The Infectious Diseases Manual

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Introduction

Chapter 1

Introduction

There have been many changes in the practice of microbiology and clinical infectious diseases since the first edition of this manual was published in 1995. Molecular techniques, which had only recently been discovered, are now in routine use. New antivirals and a new understanding of viral kinetics have revolutionized HIV care, and clinical guidelines, which were few and far between then, are now available in almost every area. Antibiotic-resistant organisms become more prevalent month by month, and for the first time in decades drugs from totally novel classes of antibiotics have been licensed. We were very encouraged by the positive response given to the first edition of the *Manual* by working clinicians, and we believe that there is even more need now for a convenient and portable source of detailed and practical information on all aspects of infectious diseases and microbiology.

For the second edition, the entire text of the manual has been carefully revised. Some sections, such as the chapter about HIV infection, have been completely rewritten. Our aim has been to produce a handbook that every SpR in infectious diseases will want in their white-coat pocket for consultant ward rounds, and every SpR in microbiology will keep by the telephone in the reporting room. As before, common conditions are described in detail. The clinical presentation of rarely seen and usually tropical conditions is described in sufficient detail to allow their recognition, whereas their treatment, which would always be a matter for specialist referral, is described in outline only. Some areas have been given a more detailed treatment than their frequency might suggest, either because of their potential significance, or because we think they are interesting. Some areas of specialist interest have been described in more detail, because patients with neutropenia or HIV may present outside their usual units, and specialist help may not always be immediately available.

We have not attempted to reference the manual comprehensively, but we have tried to demonstrate its evidence base by including key references such as national guidelines, recent authoritative reviews, or unique papers that have significantly changed practice. We have also included many useful website addresses which satisfy the same criteria and which are likely to remain accessible during the life of this edition (in general we have omitted the prefix http:// to save space).

To make the best use of space, we have used symbols and abbreviations, defined on the following pages. Throughout the text, the symbol (➢000) indicates that further information is available on that particular page.

Tables of antibiotics, doses and side effects are located in section IV. Whilst every care has been taken to ensure that these tables contain no errors, we cannot accept responsibility for any that have occurred. We regard it as good practice for prescribers to check the dose of any drug with which they are unfamiliar by reference to the manufacturer's data sheet or the *British National Formulary*.

bnf.vhn.net/home/

Abbreviations

Abbreviations which are used only within one or two sections of the manual are defined therein. Abbreviations listed here are those that are used many times throughout the manual.

AFB	acid-fast bacillus
AIDS	acquired immune deficiency syndrome
ARDS	adult respiratory distress syndrome
ASOT	anti-streptolysin O titre
BAL	broncho-alveolar lavage
BT	bioterrorism
CAPD	chronic ambulatory peritoneal dialysis
CCDC	Consultant in Communicable Disease Control
CDSC	Communicable Disease Surveillance Centre (Colindale)
CF	cystic fibrosis
CMI	cell-mediated immunity
CMV	cytomegalovirus
CNS	central nervous system
CNSt	coagulase-negative staphylococcus
COAD	chronic obstructive airways disease
CSF	cerebrospinal fluid
CT	computed tomography (scan)
CXR	chest X-ray
DIC	disseminated intravascular coagulation
EBV	Epstein–Barr virus
ECHO	echocardiogram
ELISA	enzyme-linked immunosorbent assay
ENT	ear, nose and throat
ERCP	endoscopic retrograde cholecystopancreatogram
FBC	full blood count
G6PD	glucose-6-phosphate dehydrogenase
GAS	group A β-haemolytic streptococcus
GI	gastrointestinal
GN	glomerulonephritis
h	hour
HAV	hepatitis A virus
HBV	hepatitis B virus
HCV	hepatitis C virus
HD	% drug removed by haemodialysis
HDV	hepatitis D virus
HEPA	high-efficiency particulate arrester
HHV-6	human herpes virus type 6
Hib	*Haemophilus influenzae* type b
HIG	normal human immunoglobulin
HIV	human immunodeficiency virus
HLGR	high-level gentamicin-resistant
HSV	herpes simplex virus
IA	invasive aspergillosis
ICU	intensive-care unit
id	intradermal
IE	infective endocarditis
IFAT	indirect fluorescent antibody test
im/IM	intramuscular
ip	intraperitoneal
IUD	intrauterine device
iv/IV	intravenous
IVDU	intravenous drug use(r)
LP	lumbar puncture
LRTI	lower respiratory tract infection
MAI	*Mycobacterium avium-intracellulare*
MBC	minimum bactericidal concentration
MDa	megadalton
MIC	minimum inhibitory concentration
min	minute
MOSF	multi-organ system failure
MRI	magnetic resonance imaging
MRSA	methicillin-resistant *Staphylococcus aureus*
MSU	mid-stream urine
MW	molecular weight
NSAID	non-steroidal anti-inflammatory drug
PCP	*Pneumocystis carinii* pneumonia
PD	% drug removed by peritoneal dialysis
PHLS	Public Health Laboratory Service
PID	pelvic inflammatory disease
po	orally (per os)
PUO	pyrexia of unknown origin
PVE	prosthetic valve endocarditis
RSV	respiratory syncytial virus
RUQ	right upper quadrant
SBC	serum bactericidal concentration
sc	subcutaneous
SLE	systemic lupus erythematosus
SRSV	small round structured virus
STD	sexually transmitted disease

TB	tuberculosis
TPHA	*Treponema pallidum* haemagglutination assay
TSS(T)	toxic shock syndrome (toxin)
URTI	upper respiratory tract infection
USS	ultrasound scan
UTI	urinary tract infection
VDRL	Venereal Disease Research Laboratory (syphilis)
VHF	viral haemorrhagic fever
VZV	varicella zoster virus
WBC	white blood cell (count)
WHO	World Health Organization
ZN	Ziehl–Nielsen

Symbols

Symbol	Meaning	Further details
➢	Refer to page number	
☎	Discussion with microbiology/specialist referral recommended	
🔔	Antibiotic level assay required	➢388
Σ	Cases per annum reported in England and Wales	
✈	Test performed by a reference laboratory	
✉	Notifiable disease	➢7
①	Standard isolation	➢8
②	Body fluids isolation	➢8
③	Infection risk from blood isolation	➢8
④	Strict isolation	➢8
✓	Antibiotic penetrates this fluid (e.g. CSF✓)	
✗	Antibiotic does **not** penetrate this fluid (e.g. CSF✗)	
💻	Internet resource—usually a website address (the prefix http:// is omitted to save space)	
🗝	Key reference. Usually a national guideline, a recent authoritative review, or a unique paper that has significantly changed practice	
☠	Organisms which are a hazard to laboratory staff	
📄	See manufacturer's data sheet	

✉ Notifiable diseases

In England and Wales, the following diseases must be notified to the local authority, via the local consultant in communicable disease control (CCDC).

Acute encephalitis	(➢101)	Paratyphoid fever	(➢280)
Acute poliomyelitis	(➢348)	Plague	(➢305)
Anthrax	(➢263)	Rabies	(➢357)
Cholera	(➢285)	Relapsing fever	(➢326)
Diphtheria	(➢268)	Rubella	(➢127)
Dysentery (amoebic or bacillary)	(➢209)	Scarlet fever	(➢135)
Food poisoning	(➢57)	Smallpox	(➢341)
Leprosy	(➢46)	Tetanus	(➢315)
Leptospirosis	(➢327)	Tuberculosis	(➢38)
Malaria	(➢211)	Typhoid fever	(➢280)
Measles	(➢126)	Typhus	(➢329)
Meningitis	(➢96)	Viral haemorrhagic fever	(➢206)
Meningococcaemia	(➢185)	Viral hepatitis	(➢70)
Mumps	(➢128)	Whooping cough	(➢136)
Ophthalmia neonatorum	(➢107)	Yellow fever	(➢352)

Chickenpox (➢130) is a notifiable disease in Scotland. Certain other diseases may be made **locally** notifiable.

Isolation

Isolation is a key technique for preventing spread of infectious diseases in hospitals. It can be physically and emotionally disturbing, and disruptive of clinical care, and therefore should only be used where there is proven or likely benefit. Strong evidence of efficacy is available for some infections including MRSA, tuberculosis and multiply-resistant coliforms. Isolation policies are made at individual hospitals, and local protocols should always be consulted. If these are not available, consult your microbiologists ☎ and infection control team. We have not included detailed instructions for medical and nursing procedures for the surveillance, control and prevention of infection in hospital; we refer readers searching for this information to the excellent handbooks and comprehensive reference texts that cover nosocomial infection control. Systematic reviews of the evidence for infection control interventions are being published, e.g.

www.epic.tvu.ac.uk

www.cdc.gov/ncidod/hip

Source isolation is designed to prevent infected patients from transmitting their disease to others. It may generally be considered in four categories:

Level of isolation	Examples	Route	Main suggested precautions
SUP (standard universal precautions)	All patients		Aprons, gloves and handwashing, but no need for separate room. Aprons and gloves should be used whenever there is the possibility of contact with patients' body fluids, and hands should be cleaned after every patient contact, irrespective of the diagnosis. These simple measures form the backbone of infection control in hospital
① Standard	*Neisseria meningitidis*, Group A β-haemolytic streptococci	Airborne or direct contact	Separate room. Negative pressure ventilation if available. Aprons, gloves ± masks for all entering room
② Body fluids	*Salmonella* spp., *Shigella* spp., multiply-resistant *Acinetobacter* spp.	Contact with urine, faeces and secretions	Separate room. Aprons and gloves for patient contact
③ Infection risk from blood	Hepatitis B, HIV	Contact with blood or blood-stained body fluids*	Separate room only required if patients are bleeding, likely to bleed, undergoing major invasive procedure, incontinent or confused. Plastic aprons, gloves (±visors) for procedures where contact with body fluids is possible
④ Strict	Lassa fever	Airborne or direct contact	Strict isolation in specialist unit—usually regional infectious diseases centre. **Do not send any specimens without discussion with lab**

*Including CSF, pleural fluid, vaginal secretions, peritoneal fluid, synovial fluid, semen, pericardial fluid, amniotic fluid and breast milk.

Throughout text, recommended levels of isolation are indicated by the use of symbols (e.g. ④).

Protective isolation is used to prevent immunocompromised patients from acquiring infection. It is of less certain value, particularly as most infections in neutropenic patients are endogenous (➢174). Most units concentrate on protecting against specific organisms, e.g. nursing in HEPA-filtered air (vs. aspergillosis), antibiotic prophylaxis and microbiologically clean food (to avoid colonization with new strains of Gram-negative bacteria).

Recommendations for isolation

For category codes ➢8.

Disease	Category	See
Anthrax ✉	SUP	263
Bordetella pertussis[1] ✉	①	136
Borrelia recurrentis[2] ✉	①	326
Bronchiolitis (RSV)[24]	①	23
Campylobacter jejuni[3]	②	288
Candida spp.[4]	②	367
Chickenpox ✉[6]	①	130
Chlamydia trachomatis[5]	②	329
(ophthalmia neonatorum ✉, conjunctivitis, genital infection)		
Cholera[7] ✉	②	285
Clostridium difficile[8]	②	63
Coxsackievirus[9]	②	349
Cryptosporidium parvum	②	230
Dermatitis[10] (severely infected)	①	111
Diarrhoea of unknown cause[12]	②	57
Diphtheria[11] ✉	①	268
Dysentery ✉		
Amoebic[13] or bacillary[14]	②	209
Ebola virus ✉	④	206
Eczema[10] (severely infected)	①	111
Encephalitis ?cause ✉	①	101
Erysipelas[10]	①	113
Erythema infectiosum	①	135
Escherichia coli diarrhoea, travellers' diarrhoea, haemolytic uraemic syndrome (O157, VTEC, EIEC, EPEC, EAggEC, ETEC, etc.)	②	275
Exanthem subitum	①	134
Food poisoning ✉		
Undiagnosed cause[12]	②	57
Campylobacter jejuni[3]	②	
Salmonella[15]	②	
Francisella tularensis[15]	①	307
Gastroenteritis, viral	②	350
Giardiasis	②	218
Gonococcal conjunctivitis[1]	②	86
Haemolytic streptococcus[10]	①	254
Lancefield group A, B[3], C or G (*Streptococcus pyogenes*)		
Hepatitis ?cause ✉	②	
Hepatitis A	②	70
Hepatitis B, fulminant liver failure of undetermined cause	③	70
Hepatitis C	③	73
Herpes simplex[17]	①	334
Herpes zoster[6]	①	130
HIV	③	143
Impetigo[10]	①	111
Lassa fever ✉	④	206
Leprosy ✉		46
Smear negative	—	
Smear positive	①	
Leptospirosis[1] ✉	②	327
Lice, fleas[1]	②	94
Listeriosis[18]	②	267
Marburg virus disease ✉	④	206
Measles[19] ✉	①	126
Melioidosis[15]	①	293
Meningitis ✉		
Neisseria meningitidis[1]	①	96
(including meningococcal septicaemia/other invasive meningococcal infections)		
Neonatal	②	139
Viral[9]	①	100
Meningoencephalitis, acute (acute poliomyelitis) ✉	①	348
MRSA[20]	①	251
Multiply-resistant Gram-negative bacteria[20]	②	
Mumps[9] ✉	①	128
Ophthalmia neonatorum[1] ✉	②	107
Parvovirus B19	①	135
Penicillin-resistant *Streptococcus pneumoniae*[11]	①	261
Pertussis[1] ✉	①	136
Plague ✉	④	305
Poliomyelitis, acute ✉	①	348
Pseudomonas pseudomallei[15]	①	293

(*continued*...)

Disease	Category	See
Psittacosis	①	329
PUO[21]	①	179
Rabies ✉	④	357
Ratbite fever[1]	②	306
Relapsing fever[2] ✉	①	326
Respiratory syncytial virus[24]	①	23
Rotavirus	②	350
Rubella[16] ✉	①	127
Salmonellosis[15] (excluding typhoid and paratyphoid)	②	57
Scabies[1]	①	95
Scarlet fever[10] ✉	①	135
Smallpox[22] ✉	④	341
Streptococcus pyogenes—see Haemolytic streptococcus		
Syphilis (1° or 2° only)[1]	②	89
Tapeworms	②	237
Tuberculosis[23] (open pulmonary, wound, urinary) ✉	①	38
Tularaemia[15]	①	307
Typhoid, paratyphoid and carriers[7] ✉	②	280
Typhus[2] ✉	①	329
Vaccinia, generalized	④	341
Vancomycin-resistant Gram-positive organisms[20] (usually *Enterococcus faecalis* or *faecium*)	①	262
Varicella ✉[6]	①	130
Vibrio parahaemolyticus[15]	②	287
Viral haemorrhagic fever ✉	④	206
Whooping cough[1] ✉	①	136
Yersinia enterocolitica and *pseudotuberculosis*[15]	②	284

[1] For first 24 h of treatment. [2] Until patient and contacts deloused. [3] Neonates only. [4] If part of proven outbreak. [5] For first 48 h of treatment. [6] Until vesicles are crusted and dry. Staff in contact should be immune. Notifiable in Scotland. [7] Until asymptomatic with three negative stool cultures. [8] Until asymptomatic for 3 days. [9] For 10 days after onset. [10] Until cultures known to be negative for β-haemolytic streptococci. [11] Until culture negative. [12] Until transmissible pathogens excluded. [13] Until asymptomatic and treated for cyst carriage. [14] Until asymptomatic and one negative stool culture. [15] Until asymptomatic. [16] Until 7 days after onset of rash. [17] Only for infants with disseminated infection. [18] Infants and mothers only. [19] Until 4 days after onset of rash. [20] Until agreed by microbiologist. [21] If outside Europe and N. America within 4 weeks. [22] Even if only suspected. [23] For first 14 days of therapy. [24] Cohorting on children's ward whilst symptomatic.

Microbiological specimens

Getting the best out of your microbiology service depends on . . .

- Collecting the right specimens in the right way, before starting antibiotics
- Always giving the lab full clinical details
- Discussing unusual specimen requirements, and unusual or unexpected results

Details of **sample collection** and transport vary from laboratory to laboratory, but a general summary of principles follows. Laboratories differ (based on local prevalence) on whether they routinely perform certain tests on particular specimens (e.g. *Clostridium difficile* toxin on all faeces). The importance of listing **full clinical details** has been emphasized throughout this book. **Always** give details of recent hospital in-patient stays and travel, and also occupation if the patient has diarrhoea or skin infection and works in catering, school or hospital. Similarly, **details of past, current and intended antibiotic therapy** are valuable for interpretation of many culture results. **Virus culture** is usually only worth attempting early in the course of infection. Specimens for **culture of bacteria and fungi** should always be taken **before antibiotic therapy is commenced**; sputum, mucosae and open wounds become colonized particularly rapidly with resistant bacteria.

- **Screening of contacts, or of cases for clearance**, is only occasionally useful for any pathogen out of hospital, and should always be done only according to locally written policies or after discussion with a microbiologist, ID physician or CCDC.
- Specimens are always best transported immediately to the laboratory. If delay is necessary, **in general all samples should be refrigerated at 4°C**, except inoculated blood culture bottles, which should be incubated at 37°C.

Swabs, tissue and pus

Send pus, if available, in a sterile universal container, because additional rapid tests can be performed (e.g. HPLC for short-chain fatty acids from anaerobes); a swab is an inferior substitute upon which delicate organisms die. Use firm pressure when taking swabs and always use the appropriate swab transport medium (bacterial, viral, chlamydial). Inclusion of charcoal in transport media or swab tips increases recovery of many bacteria, especially *Neisseria gonorrhoeae*. Use special **pernasal swabs** for *Bordetella pertussis*. Gonococcal culture plates are best inoculated at the bedside. Surface swabs of deeply infected lesions (e.g. sinus tracks from osteomyelitis) usually grow surface contaminants (e.g. coliforms and pseudomonads) and rarely grow the causative organism. Only isolation of *Staphylococcus aureus* from this type of specimen correlates with true deep infection. Culture of bone marrow, liver biopsies etc. is occasionally useful, but should be discussed in advance with a microbiologist. Samples from drainage bags (e.g. biliary, wound, nephrostomy) are not representative of the microbial population within the patient; cultures are frequently overgrown with commensal bacteria, especially *Bacillus* spp. Take samples of freshly drained fluid from close to the patient.

Medical devices

The tips of iv catheters suspected of being infected should be cut off with alcohol-wiped scissors and sent in a sterile universal container for semiquantitative culture. Growth of >15–20 colonies of coagulase-negative staphylococci or diphtheroids suggests infection, and any growth of other bacteria or fungi is likely to be significant. Small infected prostheses (e.g. heart valves) can be sent entire, but it is best to scrape adherent material from larger prostheses and send that.

Urine

Prepuce and labia should be held away from the urine stream, but periurethral cleaning does not additionally reduce contamination of MSUs from adults as long as the initial stream is discarded. Most laboratories supply universal containers with borate preservative, or dip-slides for urine collection in domiciliary practice. The former preserves both host and bacterial cells for 48 h. Dip-slides should be only dipped into urine, and the transport container should not

be filled with it. Catheter urine specimens should be taken by aseptic puncture of the sampling area close to the patient. Culturing urinary catheter tips is a waste of time. Paediatric bag collection systems are often contaminated, but this is reduced by cleaning the perineum with antiseptic; a negative culture is useful, but positive results must be interpreted with care. Suprapubic aspiration is the gold standard for detecting bladder urine infection. Early morning urine (EMU) specimens for AFB microscopy and culture should be ≈150 mL volumes, and taken on different days.

Sputum

Efforts, such as vigorous physiotherapy, to obtain expectorated sputum before antibiotics have been given improve the isolation rate of pneumococci and other significant pathogens. Three samples on successive days are needed to exclude open pulmonary tuberculosis. Broncho-alveolar lavage is the most sensitive diagnostic procedure, but induced sputum is simpler, with adequate sensitivity for *Pneumocystis carinii* diagnosis. In ventilated patients, non-directed lavage allows recognition of significant isolates by quantitative culture ($>10^5$/mL).

Faeces

A walnut-sized sample is needed; this is most easily collected by passing stool onto folded toilet paper in the lavatory bowl, and scooping the sample into a universal container with a spatula attached to the inside of the lid. The best chance of isolating causative agents of acute diarrhoea is on the first sample, and only if it is taken early in the course of illness. Many pathogens are only transiently excreted (e.g. *Escherichia coli* O157), so multiple samples are only required for exclusion of some parasites (e.g. *Giardia*) and to detect carriage of typhoid bacilli in food handlers (➢63). 'Hot' stool samples for visualization of trophozoites of *Entamoeba histolytica* are only useful if the patient has dysentery, i.e. bloody diarrhoea.

Blood cultures

Blood cultures should be taken from any patient who is systemically ill in whom an infective diagnosis is being considered. Before venepuncture, the skin should be carefully disinfected with an alcoholic antiseptic, which is allowed to dry. Most laboratories now use automated blood culture systems, which come with instruction sheets and should be inoculated with the specified volumes of blood (both over- and under-inoculation impair performance). Check the expiry date on the bottles and do not use if cloudy. Modern systems have greatly improved efficiency, and 2–3 cultures are sufficient for all indications, except when the patient has received antibiotics recently. In this case, when IE is suspected, it is worth taking two cultures on day 1, and daily cultures for the next 3–4 days. It is not necessary to change needles before injecting the culture bottles. It is often recommended to inoculate small volumes of normally sterile fluids (e.g. CAPD, ascitic, joint) to blood culture bottles. Unfortunately, blood culture broths are optimized for bacterial recovery only when blood is included, and other laboratory procedures become impossible (e.g. microscopy, incubation at different temperatures and atmospheres, mycobacterial culture). Always also send some fluid in a sterile universal container or capped syringe if blood culture broths are inoculated.

CSF

Best taken in three consecutively labelled bottles, and transported immediately to the laboratory. Take simultaneous blood glucose. For a reasonable chance of detecting AFB, 10 mL or more CSF is required.

Serum

Listing the **times of doses and samples** is important for interpretation of antibiotic assays. Specifying the **date of onset of illness** is vital for choosing and interpreting serological tests; acute and convalescent (10–14 days later) sera are often needed to prove recent infection. Most laboratories will store many such sera, issue a request for a convalescent sample, and only perform the assays (in parallel) if a later serum is received. IgM assay diagnosis on single acute sera is possible for some infections (e.g. *Mycoplasma*, *Rubella*, hepatitis viruses, *Toxoplasma*), and very high single titres are

diagnostic for others (e.g. *Legionella*, respiratory *Chlamydia*, *Coxiella*). **Exposure history** and **date of leaving the endemic area** are essential for performance of tests for many geographically-restricted infections (e.g. brucellosis, schistosomiasis).

Molecular tests

Local protocols for sampling and transport should always be followed. Care with these stages is as important as for conventional diagnostic testing if potential cross-reactions and inhibition of PCRs are to be avoided. Details of construction of the swab and of the composition of the transport medium may affect the sensitivity and specificity of the result. EDTA blood samples are preferred by many laboratories, but these bottles are frequently contaminated with pseudomonads.

Section II

Clinical Infectious Diseases

Chapter 2

Upper respiratory tract infections

Sinusitis

Most often affects the maxillary sinuses. May be acute or chronic and recurrent. Complications are due to the proximity of the orbits and intracranial structures.

Risk factors: Frequently secondary to: acute viral URTI, complicating ≈0.5% of childhood URTIs. Dental sepsis or procedures, nasal polyps or deviated septum. Rarely, immunodeficiency (AIDS, IgG, IgA deficiency), cystic fibrosis, immotile cilia syndrome.

Clinical features: Facial pain, fever and purulent nasal discharge. Headache, nasal obstruction, halitosis, toothache and anosmia may occur. Cough is frequent in children.

Organisms: Acute: *Streptococcus pneumoniae*, *Haemophilus influenzae*, viruses, *Moraxella catarrhalis*, rarely *Staphylococcus aureus*. **Chronic:** *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Streptococcus 'milleri'*, mixed oral anaerobes, *Staphylococcus aureus*.

Microbiological investigations: Nasal swabs are **not** helpful. Sinus aspiration to obtain material for Gram staining and culture for persistent or recurrent infections.

Other investigations: Severe or persistent infection merits sinus X-rays. Fluid level or opacity suggest acute infection. Complete opacity or mucosal thickening alone may be seen in chronic infection. CT, MRI are more sensitive.

Differential diagnosis: Consider immunodeficiency, rare non-infectious causes (Wegener's, carcinoma, lymphoma) unusual infections (TB, leprosy, syphilis).

Antibiotic management: Amoxicillin or co-amoxiclav or cefuroxime, but dubious clinical efficacy.

Supportive management: Nasal decongestants: oxymetazoline hydrochloride nasal spray, 0.05%, 1–2 sprays each nostril 8hly, or pseudoephedrine hydrochloride, 60 mg 8hly, po. ENT referral for persistent or recurrent infection.

Complications: Rare but serious. Orbital cellulitis (➢109), osteomyelitis of facial bones (➢123), intracranial abscess (➢103), meningitis (➢96), cavernous and superior sagittal sinus thrombosis, orbital fissure syndrome (sphenoid sinus).

Comments: Chronic recurrent sinusitis reflects impaired drainage from the sinuses and merits ENT referral. Infection is usually due to mixed aerobic and anaerobic oral flora and responds poorly to antibiotic therapy alone. Immunocompromised patients may develop fungal sinusitis (*Aspergillus* spp., *Mucor* spp. and relatives ➢369). Urgent ENT referral is required.

Otitis media (OM)

Risk factors: Frequently follows URTI. Common in children because of short, straight Eustachian tubes and blockage secondary to lymphoid hyperplasia.

Clinical features: Fever and earache. Otorrhoea if perforation has occurred. Presentation may be non-specific in infants. Tenderness over the mastoid process and redness and bulging of the tympanic membrane, which may have perforated.

Organisms: *Streptococcus pneumoniae*, non-capsulate *Haemophilus influenzae*, *Moraxella catarrhalis*; ≈30% are viral, frequently due to respiratory syncytial virus. *Staphylococcus aureus*, *Mycoplasma pneumoniae*, and GAS are seen rarely. Chronic infection may proceed to cholesteatoma with involvement of *Proteus* spp. and pseudomonads.

Microbiological investigations: In uncomplicated cases, none.

Antibiotic management: Role of antibiotics controversial. Distinguish between acute OM with fever, otalgia and erythema of tympanic membrane, which may merit antibiotics, and chronic OM with effusion, which does not. Chronic suppurative OM with perforation has a different microbial aetiology and requires ENT referral.

Goal of therapy in acute OM is to reduce the duration of pain and to prevent complications (mastoiditis, meningitis, intracranial abscess) In the pre-antibiotic era, these affected up to 40%, but they are now very rare. Spontaneous recovery occurs in ≈80% of acute OM without antibiotics. Systematic review suggests small benefit from antibiotics, especially in prevention of complications. We recommend giving antibiotics for acute OM; they can be withheld in patients over 2 years, who are not systemically unwell, have normal host defences and who are likely to return for follow-up assessment at 48 h. If not improved at 48 h, commence antibiotics. All authorities agree that children under 6 months should receive antibiotics. Amoxicillin is the drug of choice (erythromycin if allergic).

Supportive management: Analgesia.

🗝 Schloss MD, Can Respir J 1999; 6 (Suppl. A): 51A

Otitis externa

A hypersensitivity reaction of the skin lining the external auditory canal. Symptoms include itching, pain and a feeling of fullness. On otoscopy, oedema and redness of the walls of the meatus. Often responds to careful cleansing and topical steroids. If infection is present, it is usually mixed due to diphtheroids, pseudomonads and coliforms. Neomycin and hydrocortisone drops may be used. If there is evidence of local skin infection, such as a boil, flucloxacillin is given. Perforation must be excluded before drops are prescribed. *Aspergillus* and other fungal infections are best treated with clotrimazole drops.

Malignant otitis externa is a rare infection usually with *Pseudomonas aeruginosa* which affects diabetics and the immunocompromised. It has a significant mortality, due to infection of adjacent bone and soft tissue, and requires aggressive systemic treatment with anti-pseudomonal antibiotics and surgical debridement. Urgent ENT referral is essential.

Dental and oral infections

Dental caries is related to acid production from fermentation of dietary carbohydrates by bacteria, including *Streptococcus mutans* and lactobacilli. Its significance for the physician lies in its effects on nutrition and as a risk factor for gingival disease, dental abscesses and Vincent's angina.

Vincent's angina

Risk factors: Poor oral hygiene, poor nutrition, smoking and severe intercurrent illness.

Clinical features: Oral pain, gingival bleeding, halitosis, fever and anorexia. On examination there is necrosis and pseudomembrane formation on tonsils and gums. There may be local lymphadenopathy and excess salivation.

Organisms: Mixed infection due to *Leptotrichia* spp., *Bacteroides* spp. and *Fusobacterium* spp.

Differential diagnosis: Candidiasis (➢367), herpes simplex stomatitis (➢129), diphtheria (➢268).

Microbiological investigations: Gram stain of scrapings from the affected area. Throat swab for *Candida albicans* and *Corynebacterium diphtheriae* if suspected.

Antibiotic management: Penicillin V/amoxicillin + metronidazole **or** co-amoxiclav.

Supportive management: Attention to oral and dental hygiene.

Complications: In the severely malnourished or immunocompromised patient progression to noma, a severe gangrenous stomatitis, may occur rarely.

Practice point

Patients with agranulocytosis may present with severe oral and pharyngeal ulceration due to *Candida* spp., herpes simplex or *Capnocytophaga* spp. infection, which may subsequently act as a portal of entry for oral streptococcal bacteraemia.

Dental abscess

Risk factors: Poor dental hygiene, pregnancy.

Clinical features: Fever, toothache, facial pain and swelling.

Organisms: Mixed oral aerobes and anaerobes.

Antibiotic management: Penicillin V/amoxicillin + metronidazole **or** co-amoxiclav.

Ludwig's angina refers to a severe cellulitis of the floor of the mouth, almost always arising from the second or third mandibular molars. Infection is polymicrobial and may become extensive.

Parapharyngeal abscess

May complicate quinsy (➢21), but usually arises from dental abscess. Infection by mixed oral flora in lateral pharyngeal space displaces tonsil towards midline and causes lateral neck swelling below mandible. Severe **trismus** is characteristic; may progress rapidly to systemic sepsis and local suppurative complications, including involvement of jugular vein and carotid artery (see also Lemierre's disease ➢20).

Pharyngitis

Infection of the posterior oral cavity, often involving the lymphoid tissue of Waldeyer's ring. Most cases are viral; management is aimed at relieving symptoms. Differential diagnosis includes acute bacterial epiglottitis and, rarely, diphtheria.

Clinical features: Fever, malaise, sore throat and myalgia. On examination, erythema and oedema of the tonsils and pharyngeal mucosa. It is usually impossible to determine the cause clinically, although some features are suggestive of particular organisms. Cough and coryza suggest influenza or rhinoviruses, whereas conjunctivitis suggests adenovirus. Vesicles and ulceration affecting both the pharynx and mouth are seen in herpes simplex stomatitis; in Coxsackie A herpangina (➢135), small vesicles and ulcers are usually confined to the posterior pharynx. Purulent tonsillar exudate suggests streptococcal infection or EBV; the latter is often accompanied by generalized lymphadenopathy and/or hepatosplenomegaly. Purulent tonsillar exudate is rare in influenza or rhinovirus infection.

Organisms: Rhinovirus, coronavirus, adenovirus, influenza A and B, parainfluenza, herpes simplex virus, coxsackievirus A, EBV, and CMV infection. Group A β-haemolytic streptococci (GAS), less often groups C or G. Rarely, *Arcanobacterium haemolyticum*, *Neisseria gonorrhoeae*. Very rarely, *Corynebacterium diphtheriae*.

Microbiological investigations: A rise in ASOT may give retrospective confirmation of streptococcal infection. Throat swab is often sent. Latex agglutination tests for the rapid diagnosis of GAS antigens in throat swabs are widely used in USA, and are specific and quite sensitive when compared to throat swab. However, neither antigen tests nor throat swabs are sensitive or specific for GAS infection when compared to ASOT, due to asymptomatic GAS carriage. Flora recovered from the surface of the tonsil correlates poorly with that of tonsillar crypt but quantitative culture may predict true infection. Viral culture may be positive, particularly in HSV infection. Viral serology may be useful in retrospect.

med.mssm.edu/ebm/cpr/strep_cpr.html

Differential diagnosis: Diphtheria is extremely rare in the developed world, but has recently become endemic in parts of the former Soviet Union and should be suspected in an unimmunized patient who is unwell, particularly if there is a grey tonsillar exudate spreading from the tonsils to involve the uvula, palate or posterior pharyngeal wall (➢268). If diphtheria is suspected, liaison with the microbiology department is essential ☎.

Antibiotic management: As most cases are viral, the value of antibiotics for sore throat has been questioned. Trial of penicillin vs. no treatment vs. delayed treatment showed no benefit, although patients who were unwell, had recurrent tonsillitis or suspected rheumatic fever were excluded. Immunological sequelae of GAS infection (➢256) are now very rare in the UK, so value of antibiotics in preventing them is unquantifiable. There is some evidence to suggest that antibiotic therapy prevents local suppurative complications such as quinsy. For a full discussion see:

www.sign.ac.uk/guidelines/fulltext/34/

Zwart S, BMJ 2000; 320: 150

If patients are unwell, give penicillin V for 10 days. For **recurrent tonsillitis**, cefuroxime and clindamycin have been shown to be superior to penicillin V. Consider ENT referral.

Practice point

Patients with 1° EBV infection develop a widespread maculopapular rash after treatment with ampicillin or amoxicillin. These antibiotics should be avoided in sore throat unless the diagnosis of bacterial infection has been firmly established.

Complications: Lower respiratory tract infection, peritonsillar (➢21) and retropharyngeal abscess (➢21).

Comments: Scarlet fever ✉, now rare in the UK, is caused by streptococcal erythrodermic toxin, which may be produced in streptococcal infection at any site (➢254).

Lemierre's disease

'Anaerobic tonsillitis': Severe pharyngitis associated with fever, septicaemia, metastatic pulmonary infection and jugular vein thrombosis is rarely seen in young adults and is caused by *Fusobacterium necrophorum* (➢321).

Laryngitis

In addition to the symptoms of pharyngitis, some patients with URTI may develop hoarseness and odynophagia. Laryngitis is usually viral in aetiology, although it may accompany infection by streptococci or *Mycoplasma pneumoniae*. Persistent hoarseness is usually due to non-infectious causes, but may indicate chronic granulomatous laryngitis. Causes include *Candida albicans* and herpes simplex virus; diagnosed on biopsy.

Croup (acute laryngotracheobronchitis)

Croup typically affects children from a few months old to the age of 3 years, and occurs in epidemics in autumn and early spring. During the course of a viral URTI, inspiratory stridor and a distinctive 'seal's bark' cough develop. Cyanosis and intercostal recession indicate more severe airway obstruction. Antibiotics, steroids and mist inhalation have not been shown to be of value. Hypoxia is common. Careful observation is needed, with a view to timely intubation or tracheotomy should airway obstruction progress. The important differential diagnosis is acute epiglottitis (➢21).

Bacterial tracheitis

Retrosternal discomfort commonly accompanies viral URTI. Rarely, bacterial tracheitis may follow with fever, dyspnoea and stridor with purulent sputum. Gram stain and culture of sputum and blood culture are required if severe. Infection is most often due to *Staphylococcus aureus*, GAS and *Haemophilus influenzae* type b. Lateral soft-tissue X-ray of neck may show subglottic narrowing with a normal epiglottis ('pencil sign'). Bacterial tracheitis may follow intubation and trauma.

Antibiotic management: Flucloxacillin **or** co-amoxiclav **or** parenteral cephalosporin—to be guided by the results of sputum culture.

Quinsy

Quinsy (peritonsillar abscess) usually follows bacterial pharyngitis. It is usually polymicrobial in origin, with oral anaerobes and GAS predominating. Patients present with abrupt increase in pain and dysphagia. On examination, there is asymmetrical tonsillar enlargement with swelling in the neck and often a palpable fluctuant mass. Management consists of ENT referral for consideration of surgical drainage and benzylpenicillin or co-amoxiclav, given parenterally.

Retropharyngeal abscess

Unusual but important complication of bacterial pharyngitis and pharyngeal trauma (e.g. fishbone). Retropharyngeal space lies posterior to pharynx, anterior to cervical vertebrae and contains lymphatic tissue. Commoner in children.

Clinical features: Sore throat, dysphagia and neck pain. Bulging of the posterior pharyngeal wall may only be visible with indirect laryngoscopy. Lateral soft tissue X-ray of neck shows widening of pre-vertebral tissue, ±gas in tissues. Airway obstruction may occur.

Organisms: GAS and mixed oral flora.

Differential diagnosis: Cervical osteomyelitis, meningitis.

Antibiotic management: Benzylpenicillin **plus** clindamycin *or* parenteral cephalosporin **plus** metronidazole.

Supportive management: Urgent ENT referral for incision and drainage; ≈30% require tracheostomy.

Comments: Consider the diagnosis in the patient with neck stiffness and fever who has a normal lumbar puncture.

Acute epiglottitis

Inflammation, oedema and obstruction of the supraglottic structures including the epiglottis due to *Haemophilus influenzae* type b (rarely other capsular types) typically affecting children aged 3 to 7 yrs.

Clinical features: Abrupt onset, over hours, of severe sore throat and fever. Children are unwell, with stridor, drooling and dysphagia. They may adopt a typical posture, sitting up and leaning forward. The swollen, cherry red epiglottis may be visible, but attempts to use a tongue depressor should be avoided, as this may precipitate fatal acute total obstruction.

Antibiotic management: Parenteral cephalosporin **or** amoxicillin plus chloramphenicol should be given. Rifampicin prophylaxis should be given to the patient and all household and nursery/day-care contacts including adults if there are other susceptible children in the family (➢100).

Supportive management: Management of the airway is paramount. **Elective intubation is associated with reduced mortality, as emergency intubation may be very difficult.** Throat examination and iv cannulation should be delayed until arrival of suitably experienced anaesthetist.

Other investigations: Lateral soft-tissue neck X-ray may show the engorged epiglottis (the 'thumb sign').

Differential diagnosis: It is essential to distinguish between viral croup and epiglottitis. Salient features are the abrupt onset, toxic appearance, dysphagia and drooling associated with epiglottitis. Diphtheria and inhaled foreign body may also need to be considered.

Complications: Systemic spread, bacteraemia, meningitis, arthritis and cellulitis.

Comments: This condition has been reported rarely in adults. All forms of invasive *Haemophilus influenzae* type b are less common with the introduction of the Hib vaccine.

Thyroiditis

Sudden onset of pain, tenderness and swelling in the thyroid may be due to infection by *Staphylococcus aureus*, *Streptococcus pneumoniae* or mixed oral anaerobes. ENT referral for consideration of needle aspiration (send for

culture). Acute suppurative thyroiditis is rare. Often associated with a persistent thyroglossal duct, or a third or fourth branchial arch anomaly with a congenital fistula from the pyriform fossa to the thyroid. Confirmation by barium swallow. Inflammation is more often subacute, sometimes related to recent viral infection (e.g. mumps, measles, influenza and EBV).