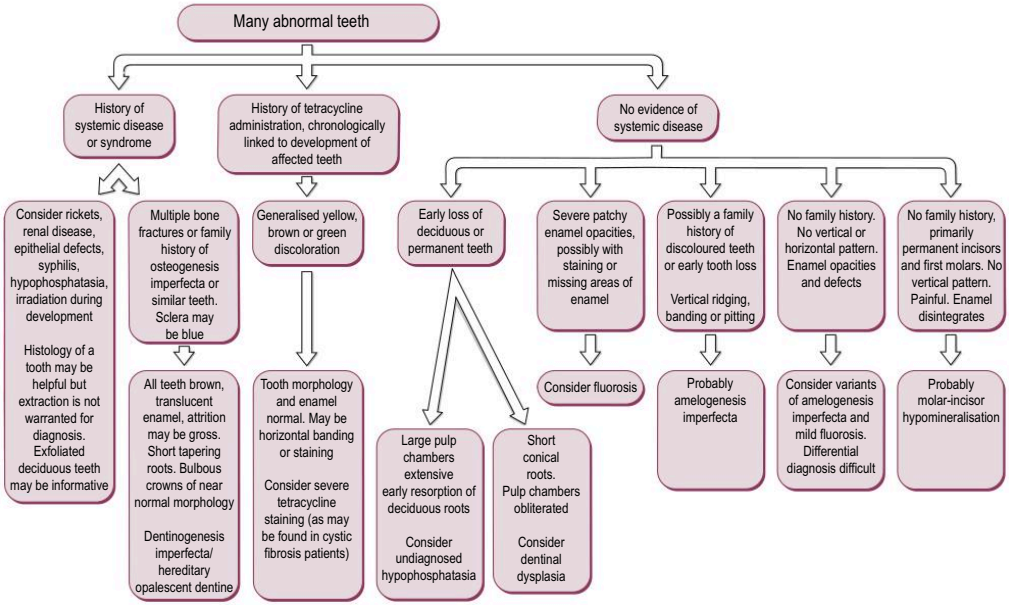
Oligodontia or anodontia with systemic defects

Anhidrotic (hereditary) ectodermal dysplasia

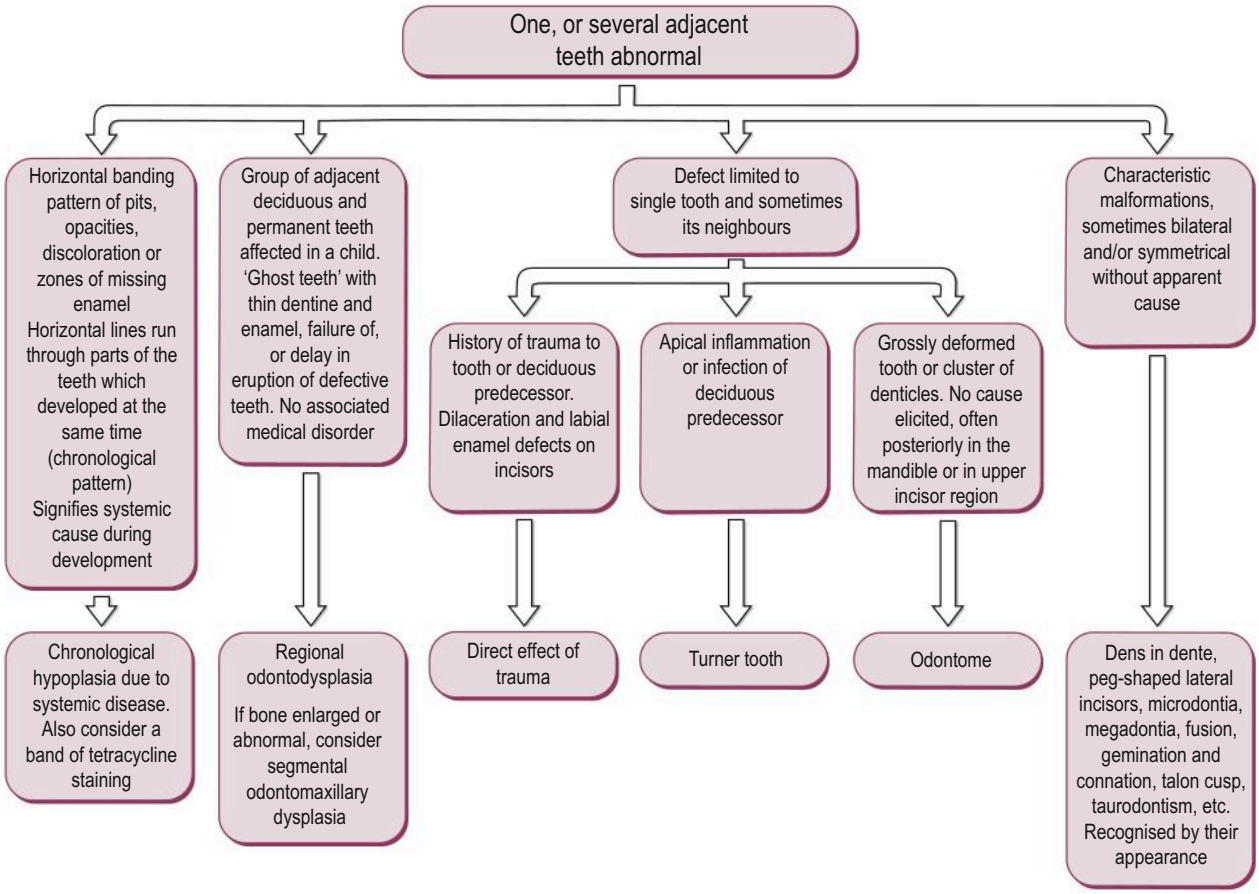
Ectodermal dysplasia has several forms. The most common is the type 1 or X-linked hypohidrotic form described here, but there are other modes of inheritance and clinical variations. Ectodermal dysplasia 1 is caused by mutation in the

Table 2.1 Disorders of development of teeth

Abnormality	Examples
Number	Anodontia Oligodontia (hypodontia) Additional teeth (supernumerary and supplemental)
Eruption	Delayed eruption Primary eruption failure Natal teeth Cleidocranial dysplasia
Enamel	Amelogenesis imperfecta Chronological hypoplasia Molar-incisor hypomineralisation Fluorosis
Dentine	Dentinogenesis imperfecta Dentinal dysplasia Vitamin D-resistant rickets
Cementum	Hypophosphatasia
All dental hard tissues	Regional odontodysplasia
Dental hard tissues and bone	Segmental odontomaxillary dysplasia
Pigmentation	Tetracycline pigmentation Rhesus incompatibility and jaundice Porphyria
Effects of systemic disease	Congenital syphilis Developmental arrest or delay
Minor tooth anomalies and abnormal tooth shape	Geminated (double) teeth Macrodontia Microdontia Dens invaginatus and evaginatus Talon cusp Additional roots or cusps Enamel pearls



Summary chart 2.1 Differential diagnosis of developmental defects of the teeth.



Summary chart 2.2 Differential diagnosis of developmental and acquired abnormalities of one or a group of teeth.

EDA or ectodysplasin-A gene on the X chromosome. Female carriers have minimal features, sometimes only peg-shaped upper lateral incisors.

The main features are summarised in Box 2.2. In severe cases, no teeth form. More often, most of the deciduous teeth form, but there are few or no permanent teeth. The teeth are usually peg-shaped or conical (Fig. 2.2).

When there is anodontia, the alveolar process, without teeth to support, fails to develop and has too little bone to support standard implants without surgical bone augmentation. The profile then resembles that of an older person because of the gross loss of vertical dimension. The hair is fine and sparse (Fig. 2.3), particularly in the tonsural region. The skin is smooth, shiny and dry due to absence of sweat glands. Heat is therefore poorly tolerated. The fingernails are usually also defective. As a temporary measure, composite restorations can disguise peg-shaped teeth and dentures or overdentures are usually well tolerated by children. Implants cannot be placed in the maxilla during growth, but it may be possible to use mini-implants or implants in the anterior mandible from a young age because, without teeth to erupt, alveolar growth is complete. Ultimately, a tooth-supported fixed partial denture or implant-supported overdenture is often a good solution.

Web URL 2.1 Ectodermal dysplasia URL: http://rarediseases.org/rare-diseases/hypohidrotic-ectodermal-dysplasia/

Other conditions associated with oligodontia

There are over 100 rare syndromes in which oligodontia is a feature, but the only common one is Down's syndrome (Ch. 40). One or more third molars are absent in more than 90% of patients with the syndrome, and absence of individual teeth is also common. Very rarely anodontia occurs. Less frequent disorders with oligodontia include cleft lip and palate, chondroectodermal dysplasia and oro-facial-digital syndrome.

Additional teeth: hyperdontia

Additional teeth are relatively common in the permanent dentition, affecting 1%–3% of the population, more frequently males. The teeth are usually of simple conical shape and less frequently resemble teeth of the normal series. These are the results of organised development and maturation under genetic control, not simple excessive growth of the dental lamina.

Supernumerary teeth are any additional teeth (Fig. 2.4). Conical or more seriously malformed additional teeth form most frequently in the incisor or molar region and, very occasionally, in the midline of the maxilla (mesiodens, Fig. 2.5).

Supplemental teeth are supernumerary teeth with a normal morphology, and they are usually an extra tooth at the end of the incisor, premolar or molar series (also seen in Fig. 2.5). Most supernumerary teeth in the deciduous dentition are supplemental.

Effects and treatment

Additional teeth usually erupt in abnormal positions, labial or buccal to the arch, creating stagnation areas and greater susceptibility to caries, gingivitis and periodontitis. Alternatively, a supernumerary tooth may prevent a normal tooth

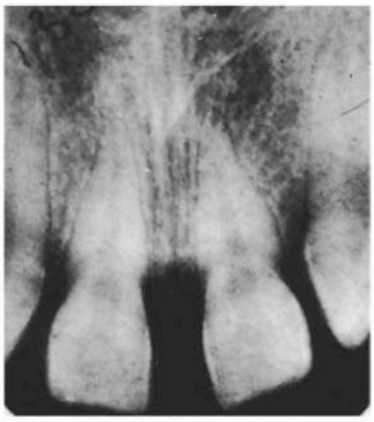


Fig. 2.1 Congenital absence of lateral incisors with spacing of the anterior teeth.

Box 2.2 Hypohidrotic ectodermal dysplasia 1: major features

- Usually an X-linked recessive trait with features more marked in males
- Missing teeth or pointed conical crowns
- Hypotrichosis (scanty fine hair)
- Reduced or absent sweating caused by lack of sweat glands.
- Reduced skin pigmentation generally, but hyperpigmented and finely wrinkled periorbital skin

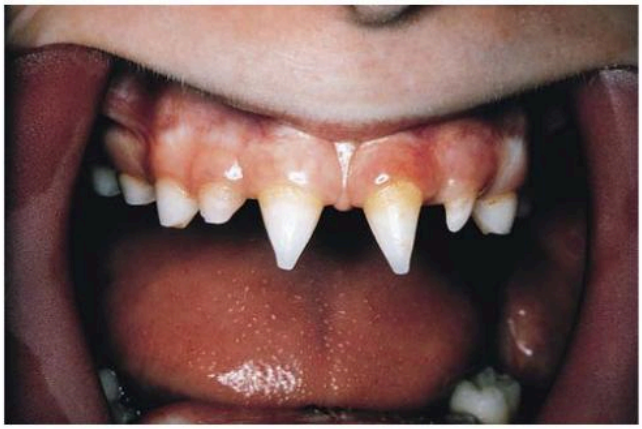


Fig. 2.2 Anhidrotic ectodermal dysplasia showing conical teeth.

from erupting, resorb roots of adjacent teeth or cause crowding and malalignment. These additional teeth are usually best extracted.

Review PMID: 24124058

Syndromes associated with hyperdontia

These syndromes are all rare, but probably the best known are cleidocranial dysplasia (Ch. 13), in which many additional teeth develop but fail to erupt, and the Gardner variant of familial adenomatous polyposis (Ch. 12).

DEFECTIVE ENAMEL FORMATION

Structural defects of the enamel, such as pitting, discoloration or failure to form can only arise during development.

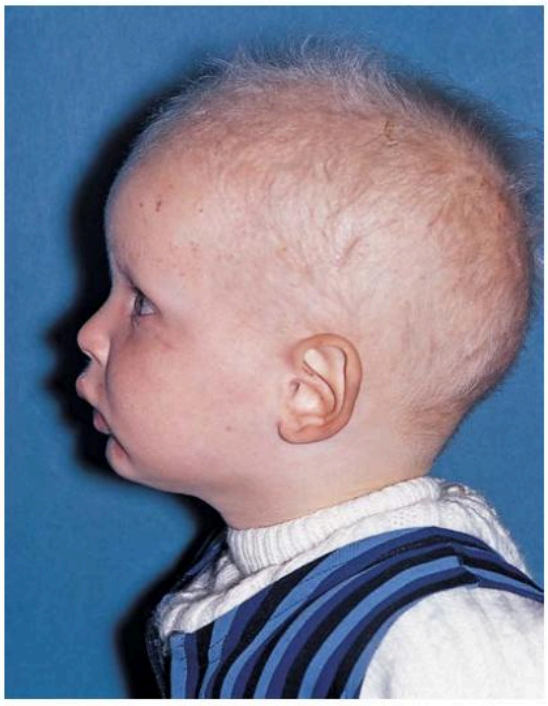


Fig. 2.3 Anhidrotic ectodermal dysplasia showing typical fine and scanty hair and loss of support for the facial soft tissues.

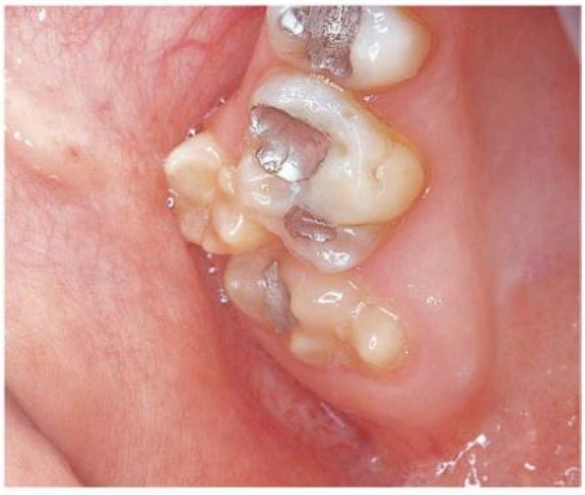


Fig. 2.4 A paramolar, a buccally placed supernumerary molar tooth.

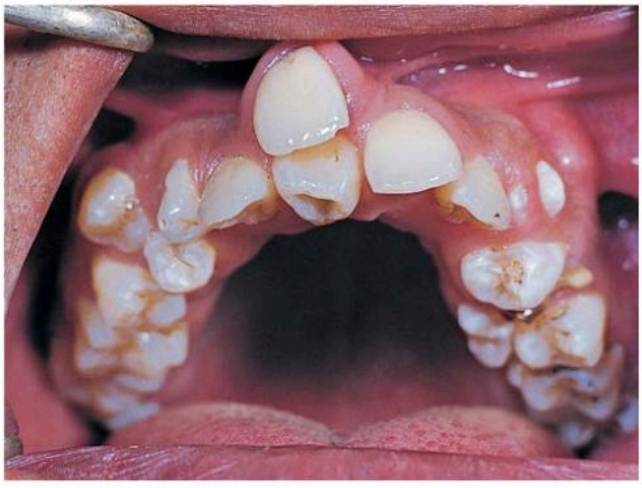


Fig. 2.5 Maleruption of a midline tuberculate supernumerary and two supplemental premolars causing ectopic eruption of adjacent teeth through gross crowding.

Hypoplasia of enamel is not an important contributory cause of dental caries. Only normally formed enamel can become carious, and hypoplasia due to fluorosis is associated with enhanced resistance. Diagnosis of developmental defects can be challenging and molecular diagnosis is becoming available for indeterminate cases.

Molecular diagnosis PMID: 26502894

Defects of deciduous teeth

Calcification of deciduous teeth begins at approximately the fourth month of intrauterine life. Disturbances of metabolism or infections that affect the foetus at this early stage without causing abortion are rare. Defective structure of the deciduous teeth is therefore uncommon but, in a few places, such as parts of India, where the fluoride content of the water is very high, the deciduous teeth may be mottled.

The deciduous teeth may be discoloured by abnormal pigments circulating in the blood. Severe neonatal jaundice may cause the teeth to become yellow, or there may be bands of greenish discoloration. In congenital porphyria, a rare disorder of haemoglobin metabolism, the teeth are red or purple. Tetracycline given during dental development, contrary to guidelines, is now a rare cause of permanent discoloration. These conditions usually also affect the permanent teeth and are discussed later in this chapter.

Defects of permanent teeth

Single permanent teeth may be malformed as a result of local causes such as periapical infection of a predecessor ('Turner tooth' – Fig. 2.6), or trauma from intubation while a preterm neonate (Fig. 2.7). Defects of multiple teeth usually indicate previous systemic disease as summarised in Box 2.3.

Amelogenesis imperfecta

➔ Summary chart 2.1 p. 24

Amelogenesis imperfecta is a group of conditions caused by defects in the genes that encode enamel matrix proteins or other proteins or enzymes required to process or mineralise the matrix. Classification is complex and based on pattern of inheritance, type of defect (enamel hypoplasia, hypomineralisation or hypomaturation) and appearance (smooth, rough or pitted). At least 16 presentations have been recognised on clinical grounds, but some are the same genetic condition with differing severity, and the classification is contentious.

Inheritance can be autosomal dominant, recessive or X-linked and occasional cases are sporadic. However, the most common types have an autosomal inheritance and are thought to be caused by mutations in the genes for ameloblastin (C4), enamelin (C4) or tuftelin (C1). In the case of the autosomal dominant type of amelogenesis imperfecta, the defective gene is enamelin (C4).

The less common X-linked types are caused by a variety of defects in the *AMELX* gene encoding amelogenin, located on the X and Y chromosomes (the copy on the Y gene being inactive) and, confusingly, it seems the same mutation can sometimes cause hypoplasia, hypomineralisation or hypomaturation in different patients.

Fig. 2.6 Turner tooth, a hypoplastic tooth resulting from periapical infection, usually of a deciduous predecessor.

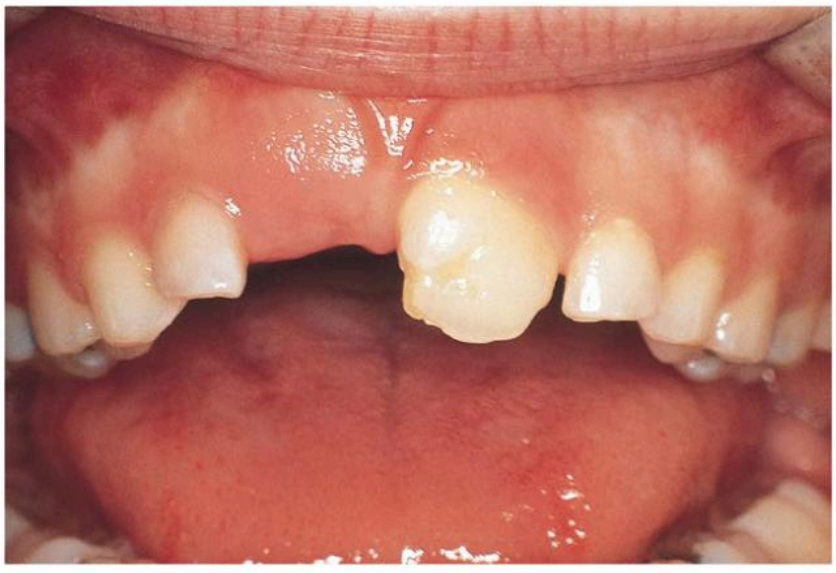


Fig. 2.7 Localised dental disturbance caused by prolonged intubation during tooth development. The upper left central incisor shows enamel pitting incisally, and the upper right central incisor is deformed and has failed to erupt.

Genetic factors act throughout the whole duration of amelogenesis. Characteristically, therefore, all teeth are affected, and defects involve the whole enamel or randomly distributed patches of it. By contrast, exogenous factors affecting enamel formation (with the important exception of fluorosis) tend to act for a relatively brief period and produce defects related to that period of enamel formation (a chronological pattern).

Until there is a better understanding, dentists should at least be able to identify the three clinical types of hypoplasia, hypocalcification and hypomaturation and take a family history, which may reveal an inheritance pattern.

Review types and causes PMID: 16838342

Detailed molecular mechanisms PMID: 28694781

Box 2.3 Multiple malformed permanent teeth: important causes

Genetic

- Amelogenesis imperfecta
  - Hypoplastic
  - Hypomaturation
  - Hypocalcified
- Chronological hypoplasia
- Molar-incisor hypomineralisation
- Dentinogenesis imperfecta
- Dentinal dysplasia
- Regional odontodysplasia
- Segmental odontomaxillary dysplasia
- Multisystem disorders with associated dental defects
- Hypophosphatasia

Infective

- Congenital syphilis

Metabolic

- Rickets
- Hypoparathyroidism

Drugs

- Tetracycline pigmentation
- Cytotoxic chemotherapy

Fluorosis

Other acquired developmental anomalies

- Fetal alcohol syndrome
- Radiotherapy

Hypoplastic amelogenesis imperfecta

The main defect in this type is deficient formation of matrix, so that the amount of enamel is reduced but normally mineralised. The enamel is either randomly pitted, grooved or uniformly very thin, but hard and translucent (Fig. 2.8). The defects tend to become stained, but the teeth are not especially susceptible to caries unless the enamel is scanty and fractures to expose dentine.

The main patterns of inheritance are autosomal dominant and recessive, X-linked and (a genetic rarity) an X-linked dominant type. In the last type, there is almost complete failure of enamel formation in affected males, whereas in females the enamel is vertically ridged (Figs 2.9–2.11). Tooth eruption can be delayed and some types are associated with anterior or lateral open bite. The irregular enamel outline but normal mineralization allow diagnosis before eruption radiographically (Figs 2.12-13). Occasionally, cases are difficult to classify (Fig. 2.14).

Hypomaturation amelogenesis imperfecta

The enamel is normal in thickness on eruption but with opaque, white to brownish-yellow patches caused by failure of maturation, a process of matrix removal and increasing mineralisation that is partly developmental and partly post-eruptive. The appearance can mimic fluorotic mottling if the spots are small (Figs 2.15 and 2.16). However, affected enamel is soft and vulnerable to attrition, though not as severely as the hypocalcified type.

There are several variants of hypomaturation defects such as a more severe, autosomal dominant type combined with hypoplasia and milder forms limited to only some tooth surfaces.

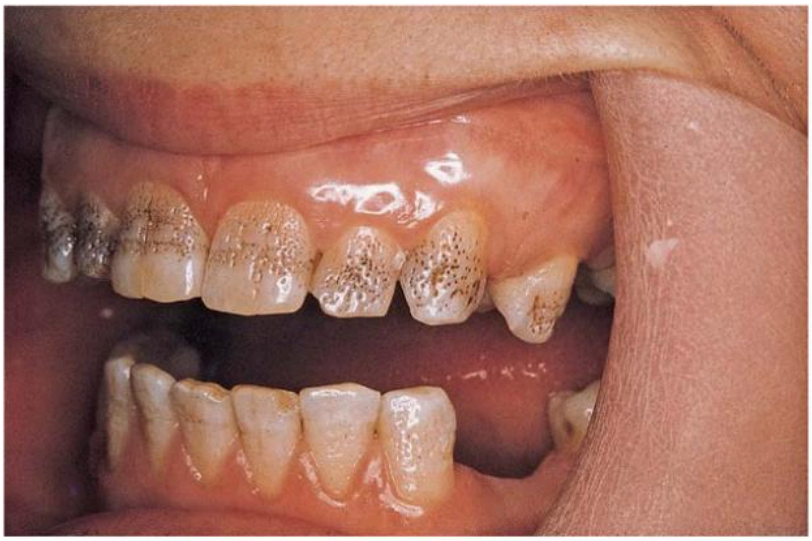


Fig. 2.8 Amelogenesis imperfecta, hypoplastic pitted type. Enamel between pits appears normal.

Fig. 2.9 Close-up of X-linked dominant hypoplastic type amelogenesis imperfecta. These teeth, from an affected female, show the typical vertical ridged pattern of normal and abnormal enamel as a result of Lyonisation.

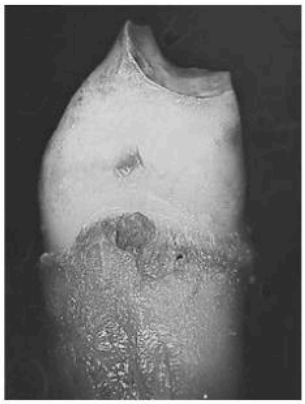


Fig. 2.10 Amelogenesis imperfecta X-linked dominant hypoplastic form in a male. This premolar has a cap of enamel so thin that the shape of the crown is virtually that of the dentine core.

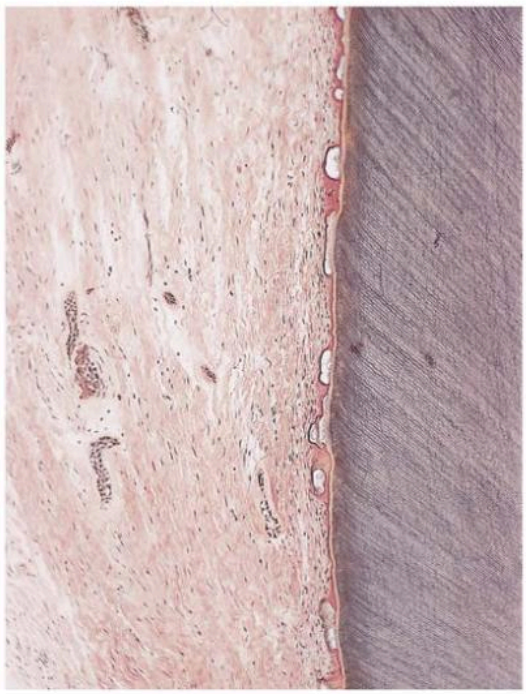


Fig. 2.11 Amelogenesis imperfecta X-linked dominant hypoplastic type in a male showing a thin translucent layer of defective enamel on the dentine surface (dentine right).

Fig. 2.12 Amelogenesis imperfecta, hypoplastic type. In this pitted hypoplastic type, the pits are seen to be focal areas of reduced enamel formation with incremental lines diverted around them. No enamel has been lost from the pit, it has developed this shape.

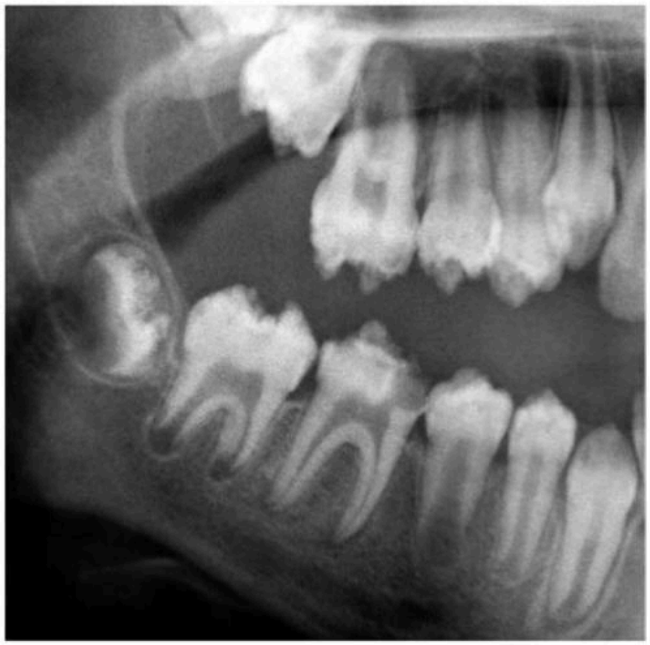


Fig. 2.13 Radiographic appearance of amelogenesis imperfecta hypoplastic pitted type, from the same patient as in Fig. 2.12. The irregular outline is visible. Note the normal enamel radiodensity where enamel is continuous enough to assess it.

Hypocalcified amelogenesis imperfecta

Enamel matrix is formed in normal quantity but is poorly calcified. When newly erupted, the enamel is normal in thickness and form, but weak, chalky and opaque in appearance.

The teeth tend to become stained, and enamel is relatively rapidly worn away. The upper incisors may acquire a shoulder due to the chipping away of the thin, soft enamel of the

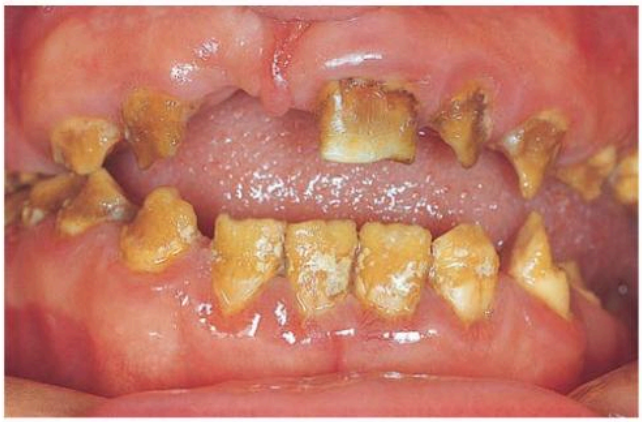


Fig. 2.14 Amelogenesis imperfecta, indeterminate type. Some cases, such as this, are difficult to classify but are clearly inherited, as shown by their long family history.

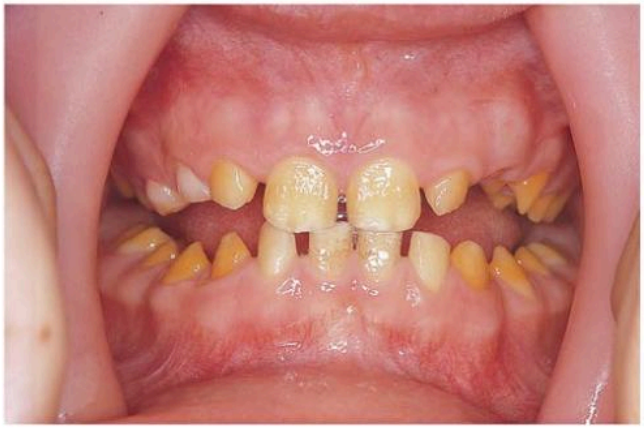


Fig. 2.15 Amelogenesis imperfecta, hypomaturation type. Tooth morphology is normal, but there are opaque white and discoloured patches.

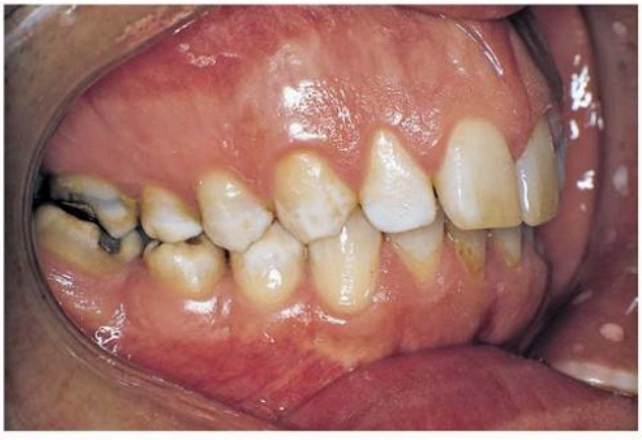


Fig. 2.16 Amelogenesis imperfecta, one of the several hypomaturation types. In this form there are opaque white flecks and patches affecting the occlusal half of the tooth surface.

incisal edges (Fig. 2.17). There are dominant and recessive patterns of inheritance.

Chronological hypoplasia

➔ Summary chart 2.1 p. 24

Any severe disturbance of metabolism can halt enamel formation. Dentine formation is less sensitive to insult,

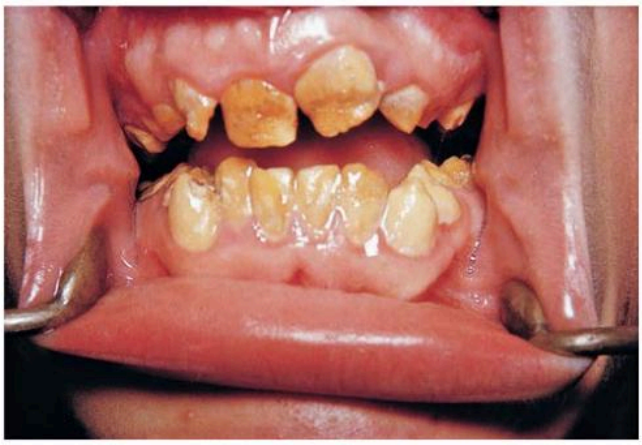


Fig. 2.17 Amelogenesis imperfecta, hypocalcified type. The soft chalky enamel was virtually of normal thickness and form but has chipped away during mastication leaving a characteristic shoulder, seen best on the upper left central incisor.

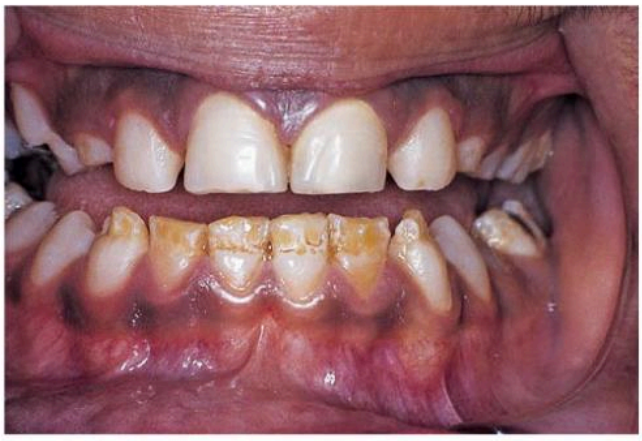


Fig. 2.18 Chronological hypoplasia due to metabolic upset. Defects are linear and run horizontally across the crown corresponding to the level of enamel forming during a severe illness.

so tooth formation will usually continue to produce a normally shaped tooth with only a band of enamel missing. The usual causes are the childhood fevers or severe infantile gastroenteritis. Measles with severe secondary bacterial infection was the most common cause of chronological hypoplasia but is rare since measles vaccination.

Unlike inherited forms of hypoplasia, only a restricted area of enamel is missing, corresponding to the sites of development at the time of the illness. Since enamel forms progressively from the incisal edges and cusp tips, the hypoplasia is characterised by a pattern of horizontal defects, either pits, grooves or a completely missing band of enamel across the crowns of the teeth.

Defects are usually in the incisal third of incisors, suggesting that the disorder had its effect during the first year or two of life, when such infections cause the most severe systemic upset (Fig. 2.18). Metabolic disturbance *in utero* or around birth affects the primary teeth in addition (Fig. 2.19). The horizontal pattern is important in distinguishing chronological hypoplasia from genetic causes of hypoplasia and determining the timing of the systemic disease (Fig. 2.20).

Molar-incisor hypomineralisation

➔ Summary chart 2.1 p. 24

Molar incisor hypomineralisation is an unexplained, apparently recently recognised and increasingly frequent condition defined by hypomineralisation of some or all first permanent molars and incisors (Fig. 2.21). The teeth erupt normally and have patchy opaque and yellow-brown patches on the enamel of the occlusal third of the crowns. The enamel surface is hard, but the underlying enamel is soft and breaks down, leaving a stained rough and soft surface that is prone to caries. The defects are sharply demarcated. Cervical enamel is usually normal and the pattern may mimic the appearance of a chronological horizontal defect.

The cause is probably failure of enamel maturation, but the presentation and family history are distinct from amelogenesis imperfecta and chronological hypoplasia. It appears that many cases are similar to chronological hypoplasia in aetiology, but the systemic upset is milder and insufficient to cause the more severe defect of hypoplasia. A very wide range of types of illness appear to be able to cause hypomineralisation.

Molars are usually affected more severely than incisors. The affected teeth are characteristically hypersensitive and difficult to anaesthetise. Restorations often fail, partly due

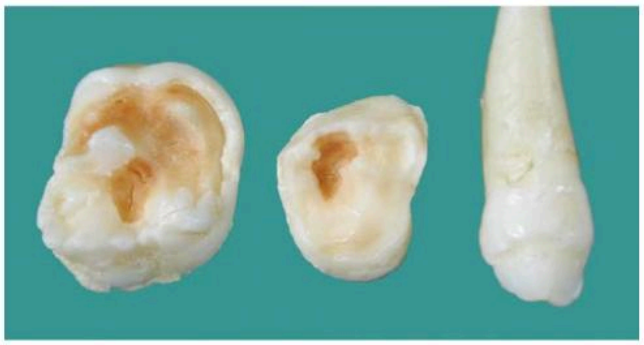


Fig. 2.19 Chronological hypoplasia with loss of primary molar occlusal enamel and a horizontal ridge on the upper canine.

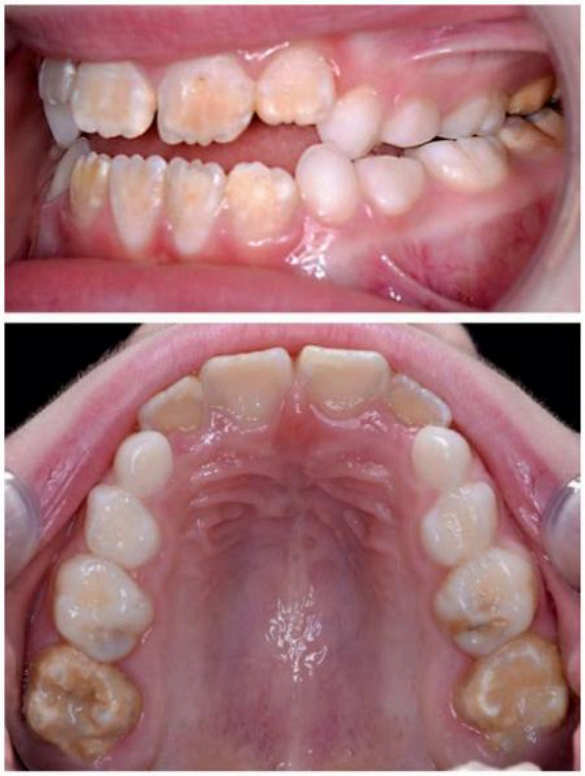


Fig. 2.21 Molar-incisor hypomineralisation. Typical appearance with discolouration and breakdown of enamel almost exclusively on permanent incisors and first molars.

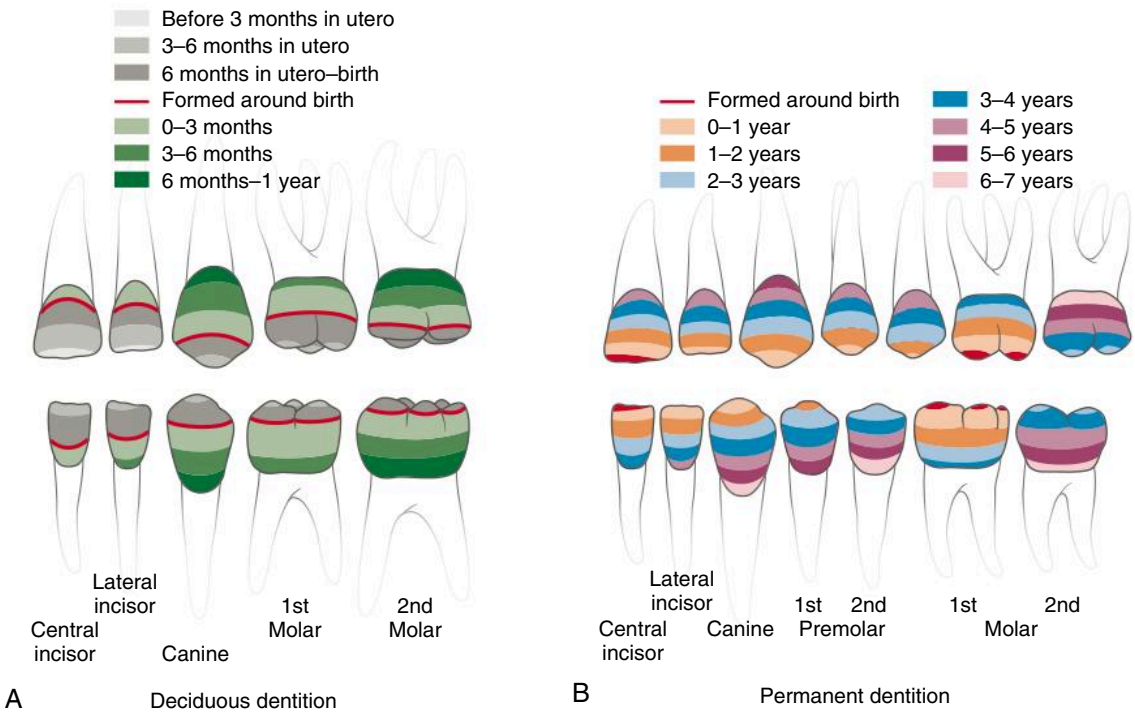


Fig. 2.20 Charts to determine the chronology of enamel hypoplasia. Chronological hypoplasia should affect many teeth symmetrically consistent with the time of illness.

to the adverse crown shape and partly because the enamel is not amenable to use of adhesive materials, even away from the clinically detectable defects. This makes treatment difficult, and after a period of preventive care to remineralise the molars and preserve them as space maintainers, extraction is often the best course of action. Otherwise, full coverage restorations are required. Microabrasion is not sufficient to restore most affected incisors because the soft enamel extends deeply, and restorations or veneers are usually required.

Aetiology PMID: 27121068

Treatment PMID: 16805354, 26856002 and 23410530

Nature of enamel defect PMID: 23685033

Localised enamel defects

Localised enamel opacities and foci of hypoplasia or discolouration are very common and have been linked to locally acting causes such as trauma, infection, extraction of deciduous predecessors, prolonged neonatal intubation and periodontal ligament injection.

DEFECTIVE DENTINE FORMATION

➔ Summary chart 2.1 p. 24

The classification of hereditary dentine defects is unsatisfactory. As in amelogenesis imperfecta, the genetic findings do not correlate well with clinical presentation, and terminology is used inconsistently. The previous widely used classifications (of Witkop and of Shields) are now considered redundant, but no replacement is yet established.

The term *osteogenesis imperfecta* is used when abnormal teeth are associated with bone defects, replacing the term *dentinogenesis imperfecta* (type I). The term *dentinogenesis imperfecta* is used when only the teeth are involved, replacing the term *hereditary opalescent dentine*. Abnormal dentine is referred to as dysplastic, meaning abnormally formed, rather than hypoplastic as used for enamel.

Osteogenesis imperfecta with opalescent teeth ➔ Summary chart 2.1 p. 24

This uncommon defect of collagen formation disturbs formation of both bone and dentine. Many forms are known, and the condition is described in Chapter 13. Types III and IV are those most frequently associated with dentine defects. Both are autosomal dominant traits with mutation in the genes *COL1A1* and *COL1A2* that prevent the procollagen alpha helix polymerising into normal type 1 collagen. The dentine is soft and has abnormally high water content.

In both these types, opalescent teeth are present in over 80% of patients in the primary dentition. Tooth discoloration and attrition is often most striking in the deciduous dentition. Class III malocclusion is associated in over 70% of patients. In type III disease, dental development is delayed in 20% but, in type IV disease, it is accelerated in over 20% of patients.

Dentinogenesis imperfecta

➔ Summary chart 2.1 p. 24

This condition produces identical changes in appearance and structure of the teeth to those in osteogenesis imperfecta but is caused by mutations in the *DSPP* gene that encodes dentine sialoprotein, a dentine matrix protein, rather than collagen genes. However, the condition may be heterogeneous and other mutated genes have been found. Previously there were thought to be two types (types II and III), but the condition of shell teeth, or type III, is now thought to be just a more severe presentation of type II caused by defects in the same gene. Dentinogenesis imperfecta can be associated with developmental hearing loss.

Clinical features

The teeth are normal in shape but uniformly brownish or purplish and abnormally translucent (Fig. 2.22), giving an opal-like appearance that leads to the clinical description of 'hereditary opalescent dentine'. The appearance is caused by the dark dentine being visible through the enamel, which is usually normal but may have hypoplastic defects in a minority of patients. The shape and size of the crowns is essentially normal, but the roots are slender and stunted, giving the tooth a cervical constriction and bulbous outline radiographically (Fig. 2.23). Dentine formation progresses to obliterate the pulp chamber at an early age. The mantle dentine is relatively normal but below the thin mantle the dentine is poorly formed, so that there is a weak zone in the

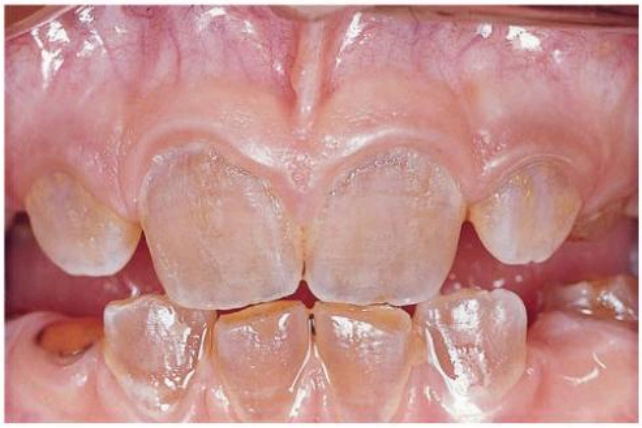


Fig. 2.22 Dentinogenesis imperfecta. Showing the grey-brown translucent appearance of the teeth which are of normal morphology.

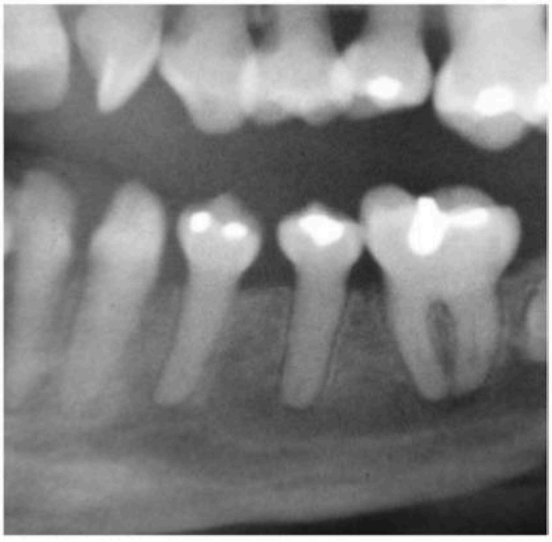


Fig. 2.23 Dentinogenesis imperfecta. Showing the slender roots and bulbous crowns of the 'tulip-shaped' teeth.

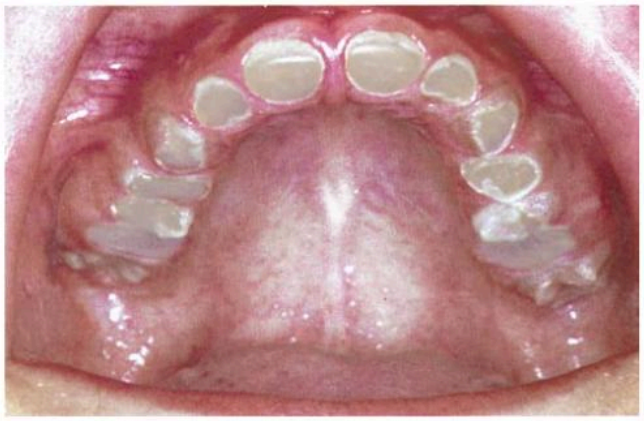


Fig. 2.24 Dentinogenesis imperfecta. In this 14-year-old, the teeth have worn down to gingival level, but the pulp chambers have become obliterated as part of the disease process. A rim of enamel remains around the necks of the teeth.

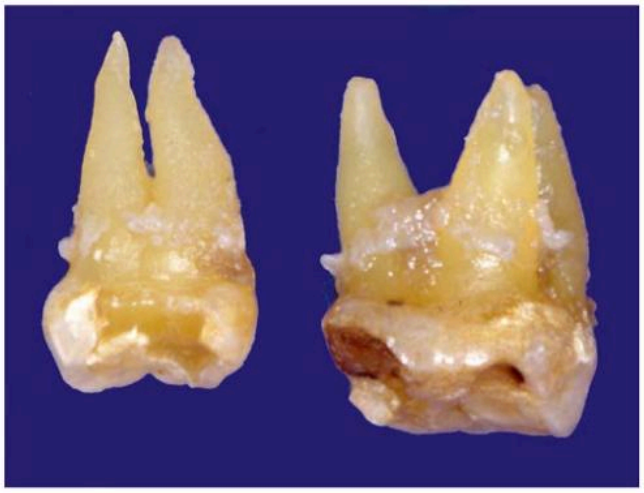


Fig. 2.25 Dentinogenesis imperfecta. Slender tapering roots and loss of enamel through fracturing.

dentine just below the amelodentinal junction. The lack of resilient dentine to support the enamel allows enamel to chip away, exposing the dentine, which is soft and rapidly wears away, eventually to the gingival level (Figs 2.24 and 2.25). In some patients, only a few teeth are severely affected, whereas the remainder appear normal.

Treatment aims to preserve vertical dimension, avoid extractions to prevent space loss and allow normal alveolar bone growth for implants later. Early application of occlusal composite onlays and preformed metal crowns on molars reduce wear. Worn roots may be used as temporary overdenture abutments but are too soft to survive long.

Severely affected patients may have shell teeth, with only a thin outer mantle layer of dentine tissue surrounding overlarge pulp chambers. Shell teeth are very difficult or impossible to manage conservatively.

Tooth structure

The earliest-formed mantle dentine under the amelodentinal junction usually appears normal. There is a sharp junction with the deeper defective dentine. This has few tubules, and they run in disorganised patterns. The uniform structure of dentine is absent; extensions of the pulp penetrate

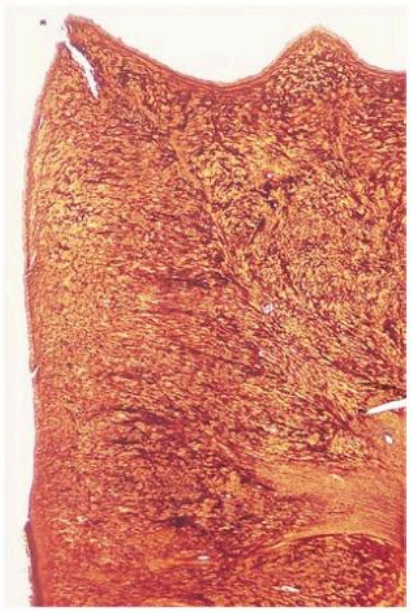


Fig. 2.26 Microscopic appearance of dentinogenesis imperfecta. Two cusps and part of the crown of a molar showing the grossly disorganised tubular structure with inclusions of pulp in the dentine and obliteration of the pulp cavity.

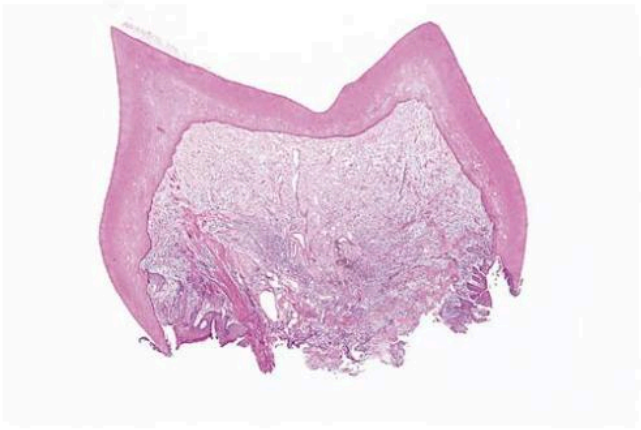


Fig. 2.27 Shell tooth. In this severe form of dentinogenesis imperfecta, only a thin mantle of dentine is formed, and no root develops.

the dentine almost to the enamel (Fig. 2.26) and can be exposed by attrition to devitalise the teeth. Calcification is incomplete and the dentine soft.

The pulp chamber becomes obliterated early, and odontoblasts degenerate. Cellular inclusions in the dentine are common. In shell teeth, the dentine layer is very thin (Fig. 2.27).

Review PMID: 19021896

Classification and types PMID: 25118030

Dentinal dysplasia ('rootless' teeth)

➔ Summary chart 2.1 p. 24

Dentinal dysplasia

This rare disorder was previously called dentinal dysplasia type 1 but is now the only type recognised. The crowns are of normal shape and size, but the roots are either absent or

very short and conical. The pulp chambers are obliterated by multiple nodules of poorly organised dentine containing tubules running in sheaves. A range of pulp shapes can result from differing severity, with almost complete obliteration producing crescent-shaped pulps at the level of the floor of the normal chamber. In the worst affected teeth, roots are absent. Teeth tend to be lost early in life (Fig. 2.28). There are pulp extensions through dentine to the enamel, and vitality is lost quickly; otherwise the lack of roots predisposes to early loss through periodontitis.

The coronal dentine and enamel are normal or almost so, but dentinal tubule patterns in the root are abnormal (Fig. 2.29). Both dentitions are affected, the deciduous more severely.

Dentinal dysplasia 'type 2'

The defect in this rare disorder is in the dentine sialoprotein gene, so this disorder is now classified as a severe form of dentinogenesis imperfecta. The tooth crowns have the same opalescent appearance as dentinogenesis imperfecta in the deciduous dentition. The permanent dentition appears normal or nearly normal in colour, but the pulps are larger than normal. A tall, wide coronal pulp extends high into the crown (thistle pulp), sometimes with pulp stones, and more marked in the permanent dentition (Fig. 2.30).

Review PMID: 19021896

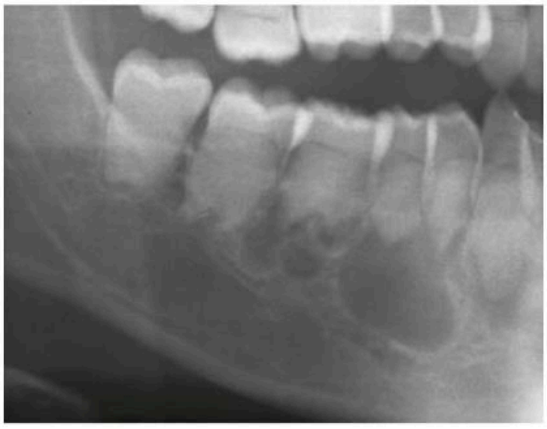


Fig. 2.28 Dentinal dysplasia type 1. Radiograph showing short roots, spontaneous pulp necrosis with apical areas, and obliterated crescent-shaped pulps.

Fig. 2.29 Dentinal dysplasia. The pulp chamber in the short, broad root is obliterated by nodules of dentine with swirling patterns of tubules.

DEFECTS OF ENAMEL AND DENTINE

➔ Summary chart 2.1 p. 24

Regional odontodysplasia (ghost teeth)

➔ Summary chart 2.2 p. 24

This localised disorder of development affects a group of teeth in which there are severe abnormalities of enamel, dentine and pulp. The disorder is not hereditary and a somatic mutation appears to be a likely cause. Although the aetiology is unknown, mutations in *PAX9* and *PIK3CA* have been detected in a few cases and a relationship to segmental odontomaxillary dysplasia proposed. A few cases are associated with facial vascular naevi or abnormalities such as hydrocephalus. There is no sex or racial predilection.

Clinically, regional odontodysplasia may be recognisable at the time of eruption of the deciduous teeth (2–4 years) or of the permanent teeth (7–11 years). The maxillary teeth are most frequently affected. Either or both dentitions, and one or, at most, two quadrants may be affected. The abnormal teeth frequently fail to erupt but, if they do, show yellowish deformed crowns with a rough surface.

Affected teeth have very thin enamel and dentine surrounding a greatly enlarged pulp chamber. In radiographs, the teeth appear crumpled and abnormally radiolucent or hazy, due to poor mineralisation, explaining the term 'ghost teeth' (Figs 2.31 - 2.33).

Histologically, the enamel thickness is highly irregular and lacks a well-defined prismatic structure. The dentine, which has a disorganised tubular structure, contains clefts and interglobular dentine mixed with amorphous mineralised tissue. The surrounding follicle soft tissue may contain numerous small calcifications, many of which are mineralized residues of enamel epithelium (Figs 2.34–2.35).

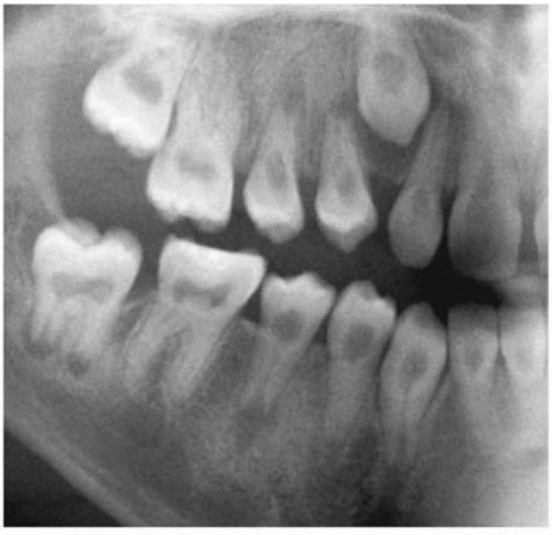


Fig. 2.30 Dentinogenesis imperfecta of dentinal dysplasia type 2 presentation. The pulp chambers are rounded, tall and wide in the developing dentition. The classical 'thistle-shaped' pulp appearance is seen in the lower canine and premolars.

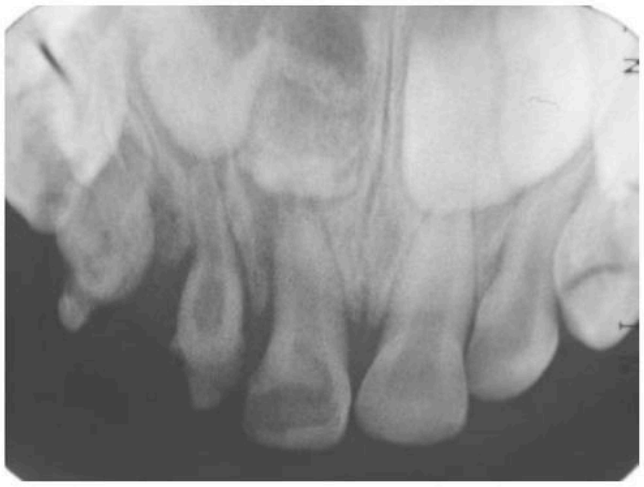


Fig. 2.31 Radiographic appearance of regional odontodysplasia. In the anterior regions the condition usually stops at the midline.

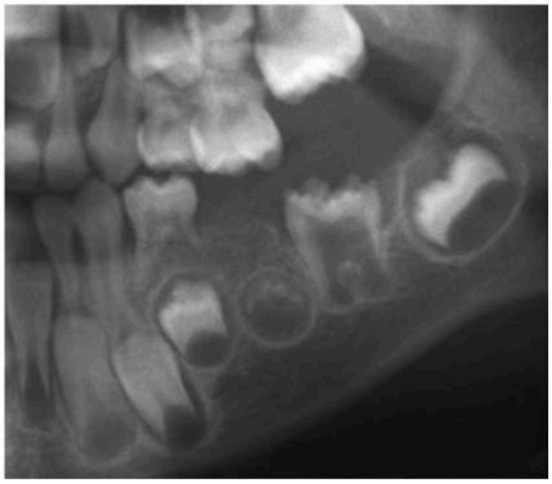


Fig. 2.32 Radiographic appearance of regional odontodysplasia. The lower left 5 and 6 are affected. Note their abnormal outline and radiodensity by comparison with the 4 and 7.

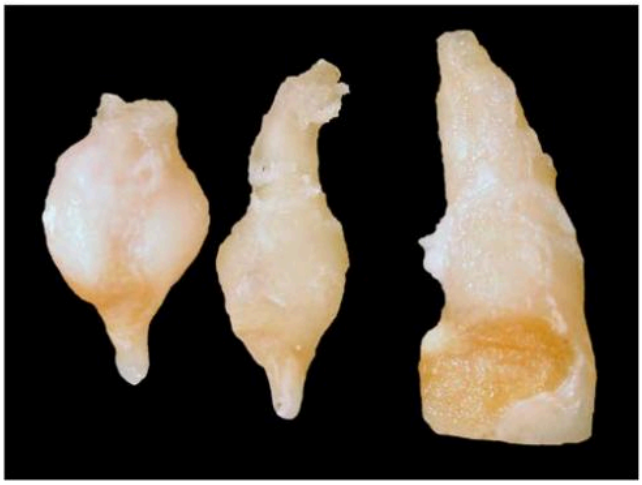


Fig. 2.33 Regional odontodysplasia. Distorted and hypoplastic teeth from the case shown in Fig. 2.31.

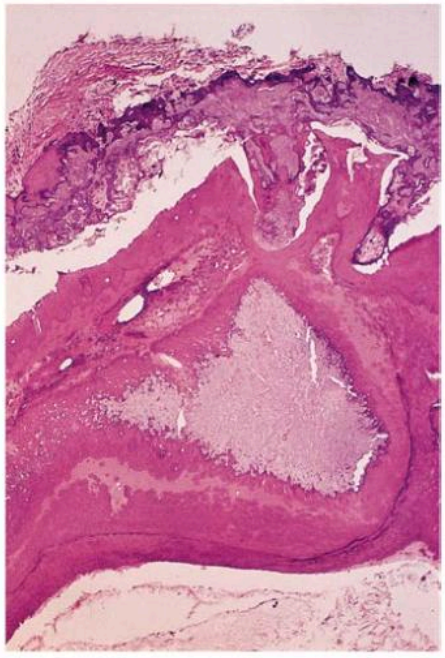


Fig. 2.34 Regional odontodysplasia. Both enamel and dentine are deformed, and there is calcification of the reduced enamel epithelium seen as a dark blue line at the top of the image.

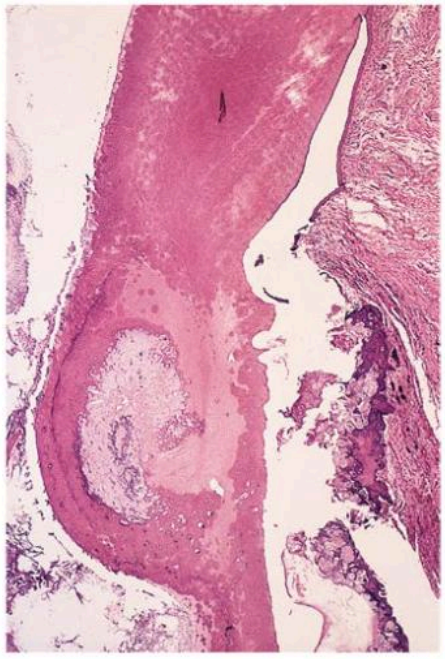


Fig. 2.35 Regional odontodysplasia. Showing dysplastic dentine with a disorganised tubule structure, an irregular enamel space and mineralised enamel epithelium.

If they erupt, the teeth are susceptible to caries and fracture. If they can be preserved and restored, crown and root dentine continue to form, and the teeth may survive long enough to allow normal development of the alveolar ridge and occlusion. However, extractions are often required eventually. This should not be done until it is certain that eruption has completely failed or the defects are too severe to be treatable. Unerupted teeth may be left in situ to preserve alveolar bone.

Review and cases PMID: 2549236

Cases PMID: 14714196

Natural history and treatment PMID: 17613259

Segmental odontomaxillary dysplasia

This rare disorder is frequently mistaken for fibrous dysplasia or regional odontodysplasia.

Segmental odontomaxillary dysplasia causes unilateral expansion of the alveolar process of the maxilla in a child in the deciduous or mixed dentition. One premolar and molar region is most frequently affected. Enlargement is due to both fibrous enlargement of the gingiva and of the alveolar bone. The antrum is small, and the maxilla is distorted, although only rarely to the extent of causing facial asymmetry. Eruption of teeth in the affected area is delayed, and they are hypoplastic to varying degrees, with enlargement of the pulps, thin pitted enamel, an irregular pulp-dentine interface and many pseudoinclusions in poorly organised dentine, and pulp stones. Permanent successors, particularly the premolars, may be absent.

Some patients have facial vascular or epidermal naevi and the combination of **H**emimaxillary enlargement, **A**symmetry of the face, **T**ooth abnormalities, and **S**kin abnormalities has been referred to as HATS syndrome. The cause of segmental odontomaxillary dysplasia is probably a somatic mutation and mosaicism of the *PIK3CA* gene, though the *ACTB* gene has also been implicated. *PIK3CA* encodes a signalling protein and *ACTB* the cytoskeletal protein actin. Similar mutations are known to cause local tissue overgrowth including epidermal naevi, explaining these apparently unconnected features. Since the cause is a somatic mutation, the condition is not inherited.

Radiographically, there is a zone of bone sclerosis with a coarse, often vertically-orientated, trabecular pattern and loss of the cortex and missing and distorted teeth (Fig. 2.36). Histologically, the sclerotic zone consists of woven bone trabeculae in bland fibrous tissue and appears superficially similar to the regressing stage of fibrous dysplasia. Both radiographs and histology are therefore necessary for diagnosis.

Case series PMID: 21684782 and 29389339

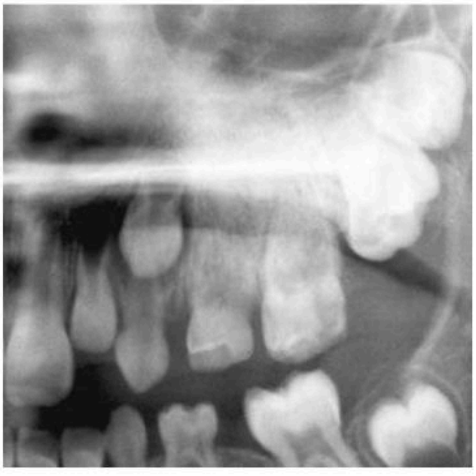


Fig. 2.36 Segmental odontomaxillary dysplasia. Showing abnormal upper primary molars that are indistinct against a background of even, coarsely trabecular bone. Permanent successors are absent.

OTHER SYSTEMIC DISEASES AFFECTING TEETH

Other metabolic disturbances

Rickets can cause hypocalcification of the teeth, but only if unusually severe (see Ch. 13).

Early-onset idiopathic hypoparathyroidism is rare. Ectodermal effects are associated. The teeth may therefore be hypoplastic with ridged enamel, short blunt roots and persistently open apices (Fig. 2.37). The nails may be defective, and there may be complete absence of hair. Patients with early-onset idiopathic hypoparathyroidism may later develop other endocrine deficiencies (polyendocrinopathy syndrome), and chronic oral candidosis may be the first sign (Ch. 15).

Hypophosphatasia. This rare genetic disorder can have severe skeletal effects as a result of failure of development of mature bone. There may also be failure of cementum formation causing early loss of teeth (Fig. 2.38). In milder forms, premature loss of the deciduous incisors is characteristic and occasionally the only overt manifestation of the disease.

Hypophosphatasia dental effects PMID: 19232125

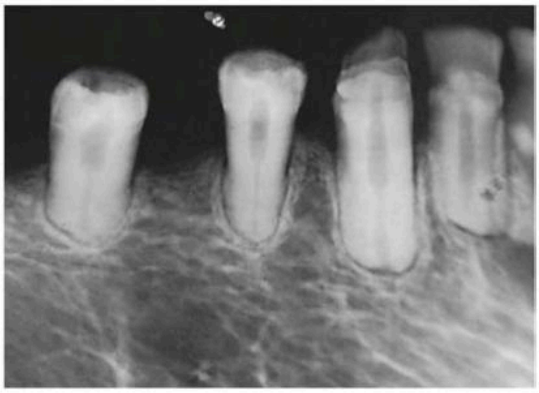


Fig. 2.37 Teeth in childhood hypoparathyroidism with short blunt roots, open apices and large pulp chambers.

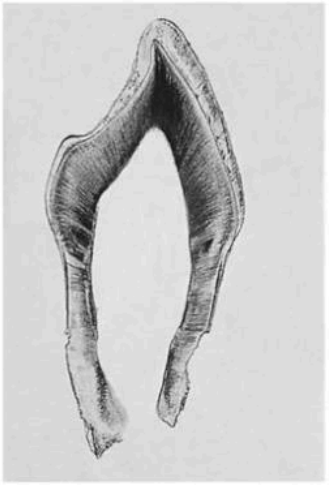


Fig. 2.38 Unstained ground section of a tooth in hypophosphatasia showing the enlarged pulp chamber and absence of cementum.

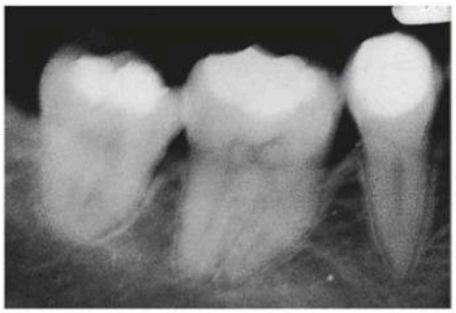


Fig. 2.39 Multiple pulp stones in a case of Ehlers–Danlos syndrome.

Ehlers–Danlos syndromes

This group of collagen disorders is characterised (to varying degrees) by hypermobile joints, loose hyperextensible skin, fragile oral mucosa and, in type VIII, early-onset periodontitis. There may also be temporomandibular joint symptoms such as recurrent dislocation (see main section in Ch. 14).

The main dental abnormalities are small teeth with short roots and multiple pulp stones (Fig. 2.39).

Gardner's syndrome (familial adenomatous polyposis)

The Gardner variant of familial adenomatous polyposis (often referred to as Gardner's syndrome) is characterised by multiple osteomas, especially of the jaws, colonic polyps and skin tumours. The majority of patients have dental abnormalities. These include impacted teeth other than third molars, supernumerary or missing teeth and abnormal root formation (Fig. 2.40). This syndrome is discussed and illustrated further in Chapter 12.

Colon carcinoma develops in almost all patients by middle age, and the mortality is high. The dental abnormalities can be detected in childhood or adolescence, and recognition of this syndrome may be life saving.

Epidermolysis bullosa

Epidermolysis bullosa is a genetic blistering disease of skin and mucosae (Ch. 16). Dental abnormalities include fine or coarse pitting defects, or thin and uneven enamel, which may also lack prismatic structure. The amelodentinal junction may be smooth. Dental defects vary in the different subtypes of the disease but are most frequent in the autosomal recessive, scarring type of epidermolysis bullosa in which there may be delayed, or failure of, eruption. The defects result from poor adhesion between ameloblasts during development.

Congenital syphilis ➔ Summary chart 2.1 p. 24

Prenatal syphilis, the result of maternal infection, can cause a characteristic dental deformity, described by Hutchinson in 1858.

If the fetus becomes infected at a very early stage, abortion follows. Infants born with stigmata of congenital syphilis result from later fetal infection, and only the permanent teeth are affected. The characteristic defects are usually seen in the upper central incisors.

The incisors (Hutchinson's incisors) are small, barrel-shaped and taper toward the tip (Fig. 2.41). The incisal edge sometimes shows a crescentic notch or deep fissure which forms before eruption and can be seen radiographically. An anterior open bite is also characteristic. The first molars may be dome-shaped (Moon's molars) or may have a rough pitted occlusal surface with compressed nodules instead of cusps (mulberry molars) (Fig. 2.42). These defects are often thought largely of historical interest, but congenital syphilis has reappeared in developed countries including the UK. Several hundred cases of congenital syphilis occur every year in the United States, and worldwide half a million infants die from it every year.

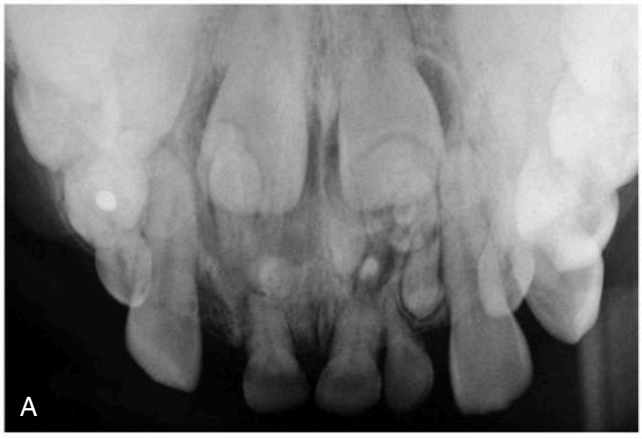


Fig. 2.40 Gardner's syndrome. Multiple unerupted abnormally formed supernumerary teeth. See also Fig. 12.8.

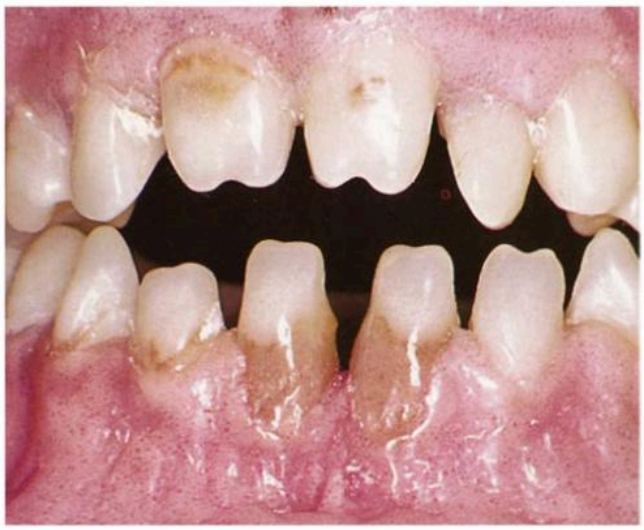


Fig. 2.41 Congenital syphilis: Hutchinson's teeth. The characteristics are the notched incisal edge and the peg shape tapering from neck to tip. *(From Cawson RA et al, 2001. Oral disease. 3rd ed. St Louis: Mosby.)*

The effects are due to infection of the dental follicle by *Treponema pallidum*. The postulated consequences are chronic inflammation, fibrosis of the tooth sac, compression of the developing tooth and distortion of the ameloblast layer. *T. pallidum* and inflammation are proposed to cause proliferation of the odontogenic epithelium, which bulges and kinks into the dentine papilla, causing the characteristic central notch.

Vitamin D-resistant rickets

This term is given to familial hypophosphataemia, a rare X-linked dominant disease that causes phosphate loss in the kidneys, and consequent rickets that does not respond to vitamin D. Patients have short legs, wide skull sutures and kyphosis develops during adulthood.

The teeth have abnormally large pulp chambers with fine extensions of the pulp horns to the tips of the cuspal dentine (Fig. 2.43). These are prone to exposure by attrition or fracture and are often invisible radiographically. A periapical granuloma on an apparently normal tooth is a common presentation.

Calcification of dentine is defective. The typical inter-globular mineralisation of rickets is seen throughout the dentine.

EXTRINSIC AGENTS AFFECTING TEETH

➔ Summary chart 2.1 p. 24

Drugs

Tetracycline pigmentation

Tetracycline is taken up by calcifying tissues, and the band of tetracycline-stained bone, dentine or enamel fluoresces bright yellow under ultraviolet light.

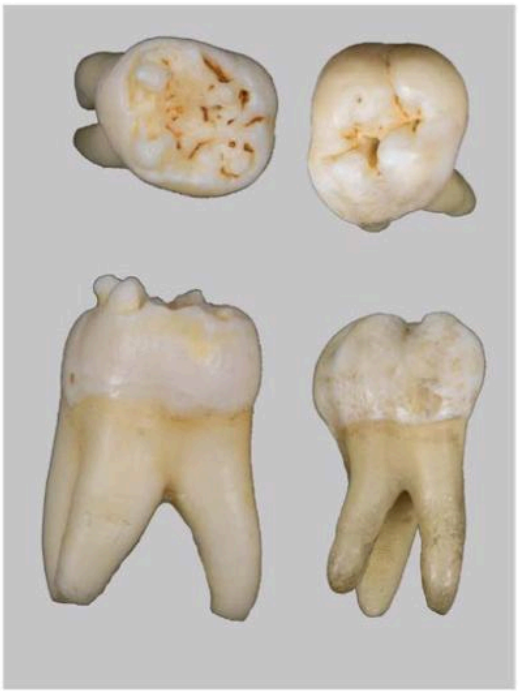


Fig. 2.42 Congenital syphilis: Molars. The molar on the left is a mulberry or Fournier molar with cusps surrounded by a hypoplastic groove producing a knobbly surface. That on the right is a Moon's molar, with a smooth rounded crown that tapers toward the occlusal surface. *(Copyright Museums at the Royal College of Surgeons.)*

The teeth become stained only when tetracycline is given during their development, and it can cross the placenta to stain the developing teeth of the fetus. More frequently, permanent teeth are stained by tetracycline given during infancy. Tetracycline is deposited along the incremental lines of the dentine and, to a lesser extent, of the enamel.

The more prolonged the course of treatment, the broader the band of stain and the deeper the discoloration. The teeth are at first bright yellow but become a dirty brown or grey (Figs 2.44 and 2.45). The stain is permanent, and when the permanent incisors are affected, the dark appearance can only be disguised. When the history is vague, the brownish colour of tetracycline-stained teeth must be distinguished from dentinogenesis imperfecta. In dentinogenesis imperfecta, the teeth are obviously more translucent than normal and, in many cases, chipping of the enamel from the dentine can be seen. In tetracycline-induced defects, the enamel is not abnormally translucent and is firmly attached to dentine. In very severe cases, intact teeth may fluoresce under ultraviolet light. Otherwise, the diagnosis can only be confirmed by linking the developmental age of the affected teeth to timing of exposure or after a tooth has been extracted. In an undecalcified section, the yellow fluorescence of the

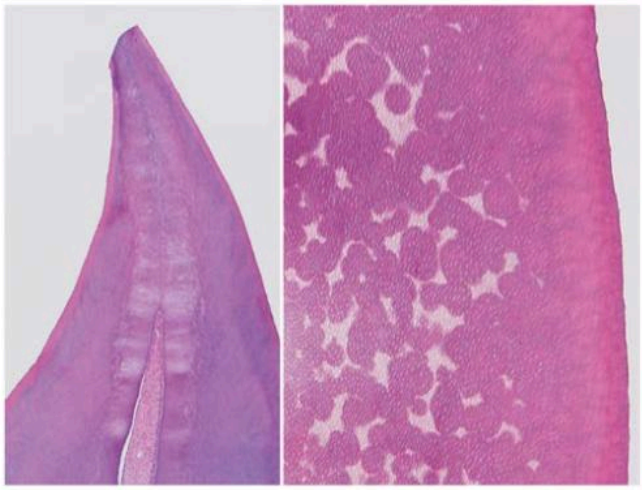


Fig. 2.43 Vitamin D-resistant rickets. A fine pulp extension into the incisal tip dentine is just visible on the left. Right, at higher power, there is prominent globular mineralisation of dentine.

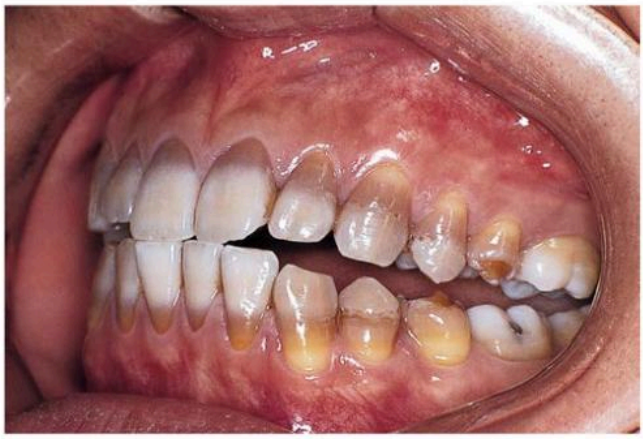


Fig. 2.44 Tetracycline staining. Note the chronological distribution of the dark-brown intrinsic stain.

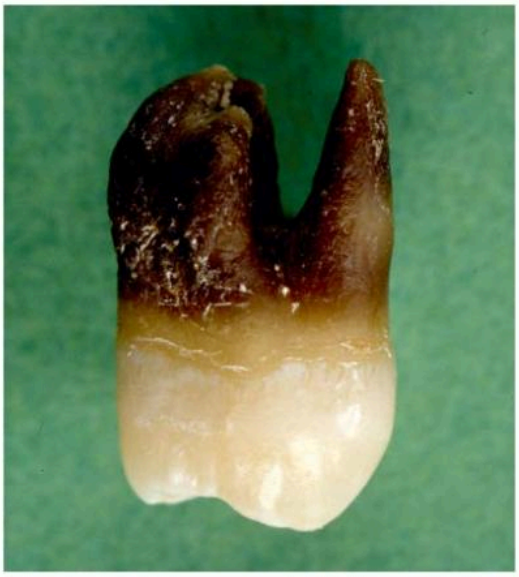


Fig. 2.45 Minocycline staining. Now one of the commoner forms of tetracycline staining since administration in childhood is controlled, limited to third molar roots from use of minocycline for acne during adolescence.

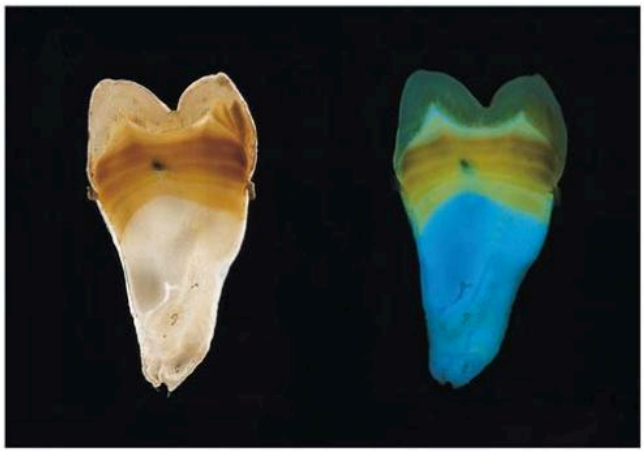


Fig. 2.46 Tetracycline pigmentation. Ground (undecalcified) section (*left*) shows the broad bands of tetracycline deposited along the incremental lines of the dentine; (*right*) same section viewed under ultraviolet light shows fluorescence of the bands of tetracycline.

tetracycline deposited along the incremental lines can be easily seen (Fig. 2.46).

It is no longer necessary to give tetracycline during dental development. There are equally effective alternatives, and it should be avoided from approximately the fourth month to at least the 12th year of childhood, ideally the 16th year. Nevertheless, tetracycline staining is still seen.

Tetracyclines that achieve a high blood level may still stain apparently fully formed teeth, for example minocycline may darken teeth in which there is reactionary dentine formation following trauma.

Minocycline stain PMID: teeth 23887527 and bone 7614206

Cytotoxic chemotherapy

Increasing numbers of children are surviving malignant disease, particularly acute leukaemia, as a result of cytotoxic chemotherapy.

Box 2.4 Dental fluorosis: distinctive features

- Clinically evident fluorosis limited to areas where fluorides in water exceed approximately 2 parts per million
- Only those who have lived in a high-fluoride area during dental development show mottling
- The defect is not acquired by older visitors to the area
- Permanent teeth are affected; mottling of deciduous teeth is rare
- Mottled teeth are less susceptible to caries than normal teeth from low-fluoride areas
- A typical effect is spotty paper-white enamel opacities
- Brown extrinsic staining of these patches may be acquired after eruption

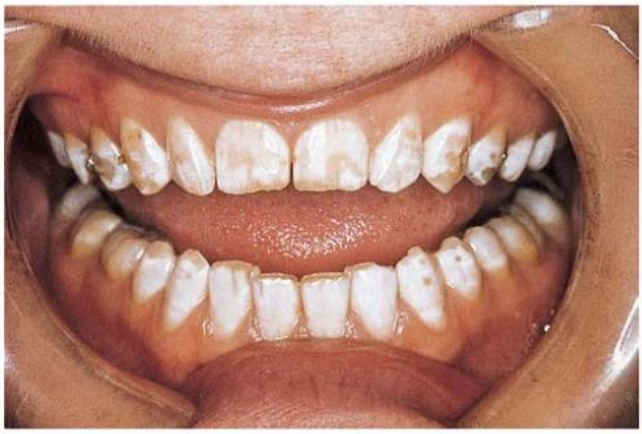


Fig. 2.47 Fluoride mottling. In this case, from an area of endemic fluorosis, there is generalised opaque white mottling with patchy enamel hypoplasia. Note the resemblance to the hypomaturation type of amelogenesis imperfecta.

Among survivors, teeth that develop during treatment may have short roots, hypoplasia of the crowns and enamel defects. Microscopically, incremental lines may be more prominent, corresponding to growth arrest or delay during the period of chemotherapy. In extreme cases, tooth formation may be aborted so that oligodontia results.

Fluorosis ➔ Summary chart 2.1 p. 24

Mottled enamel is the most frequently seen and most reliable sign of excess fluoride in the drinking water. It has distinctive features (Box 2.4). The highest fluoride levels completely disrupt amelogenesis, producing hypoplastic patches. Lower levels inhibit mineralisation and prevent enamel maturation.

Clinical features

Mottling ranges from paper-white matt patches to opaque, brown, pitted and brittle enamel. Clinically, it may be difficult to distinguish fluorotic defects from amelogenesis imperfecta when the degree of exposure to fluoride is unknown (Figs 2.47–2.49).

There is considerable individual variation in the effects of fluorides. A few patients acquire mottling after exposure to relatively low concentrations (Fig. 2.50), while others exposed to higher concentrations appear unaffected. Being a systemic effect, fluorosis is bilateral and usually affects all teeth, though a chronological pattern could result from a