GUIDELINES

For

GENERAL PRACTITIONERS

2024

Press record

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FOREWORD

It is a great honor for me to write a foreword to Guidelines for General Practitioners by General Practitioners' society, Myanmar Medical Association (Central).

General practitioners are the primary health providers in the community looking after the majority of the people of our country. They are being trusted and depend upon by every families in the surrounding area where they practice. The first and foremost care by the General Practitioners are the most important for all the people.

Guidelines based on a critical appraisal of scientific evidence (evidence-based guidelines) clarify which interventions are of proved benefit and document the quality of the supporting data. They alert clinicians to interventions unsupported by good science, reinforce the importance and methods of critical appraisal, and call attention to ineffective, dangerous, and wasteful practices.

Clinical guidelines can improve the quality of clinical decisions. They offer explicit recommendations for clinicians who are uncertain about how to proceed, overturn the beliefs of doctors accustomed to outdated practices, improve the consistency of care, and provide authoritative recommendations that reassure practitioners about the appropriateness of their treatment policies.

The Myanmar Medical Association together with the GP society has been helping out with the CME and CPD program for the Member doctors both inhouse sessions and online courses. This guideline is one of the essential parts of this CPD for the GPs.

I would like to congratulate the GP society for their effort for producing this guideline and also, I would like to encourage them to review and updated regularly.

Professor Aye Aung
President
Myanmar Medical Association

April, 2024

PREFACE

We are writing this letter to express our sincerest gratitude and appreciation for the successful completion of the **second edition** of the **General Practitioners' Guidelines**. This accomplishment is the result of an exceptional collaborative effort, and we would like to extend our thanks to all those involved.

The General Practitioners' Guidelines has been an invaluable resource since its inception with the launch of the first edition in November 2017. As per the initial plan, the guidelines were intended to be updated every three years to ensure the most up-to-date information reaches Myanmar General Practitioners, enhancing their knowledge in primary healthcare and family health.

However, the unforeseen outbreak of the Covid-19 pandemic disrupted our plans and posed numerous challenges for the team. In-person meetings became impossible due to safety concerns, making it necessary for us to find alternative means of communication and collaboration. Despite the adversity faced, the team members demonstrated remarkable resilience and adaptability by utilizing online platforms and technology to continue the update process.

We would like to extend our deepest gratitude to the dedicated team members who persevered and worked tirelessly during these trying times. Their commitment, professionalism, and unwavering dedication to the project enabled us to overcome the obstacles posed by the pandemic and successfully complete the second edition of the guideline.

Furthermore, we would like to express our sincere appreciation to the specialist societies that actively contributed to the development of the guidelines. Their expertise and invaluable insights have ensured that the content remains current, accurate, and relevant, enabling our General Practitioners to provide the highest quality of care to their patients.

We would also like to extend our heartfelt thanks to the esteemed President of the Myanmar Medical Association, for their continuous support and guidance throughout this endeavor. Their leadership and unwavering commitment to advancing medical knowledge in Myanmar have been instrumental in the success of this Guidelines.

Moreover, the decision to distribute the guideline as electronic copies reflects our commitment to ensuring easy access for all Myanmar General Practitioners. By making it available in this format, we aim to facilitate the dissemination of updated knowledge, thus empowering our healthcare professionals to deliver the best possible care to the community.

In conclusion, we would like to express our deepest gratitude to all those who contributed to the development and distribution of the General Practitioners' Guidelines Second Edition. The unwavering supports and collective efforts have made a significant impact on enhancing primary healthcare and family health care in Myanmar.

Once again, thank you for your outstanding dedication, resilience, and invaluable contributions. We look forward to our continued collaboration in advancing medical knowledge and improving healthcare outcomes for all.

Dr Khine Soe Win and Dr Win Zaw April, 2024
General Practitioners' Society (Central)
Myanmar Medical Association

EDITORIAL

It is my privilege to inform you that our updated and revised edition of "**Guidelines for General Practitioners**" will be published very soon and it is my great pleasure to be the editor-in-chief of this guideline book. There are various reasons for revising and updating the previous edition.

This is the fact that some important topics, for example, malaria and family violence are missing in the first edition and some clinical practice guidelines like Diabetes Management have been changed during the interim period. Of course, this opportunity arises due to the emergence of COVID-19 in the world. As all you know, Medicine is an ever-changing science; we need to consider updating our guidelines at least five- yearly. Hence the time is up now!

Education is achieved by assimilating information from many resources and readers of this book can enhance their learning experience in terms of reflecting in their daily Family/General Practice. We all take immerse pride in contributing good educational resource dedicated to Myanmar General Practitioners. The editors and authors anticipate that the readers will both enjoy and profit from their work in preparing this volume.

Happy studying and learning,

Dr Win Lwin Thein
Editor-in chief
Vice President (GP Society)
April, 2024

ACKNOWLEDGEMENT

We would like to thank all our talented and hard-working colleagues who have contributed to the ongoing development of the **Guidelines for General Practitioners**.

Especially, we would like to highlight the significance of the second edition which appears when the family medicine development process in Myanmar is being idle. Many factors are impeding the developing process lately, which has been accelerated previously by the commitment of the MOHS, the medical universities, and the General Practitioners' Society before the COVID-19 pandemic started.

No one can deny that the Myanmar health care system is lacking a strong and effective primary care task force. The best solution to mend this defect is retraining the thousands of general practitioners who are working individually across the country. Here comes the role of family medicine to train these GPs and primary care doctors to be able to use its principles effectively and, in turn, strengthen primary care.

Many GPs are using some family medicine principles consciously or unconsciously in varying degree of competency. Person-centered care, continuity of care, and family-oriented care became the culture of most practices for a long time. But only a few GPs can enjoy the most effective coordinated care and seamless continuity of care with secondary and tertiary care providers. The reasons behind this would be the absence of standardization in general practitioners' service quality and unawareness of the value of family medicine practitioners by other specialties and the public.

To resolve this ambiguity, primary care doctors should be involved in the retraining programs and thereafter CME/CPD and other life-long-learning programs which prescribe family medicine curricula.

We also acknowledge the effort of the contributors to make this new edition more family medicine-oriented, in addition to the Family Medicine chapter at the beginning of the book. We genuinely believe that the new edition will be a better reference for the GP/FP who wants to practice quality primary care and for future family medicine programs in Myanmar.

Finally, we would like to thank all academic writers who contributed to the General Practice Guidelines-first edition. Without their kind support, this second edition could never have happened.

Regards,

Dr. Tin Aye and Dr. Kyaw Thu

General Practitioners' Society (Central), MMA **April, 2024**

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SYMBOLS AND ABBREVIATIONS

AAA abdominal aortic aneurysm
ABC airway, breathing, circulation
ABCD airway, breathing, circulation, dextrose
ABO A, B and O blood groups
ACE angiotensin-converting enzyme
ACEI angiotensin-converting enzyme inhibitor
ACTH adrenocorticotrophic hormone
ADHD attention deficit hyperactivity disorder
ADT adult diphtheria vaccine
AFP alpha-fetoprotein
AI aortic incompetence
AIDS acquired immunodeficiency syndrome
AIIRA angiotensin II (2) reuptake antagonist
AKF acute kidney failure
ALE average life expectancy
ALL acute lymphocytic leukaemia
ALP alkaline phosphatase
ALT alanine aminotransferase
AMI acute myocardial infarction
AML acute myeloid leukaemia
ANA antinuclear antibody
ANF antinuclear factor
AP anterior–posterior
APH ante-partum haemorrhage
ASD atrial septal defect
ASIS anterior superior iliac spine
ASOT antistreptolysin O titre
AST aspartate aminotransferase
AV atrioventricular
AZT azidothymidine
BCC basal cell carcinoma
BCG bacille Calmette-Guérin
BMD bone mass density
BMI body mass index
BP blood pressure
BPH benign prostatic hyperplasia
Ca carcinoma
CABG coronary artery bypass grafting
CAD coronary artery disease
CAP community acquired pneumonia
CBT cognitive behaviour therapy
CCF congestive cardiac failure
CCU coronary care unit
CD4 T helper cell
CD8 T suppressor cell
CDT combined diphtheria/tetanus vaccine
CEA carcinoembryonic antigen
CFS chronic fatigue syndrome
CHD coronary heart disease
CHF chronic heart failure
CIN cervical intraepithelial neoplasia
CK creatinine kinase
CKD chronic kidney disease
CKF chronic kidney failure
CML chronic myeloid leukaemia
CMV cytomegalovirus
CNS central nervous system
COAD chronic obstructive airways disease
COC combined oral contraceptive
COCP combined oral contraceptive pill
COPD chronic obstructive pulmonary disease
COX cyclooxygenase
CPA cardiopulmonary arrest
CPAP continuous positive airways pressure
CPK creatine phosphokinase
CPR cardiopulmonary resuscitation
CR controlled release
CREST calcinosis cutis; Raynaud's phenomenon; oesophageal involvement; sclerodactyly; telangiectasia
CRF chronic renal failure
CR(K)F chronic renal (kidney) failure
CRP C-reactive protein
CSF cerebrospinal fluid
CT computerised tomography
CTS carpal tunnel syndrome
CVA cerebrovascular accident
CVS cardiovascular system
CXR chest X-ray
DBP diastolic blood pressure
DC direct current
DHA docosahexaenoic acid
DI diabetes insipidus
DIC disseminated intravascular coagulation
dL decilitre
DMARDs disease modifying antirheumatic drugs
DNA deoxyribose-nucleic acid
DRABC defibrillation, resuscitation, airway, breathing, circulation
drug dosage bd—twice daily, tid/tds -three times daily, qid/qds -four times daily
ds double strand
DS double strength
DSM diagnostic and statistical manual (of mental disorders)
DU duodenal ulcer
DUB dysfunctional uterine bleeding
DVT deep venous thrombosis
EBM Epstein-Barr mononucleosis (glandular fever)
EBV Epstein-Barr virus
ECG electrocardiogram
ECT electroconvulsive therapy
EDD expected due date
EEG electroencephalogram
ELISA enzyme linked immunosorbent assay
ESRF end-stage renal failure
ESR(K)F end stage renal (kidney) failure
ERCP endoscopic retrograde cholangiopancreatography
esp. especially
ESR erythrocyte sedimentation rate
FB foreign body
FBE full blood count

FEV1 forced expiratory volume in 1 second
fL femtolitre = (1e–15) litre
FSH follicle stimulating hormone
FUO fever of undetermined origin
FVC forced vital capacity
g gram
GA general anaesthetic
GABHS group A beta-haemolytic streptococcus
GBS Guillain-Barré syndrome
GFR glomerular filtration rate
GI glycaemic index
GIT gastrointestinal tract
GLP glucagon-like peptide
GnRH gonadotrophin-releasing hormone
GO gastro-oesophageal
GORD gastro-oesophageal refl ux
GP general practitioner
G-6-PD glucose-6-phosphate
GU gastric ulcer
HAV hepatitis A virus
anti-HAV hepatitis A antibody
Hb haemoglobin
HbA haemoglobin A
anti-HBc hepatitis B core antibody
HBeAg hepatitis B e antigen
anti-HBs hepatitis B surface antibody
HBsAg hepatitis B surface antigen
HBV hepatitis B virus
HCG human chorionic gonadotropin
HCV hepatitis C virus
anti-HCV hepatitis C virus antibody
HDL high-density lipoprotein
HEV hepatitis E virus
HFM hand, foot and mouth
HFV hepatitis F virus
HGV hepatitis G virus
HIV human immunodeficiency virus
HNPCC hereditary nonpolyposis colorectal cancer
HPV human papilloma virus
HRT hormone replacement therapy
HSV herpes simplex viral infection
IBS irritable bowel syndrome
ICE ice, compression, elevation
ICS inhaled corticosteroid
ICS intercondylar separation
ICT immunochromatographic test
IDDM insulin dependent diabetes mellitus
IDU injecting drug user
IgE immunoglobulin E
IgG immunoglobulin G
IgM immunoglobulin M
IHD ischaemic heart disease
IM, IMI intramuscular injection
inc. including
IPPV intermittent positive pressure variation
IR internal rotation
ITP idiopathic (or immune) thrombocytopenia purpura
IUCD intrauterine contraceptive device
IUGR intrauterine growth retardation
IV intravenous
IVI intravenous injection
IVP intravenous pyelogram
IVU intravenous urogram
JCA juvenile chronic arthritis
JVP jugular venous pulse
KA keratoacanthoma
kg kilogram
KOH potassium hydroxide
LA local anaesthetic
LABA long acting beta agonist
LBBB left branch bundle block
LBO large bowel obstruction
LBP low back pain
LDH/LH lactic dehydrogenase
LDL low-density lipoprotein
LFTs liver function tests
LH luteinising hormone
LHRH luteinising hormone releasing hormone
LIF left iliac fossa
LMN lower motor neurone
LNG levonorgestrel
LRTI lower respiratory tract infection
LSD lysergic acid
LUQ left upper quadrant
LUTS lower urinary tract symptoms
LV left ventricular
LVH left ventricular hypertrophy
mane in morning
MAOI monoamine oxidase inhibitor
mcg microgram (also µg)
MCV mean corpuscular volume
MDI metered dose inhaler
MDR multi-drug resistant TB
MI myocardial infarction
MRCP magnetic resonance cholangiography
MRI magnetic resonance imaging
MS multiple sclerosis
MSM men who have sex with men
MSU midstream urine
N normal
NAD no abnormality detected
NGU non-gonococcal urethritis
NHL non-Hodgkin's lymphoma
NIDDM non-insulin dependent diabetes mellitus
nocte at night
NSAIDs non-steroidal anti-inflammatory drugs
NSU non-specific urethritis
(o) taken orally
OA osteoarthritis
OCP oral contraceptive pill
OGTT oral glucose tolerance test
OSA obstructive sleep apnoea
OTC over the counter
PA posterior–anterior
PAN polyarteritis nodosa
Pap Papanicolaou
pc after meals
PCA percutaneous continuous analgesia
PCB post coital bleeding

PCL posterior cruciate ligament
PCOS polycystic ovarian syndrome
PCP pneumocystis carinii pneumonia
PCR polymerase chain reaction
PCV packed cell volume
PDA patent ductus arteriosus
PEF peak expiratory flow
PEFR peak expiratory flow rate
PET pre-eclamptic toxaemia
PFT pulmonary function test
PH past history
PID pelvic inflammatory disease
PLISSIT permission: limited information: specific suggestion: intensive therapy
PMS premenstrual syndrome
PMT premenstrual tension
POP plaster of Paris
POP progestogen-only pill
PPI proton-pump inhibitor
PPROM preterm premature rupture of membranes
PR per rectum
prn as and when needed
PROM premature rupture of membranes
PSA prostate specific antigen
PSIS posterior superior iliac spine
PSVT paroxysmal supraventricular tachycardia
PT prothrombin time
PTC percutaneous transhepatic cholangiography
PU peptic ulcer
PUO pyrexia of undetermined origin
pv per vagina
qds, qid four times daily
RA rheumatoid arthritis
RBBB right branch bundle block
RBC red blood cell
RCT randomised controlled trial
RF rheumatic fever
Rh rhesus
RIB rest in bed
RICE rest, ice, compression, elevation
RIF right iliac fossa
RPR rapid plasma reagin
RR relative risk
RSV respiratory syncytial virus
RT reverse transcriptase
rtPA recombinant tissue plasminogen activator
SAH subarachnoid haemorrhage
SARS severe acute respiratory distress syndrome
SBE subacute bacterial endocarditis
SBO small bowel obstruction
SBP systolic blood pressure
SC/SCI subcutaneous/subcutaneous injection
SCC squamous cell carcinoma
SCG sodium cromoglycate
SIADH syndrome of secretion of inappropriate antidiuretic hormone
SIDS sudden infant death syndrome
SIJ sacroiliac joint
SL sublingual
SLE systemic lupus erythematosus
SLR straight leg raising
SND sensorineural deafness
SNHL sensorineural hearing loss
SNRI serotonin noradrenaline reuptake inhibitor
SOB shortness of breath
sp species
SR sustained release
SSRI selective serotonin reuptake inhibitor
SSS sick sinus syndrome
stat at once
STI sexually transmitted infection
SVC superior vena cava
SVT supraventricular tachycardia
T3 tri-iodothyronine
T4 thyroxine
TB tuberculosis
tds, tid three times daily
TENS transcutaneous electrical nerve stimulation
TFTs thyroid function tests
TG triglyceride
TIA transient ischaemic attack
TIBC total iron binding capacity
TM tympanic membrane
TMJ temporomandibular joint
TNF tissue necrosis factor
TOF tracheo-oesophageal fistula
TORCH toxoplasmosis, rubella, cytomegalovirus, herpes virus
TPHA Treponema pallidum haemoglutination test
TSE testicular self-examination
TSH thyroid-stimulating hormone
TT thrombin time
TV tidal volume
U units
UC ulcerative colitis
U & E urea and electrolytes
µg microgram
UMN upper motor neurone
URTI upper respiratory tract infection
US ultrasound
UTI urinary tract infection
U ultraviolet
VC vital capacity
VDRL Venereal Disease Reference Laboratory
VF ventricular fibrillation
VMA vanillyl mandelic acid
VSD ventricular septal defect
VT ventricular tachycardia
VUR vesico-ureteric reflux
VWD von Willebrand's disease
WBC white blood cells
WCC white cell count
WHO World Health Organization
WPW Wolff-Parkinson-White
XL sex linked

CHAPTER 5

GASTRO-INTESTINAL AND HEPATO-BILIARY PROBLEMS

ACUTE GASTROENTERITIS/ DIARRHOEA

DEFINITION OF DIARRHOEA

- Passage of unusually loose or watery stools usually at least three times in a 24-hour period. (14 day or fewer in duration)
- (consistency of stool is more important than number)

CAUSATIVE AGENTS

Bacteria	Viruses	Parasites
• *Diarrheagenic Escherichia coli* • *Campylobacter jejuni* • *C. coli* • *C. upsaliensis* • *Vibrio cholerae O1* • *V cholerae 0139* • *V parahaemolyticus* • *Shigella species* • *Bacteroides fragilis* • *Nontyphoidal Salmonellae* • *Clostridium difficile* • *Yersinia enterocolitica* • *Y. pseudotuberculosis*	• *Rotavirus* • *Norovirus (calicivirus)* • *Adenovirus* • *Astrovirus* • *Cytomegalovirus*	**Protozoan** • *Cryptosporidium parvum* • *Giardia intestinalis* • *Microsporida* • *Entamoeba histoly tica* • *Jsospora belli* • *Cyclospora cayetanensis* • *Dientamoeba fragilis* • *Blastocystis hominis* **Helminths** • *Strongyloides stercoralis* • *Angiostrongylus costaricensis* • *Schistosoma mansoni,* • *Schistosoma japonicum*

Clinical manifestations

- Episodes of diarrhoea can be classified into three categories.

Category	Clinical manifestations
Acute diarrhea	Presence of three or more unusually loose or watery stools in the preceding 24 hours
Dysentery	Presence of visible blood in stools
Persistent diarrhea	Acutely starting episode of diarrhea lasting more than 14 days

Linking the main symptoms to the causes of acute diarrhea

Symptoms	Causes of acute diarrhoea
Fever	Common and associated with invasive pathogens Initially present in the majority of children with rotavirus diarrhea
Bloody stools	Invasive and cytotoxin-producing pathogens Suspect *(entero-haemorrhagic E. coli)* EHEC infection in the absence of fecal leucocytes Not with viral agents and enterotoxins producing bacteria
Vomiting	Frequently in viral diarrhea and illness caused by ingestion of bacterial toxins (e.g. Staphylococcus aureus) Common in cholera

Clinical evaluation

The initial clinical evaluation of the patient should focus on:

- Assessing the severity of the illness and the magnitude (degree) of dehydration
- Determining likely causes on the basis of the history and clinical findings, including stool characteristics

Medical assessment of diarrhoea

Patient history	Physical examination
• Onset, stool frequency, type and volume • Presence of blood • Vomiting • Dark yellow or scant urine, decreased skin turgor, orthostatic hypotension • Food history, recent and remote travel history, occupational exposure • Medicines received • Past medical history • Underlying conditions	• Body weight • Temperature • Pulse/heart and respiratory rate • Blood pressure

Character of symptoms

- Diarrhea of small bowel origin is typically watery, of large volume, and associated with abdominal cramping, bloating, and gas. Weight loss can occur if diarrhea becomes persistent. Fever is rarely a significant symptom and occult blood or inflammatory cells in the stool are rarely identified.
- In contrast, diarrhea of large intestinal origin often presents with frequent, regular, small volume, and often painful bowel movements. Fever and bloody or mucoid stools are common, and red blood cells and inflammatory cells can be seen routinely on stool microscopy.
- These inflammatory signs associated with large bowel infection (fever, bloody or mucoid stools) suggest invasive bacteria (eg, Salmonella, Shigella, or Campylobacter), enteric viruses (eg, cytomegalovirus [CMV] or adenovirus), Entamoeba histolytica, or a cytotoxic organism such as C. difficile. Visibly bloody acute diarrhea is relatively uncommon and raises the possibility of Shiga toxin-producing E. coli (STEC) (eg, E. coli O157:H7) infection.
- Other bacterial causes of visibly bloody diarrhea are Shigella, Campylobacter, and Salmonella species. Bloody diarrhea can also reflect non-infectious aetiologies such as inflammatory bowel disease or ischemic colitis
- Syndromes that begin with diarrhea but progress to fever and systemic complaints, such as headache and muscle aches, should raise the possibility of other aetiologies, including a typhoidal illness (particularly in travelers from resource-limited settings) or infection with Listeria monocytogenes (particularly if a stiff neck is also present or the patient is a pregnant woman).

Food history

- Consumption of unpasteurized dairy products, raw or undercooked meat or fish, or organic vitamin preparations may suggest certain pathogens.
- Although it is often difficult to know which food exposure was the potential source, the timing of symptom onset following exposure to the suspected offending food can be an important clue to the diagnosis.
- Within six hours: suggests ingestion of a preformed toxin of Staphylococcus aureus or Bacillus cereus, particularly if nausea and vomiting were the initial symptoms
- At 8 to 16 hours: suggests infection with Clostridium perfringens
- At more than 16 hours: suggests either viral or other bacterial infection (e.g., contamination of food with enterotoxigenic or STEC or other pathogens)

Other exposures

- Exposure to animals (poultry, turtles, petting zoos) has been associated with Salmonella infection.
- Travel to a resource-limited setting increases the risk of bacterial diarrhea and also informs the risk of certain parasitic infections.
- Occupation in daycare centers has been associated with infections with Shigella, Cryptosporidium, and Giardia. Rotavirus is a potential consideration, but in countries that routinely immunize infants against rotavirus, infection due to rotavirus has decreased substantially.

Medical history

- It is also important to ask about recent antibiotic use (as a clue to the presence of C. difficile infection), other medications (such as proton pump inhibitors, which can increase the risk of infectious diarrhea), and to obtain a complete past medical history (eg, to identify an immunocompromised host or the possibility of nosocomial infection).

Physical examination

- The examination focuses on evaluating volume status and identifying complications.
- Volume depletion can be suggested by dry mucous membranes, diminished skin turgor, postural or frank, reductions in blood pressure, and altered sensorium. These signs can be mild or absent with early hypovolemia
- The abdominal examination should evaluate for findings that can suggest ileus or peritonitis, including abdominal distension, pain with gentle percussion, abdominal rigidity, or rebound tenderness

Clinical assessment of hydration status

- Assessment of patients' hydration status is based on the presence of the symptoms and signs outlined in the following table. The presence of one of these signs or symptoms immediately classifies the patient as a more severe case.

Classification of dehydration

Severe dehydration

- Consider hospitalization depend on patient's condition
- Lethargic, unconscious
- Incapable of drinking
- Weak radial pulse
- Supine hypotension
- Skin pinch goes back very slowly
- Decrease in the urine output (oliguria)

Moderate dehydration

- Sunken eyes with ocular hypo-tony
- Dryness of the oral mucosa, tongue, and mucous membrane
- Intense thirst; drinks eagerly
- Skin pinch goes back slowly

No signs of dehydration

- None of the above

Investigations

- Blood
- Full blood count
- Urea, creatinine and electrolytes
- ESR (increased in cancer, inflammatory bowel disease)
- CRP (increased in infection, inflammatory bowel disease)
- Blood cultures (in patients with high fevers or who appear systemically ill)
- Stool/ Rectal swab
- Microbiological investigation is indicated in patients who are dehydrated or febrile or have blood or pus in their stool. A fecal specimen or rectal swab should be obtained for analysis in cases of severe, bloody, inflammatory, or persistent diarrhoea, or if cholera is suspected.

Management

- Rehydration
- Antibiotics
- Diet
- Anti-diarrhoeal agents
- Zinc supplement
- Probiotic, prebiotic

Rehydration

- The first line of treatment in acute diarrhoea is prevention and treatment of fluid and electrolyte depletion.

No signs of dehydration

- Oral rehydration salt (ORS) solution ad lib at home (liquid should be administered in small amounts frequently, every 15-30 minutes)

Moderate dehydration

- ORS + IV Ringer's lactate solution 10 ml/kg/hour

Severe dehydration

- Life-threatening condition
- Two or more IV lines should be installed.
- IV Ringer's lactate solution should be given rapidly until radial pulse is palpable and BP is raised above 90/60 mmHg.
- Then subsequent fluid therapy depends on the amount of ongoing stool loss.
- Ringer's lactate solution is the first option. If it is not available, isotonic saline solution (0.9%) can be used.
- Never use glucose solution.
- ORS should also be given at the same time.
- Closely monitor fluid balance during this phase in order to guarantee sufficient replenishment of volume.

Antibiotics

- Antibiotics are indicated if history and physical examination suggestive of bacterial infection (i.e. diarrhoea is severe and prolonged, fever, look toxic).

Cause	**Antibiotics** First choice *I Alternative(s)*
Cholera	Doxycycline 300 mg once *Azithromycin* 1.0 g as a single dose, only once *Ciprofloxacin* 500 mg 12-hourly for 3 days, or 2.0 grams as a single dose, only once
Shigellosis	Ciprofloxacin 500 mg bd/day for 3 days, or 2.0 g as a single dose only once *Ceftriaxone* 2-4 g as a single daily dose for 2-5 days
Amoebiasis	Metronidazole 750 mg tds/day for 5 days (10 days for severe disease)
Giardiasis	Metronidazole 250 mg tds/day for 5 days *Tinidazole* single dose 50 mg/kg orally; maximum dose 2 g *Ornidazole* single, 2-g dose
Campylobacter	Azithromycin 500 mg od/day for 3 days *Fluoroquinolones* such as ciprofloxacin 500 mg od/day for 3 days

Anti-diarrhoeal agents

Antimotility agents

- (Loperamide 4-6 mg/day is the agent of choice for adults)
- Should be used mostly for mild to moderate traveler's diarrhea (without clinical signs of invasive diarrhea)
- Inhibits intestinal peristalsis and has mild antisecretory properties
- Should be avoided in bloody or suspected inflammatory diarrhea (febrile patients)
- Significant abdominal pain also suggests inflammatory diarrhea (this is a contraindication for loperamide use)

Diet

- Normal feeding should be continued for those with no signs of dehydration, and food should be started immediately after correction of moderate and severe dehydration, which usually takes 2-4 hours. Adequate nutrition during an episode of acute diarrhea is important to facilitate enterocyte renewal. Boiled starches and cereals (eg, potatoes, noodles, rice, wheat, and oat) with salt are indicated in patients with watery diarrhea.
- Foods with high fat content should be avoided until the gut function returns to normal after a severe bout of diarrhea.

- Dairy products (except yogurt) may be difficult to digest in the presence of diarrheal disease. This is due to secondary lactose malabsorption, which is common following infectious enteritis and may last for several weeks to months. Thus, temporary avoidance of lactose-containing foods is reasonable.

Zinc supplement

- Zinc deficiency is widespread among children in developing countries. Routine zinc therapy, as an adjunct to ORT is useful in modest reduction of the severity but more importantly reduce diarrhea episodes. It is not routinely recommended in adults.

Probiotics and Diarrhea

- Probiotics are considered to be beneficial to the host's health and contain a sufficient amount of non-pathogenic specific live bacteria preparations, such as Lactobacillus, Yeast, Bifidobacterium, Enterococcus, and Bacillus.
- Probiotics with beneficial bacteria that assist in maintaining or recolonizing the intestine with non-pathogenic flora can also be used as alternative therapy.
- Many different probiotics are available, and each probiotic has different activity, so only specific probiotics may be useful.
- Lactobacillus GG has been shown to decrease duration of childhood infectious diarrhea and Saccharomyces boulardii may be effective in decreasing the duration of C. difficile infection.

Prebiotics

- Prebiotics are defined as "substrates that are selectively utilized by host microorganisms to confer health benefits" (Gibson et al., 2017).
- Consumption of prebiotics can improve the gut microbiota, which is beneficial to health. Some prebiotics, such as fructo-oligosaccharide, inulin, pectin oligosaccharides, etc., can resist the colonization of pathogen by acting as soluble decoy receptors that mimic the binding site of pathogens, thereby promoting the eliminating of pathogens from the intestine (Pujari and Banerjee, 2021) Previous studies have shown that prebiotics can shorten the duration of acute watery diarrhea and has a good therapeutic effect on diarrhea (Rigo Adrover et al., 2017).

Prevention of diarrhoea

- Safe water supply and water sanitation
- Food sanitation
- Hand washing habit
- Safe disposal of stool
- Fly control

Persistent diarrhea (more than 14 but fewer than 30 days in duration)

- Work-up and management for patients with persistent diarrhea or diarrhea that does not respond to empiric treatment includes testing for parasitic organisms and other evaluation for noninfectious processes.
- The spectrum of parasites associated with persistent diarrhea can vary based on exposures or populations.
- In general, Giardia, Cryptosporidium, and E. histolytica are the most common parasitic pathogens in patients with persistent diarrhea.

- Persistent diarrhea following travel to certain locations, such as mountainous regions, is associated with Giardia, Cryptosporidium, or Cyclospora. Persistent diarrhea with exposure to infants in daycare centers has been associated with Giardia and Cryptosporidium. Microsporidium should be a consideration in immunocompromised patients with persistent diarrhea.
- Most of these pathogens can be diagnosed by microscopy for ova and parasites. Three specimens should be sent on consecutive days (or each specimen separated by at least 24 hours) for ova and parasite examination since parasite excretion may be intermittent.
- Non-infectious aetiologies also become more likely when acute diarrhea persists or does not respond to empiric therapy. The evaluation of patients for a non-infectious etiology should be pursued in those patients in whom evaluation fails to identify a pathogen (eg, bacterial, viral, or protozoal) and the diarrhea worsens or becomes chronic. In some cases, this will include endoscopy, for example, to distinguish inflammatory bowel disease from infectious diarrhea.

Reference

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CHRONIC DIARRHOEA

Definition

- Diarrhoea persisting >4 weeks. Patients' perceptions of diarrhoea vary widely. Clarify what is meant.

Causes of chronic diarrhea

	Colonic	Malabsorption	Small bowel
Clinical features	Blood and mucus in stool	Steatorrhoea	Large-volume, watery stool
	Cramping lower abdominal pain	Undigested food in the stool Weight loss and nutritional disturbances	Abdominal bloating Cramping mid-abdominal pain
Some causes	Inflammatory bowel disease	Pancreatic	VIPoma (neuroendocrine tumour that secrete Vasoactive intestinal Peptide)
	Neoplasia	Chronic pancreatitis	Drug-induced
	Ischaemia	Cancer of pancreas	NSAIDs
	Irritable bowel syndrome	Cystic fibrosis	Aminosalicylates
		Cystic fibrosis	Aminosalicylates
		Enteropathy Coeliac disease	Selective serotonin re- uptake inhibitors (SSRIs)
		Tropical sprue	
		Lymphoma	
		Lymphangiectasia	
Investigations	Colonoscopy with biopsies	Ultrasound, CT and Magnetic Resonance Cholangiopancreatography (MRCP)	Stool volume
		Small bowel biopsy	Gut hormone profile
		Barium follow-through	Barium follow-through

(Davidson 's Principles and Practice of Medicine 22nd Edition)

Symptoms suggestive of organic disease

- History of <3 months duration
- history of gastrointestinal cancer, or symptom onset after the age of 50 years.
- Mainly nocturnal or continuous (as opposed to intermittent) diarrhoea
- Significant weight loss
- awakening by symptoms
- Liquid stools with blood and/or mucus

Examination and investigation

- Full examination: Look for signs of systemic disease and examine abdomen thoroughly.
- Physical exam of the abdomen may reveal localized tenderness or masses serve as an argument for further diagnostic evaluations. Measurement of blood pressure and heart rate and inspection of mucous membranes to detect anemia or dehydration.

- Check:
- Blood- FBC, ESR, Ca++, LFTs, haematinics (Fe, folic acid, B12), TFTs,
- Stool-Microscopy, C&S

Management

- If obvious identifiable cause, e.g. GI infection, constipation, drug side effect, then treat and review.
- Treat the underlying cause is the main stay of treatment.
- Clear explanation of the symptoms and diagnosis and reassurance about the benign nature of chronic functional diarrhoea are important.
- Dietary restrictions of food components, such as fructose, sorbitol, caffeine, or other precipitating foods, are generally proposed as a first approach.
- Pharmacotherapy can be considered as a first-line treatment in those who have symptoms with major impact on their quality of life or can be added in those who fail to respond sufficiently to reassurance and dietary measures.
- Antidiarrheal agents may be classified as intestinal transit inhibitors (opioids, tricyclic antidepressants and 5-HT antagonists), intraluminal agents (cholestyramine, medicinal fiber, clays, activated charcoal, and bismuth), proabsorptive agents (clonidine), and antisecretory drugs (octreotide).

Further Evaluation of Patients with Chronic Secretory Diarrhea

- Patients with chronic watery diarrhea who have little or no osmotic gap as calculated from stool electrolytes should be evaluated with three sets of investigations:
- Although bacterial infection rarely causes chronic diarrhea, it can be excluded by stool culture, including culture on special media for Aeromonas and Pleisiomonas. In addition, the stool should be examined microscopically for ova and parasites, with special tests for Cryptosporidium, Microsporidium, and Giardia. Giardia antigen, measured in stool by enzyme-linked immunosorbent assay, is the most sensitive test for giardiasis. An aspirate of small bowel contents for quantitative culture or breath tests with glucose or isotopically labeled xylose can be used to establish the presence of small bowel bacterial overgrowth but is likely to be meaningful only in patients with disorders predisposing them to bacterial overgrowth.
- Structural disease should be excluded by radiography of the small bowel, sigmoidoscopy, or colonoscopy with multiple biopsies of the colonic mucosa, computerized tomography of the abdomen, and endoscopic biopsy of the proximal small bowel mucosa. A small bowel follow-through examination is preferable to an enteroclysis study for the radiographic evaluation of patients with chronic diarrhea.
- Selective testing for plasma peptides such as gastrin, calcitonin, vasoactive intestinal polypeptide, and somatostatin, as well as urine excretion of 5-hydroxyin_dole acetic acid, metanephrine, or histamine and other tests of endocrine function, such as measurement of thyroid-stimulating hormone and serum thyroxine levels or an adrenocorticotropin-stimulation test for adrenal insufficiency, can be valuable. Because peptide secreting tumor syndromes causing chronic diarrhea are very rare, measurement of serum peptide concentrations (e.g., gastrin, vasoactive intestinal polypeptide, calcitonin) should be done only when a tumor syndrome seems likely from the clinical presentation or findings on radiographic studies.

Further Evaluation of Patients with Chronic Osmotic Diarrhea

- Most osmotic diarrhea not associated with steatorrhea is caused by ingestion of poorly absorbable carbohydrates or magnesium salts.
- A low stool pH suggests carbohydrate malabsorption, and a high stool magnesium concentration or output suggests magnesium ingestion.
- If carbohydrate malabsorption is suspected, a careful dietary history and judicious use of breath hydrogen testing with lactose as the test sugar or measurement of lactase in a mucosal biopsy specimen can be diagnostic. Patients with high stool magnesium outputs should be evaluated for inadvertent ingestion of magnesium in mineral supplements or antacids and for surreptitious laxative abuse.

Further Evaluation of Chronic Inflammatory Diarrhea

- Patients with blood and pus in the stool should undergo radiographic evaluation of the small bowel with barium (small bowel follow-through examination) and sigmoidoscopy or colonoscopy with biopsies of the colonic mucosa.
- Stool culture and analysis of stool for Clostridium difficile toxin may identify infectious causes of inflammation.

Evaluation of Chronic Fatty Diarrhea

- Patients with evidence of steatorrhea should undergo small bowel follow-through radiographic study to exclude structural problems. Small bowel biopsy specimens and an aspirate of small bowel contents for quantitative culture should be obtained, and pancreatic exocrine insufficiency should be assessed by direct tests, such as the secretin test, or by indirect tests, such as measurement of stool chymotrypsin activity or a bentiromide test.
- Studies such as D-xylose absorption tests and the Schilling test have little application in the evaluation of these patients.

Empirical Therapy for Chronic Diarrhea

- Empirical therapy is used in three situations:(1) as a temporizing or initial treatment before diagnostic testing,(2) after diagnostic testing has failed to confirm a diagnosis, and (3) when a diagnosis has been made, but no specific treatment is available or specific treatment fails to effect a cure.
- Empirical trials of antimicrobial therapy may be justified if the prevalence of bacterial or protozoal infection is high in a specific community or situation.
- An empirical trial of bile acid–binding resins, such as cholestyramine, may be the least expensive way to diagnose bile acid–induced diarrhea.
- Opiates are the most effective nonspecific antidiarrheal agents. Octreotide should be reserved as a secondary agent.
- Adequate hydration is an essential part of the treatment of diarrheal diseases, and oral rehydration solutions may be necessary in some instances. Some patients, particularly those with postresection diarrhea, may need long-term intravenous fluid administration
- Parenteral nutrition should be reserved for patients who are unable to maintain an adequate nutritional status because of the diarrheal disease.

Antibiotic associated diarrhoea

- Diarrhoea is a common adverse effect of antibiotic treatments. The frequency of antibiotic associated diarrhoea depends on the definition of diarrhoea, the inciting antimicrobial agents, and host factors. Almost all antibiotics, particularly those that act on anaerobes, can cause diarrhoea, but the risk is higher with aminopenicillins, a combination of aminopenicillins and clavulanate, cephalosporins, and clindamycin. Host factors for antibiotic associated diarrhoea include age over 65, immunosuppression, being in an intensive care unit, and prolonged hospitalisation.
- Clinical presentations of antibiotic associated diarrhoea range from mild diarrhoea to fulminant pseudomembranous colitis. The latter is characterised by a watery diarrhoea, fever (in 80% of cases), leucocytosis (80%), and the presence of pseudomembranes on endoscopic examination.
- Severe complications include toxic megacolon, perforation, and shock.
- Antibiotic associated diarrhoea results from disruption of the normal microflora of the gut by antibiotics. Antibiotics disturb the composition and the function of this flora and enable overgrowth of microorganisms that induce diarrhoea.
- Clostridium difficile has emerged as the major enteropathogen of antibiotic associated diarrhoea. Other infectious agents reported to be responsible for antibiotic associated diarrhoea include C perfringens, Staphylococcus aureus, Candida spp, Klebsiella oxytoca, and Salmonella spp.
- Antibiotic associated diarrhoea can also result from a decrease in metabolism of carbohydrates and bile acids.
- Managing the diarrhoea depends on presentation and the inciting agent. In mild to moderate diarrhoea conventional measures include rehydration or discontinuation of the inciting agent or its replacement by an antibiotic with a lower risk of inducing diarrhoea, such as quinolones, co-trimoxazole, or aminoglycosides.
- In 22% of cases of diarrhoea related to C difficile, withdrawal of the inciting agent will lead to resolution of clinical signs in three days.
- In cases of severe or persistent antibiotic associated diarrhoea, the challenge is to identify C difficile associated infections since this is the most common identifiable and treatable pathogen. Treatment of C difficile related diarrhoea is based on oral metronidazole (250 mg four times daily) or oral vancomycin (125 mg four times daily) for 10 days. Vancomycin should be reserved for those with severe illness, intolerance to metronidazole, failure to respond to metronidazole, or pregnancy.
- Antiperistaltic agents should be avoided because of the risk of retention of toxins in the lumen. About 20% of patients with C difficile related diarrhoea will relapse. The key measure for preventing antibiotic associated diarrhoea, is to limit antibiotic use.
- Probiotics have proved useful in preventing diarrhoea, Lactobacillus rhamnosus GG and Saccharomyces boulardii appear to be the most efficacious
- Choice for preventing antibiotic-associated diarrhoea, Lactobacillus casei may be the best for specifically preventing severe C. difficile-related diarrhoea

***REFER** to gastroenterologist:*

- If treatment does not relieve symptoms.
- If symptoms suggestive of functional bowel disease and <45 yr with normal investigations, irritable bowel syndrome is likely. Reassure, offer advice, and review as necessary.
- If atypical symptoms appear or the patient is unhappy with the diagnosis.
- Otherwise refer to gastroenterologist for assessment.

- Speed of referral depends on age and severity of symptoms

Refer urgently if:

•Any age with:

- Right lower abdominal mass consistent with involvement of large bowel
- A palpable rectal mass (intraluminal, not pelvic; a pelvic mass outside the bowel would warrant an urgent referral to a urologist)
- Unexplained iron deficiency anaemia (Hb≤11g/dL for male: ≤10g/dL for a non-menstruating female)
- •Aged ≥ 40 yr
- Reporting rectal bleeding with a change of bowel habit towards looser stools and/or increased stool frequency persisting ≥ 6 weeks.
- •Aged ≥ 60 yr with:
- Rectal bleeding persisting for ≥ 6 weeks without a change in bowel habit and without anal symptoms
- Change in bowel habit to looser stools and/or more frequent stool persisting for ≥ 6 weeks without rectal bleeding.
- • In a patient with equivocal symptoms who is not unduly anxious, it is reasonable to 'treat, watch and wait'.

Reference

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ACUTE GASTRITIS

Definition

- Mucosal inflammation of the stomach with no ulcer
- Type A: affects the entire stomach; associated with pernicious anaemia; pre-malignant
- Type B: affects antrum ± duodenum; associated with H. pylori
- Type C: due to irritants, e.g. NSAIDs, alcohol, bile reflux
- Other causes -stress (secondary to mucosal ischemia) and autoimmune gastritis.
- Rare causes - phlegmonous gastritis (a rare bacterial infection).

Presentation

- COMMON SYMPTOMS
- retrosternal or epigastric pam, fullness, bloating, wind, heartburn, nausea, and vomiting.

Examination

- usually normal
- Clinical anaemia
- Epigastric tenderness.
- Epigastric mass/hepatomegaly, and lymph nodes in the neck.

Investigation

- Helicobacter pylori urea breath test
- H pylori fecal antigen test
- CBC
- Endoscopy
- Gastric mucosal histology
- Serum vitamin B12

Management

- Lifestyle:reduce alcohol, stop smoking
- Mucosal coating (sucralfate, antacids) agents or short-term histamine-2 antagonists and proton-pump inhibitor (PPI) for 4-8weeks can stabilize mild to moderate cases in the short term.
- Administer fluids and electrolytes as required, particularly if the patient is vomiting.
- Treat the cause where possible: (e.g. vitamin B12 injections; H. pylori eradication; avoidance of nonsteroidal anti-inflammatory drugs, caffeine, alcohol)
- Re-endoscope to confirm healing
- Consult a gastroenterologist in complicated cases.
- Surgical intervention is not necessary for gastritis, except in the case of phlegmonous gastritis or acute necrotizing gastritis.

Complications

- Haemorrhage, gastric atrophy ± gastric cancer (type A only)

Prevention

- In patients with gastritis, it is recommended to eradicate *H pylori* infection before starting nonsteroidal anti-inflammatory drug (NSAIDs)/aspirin treatment for the first time, as this will decrease the possibility of inducing gastroduodenal ulceration.

Reference

1. *Oxford Handbook of General Practice, 4th Edition*
2. *https://bestpractice.bmj.com/topics/en-us/8163*
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PEPTIC ULCERATION

Definition

- Peptic ulceration (PU) is a term which includes both gastric and duodenal ulceration. Most patients present with dyspepsia
- **Gastric** – referring to the stomach.
- **Duodenal** – referring to the beginning of the small intestine or duodenum.

Features of gastric and duodenal ulcers

	Gastric Ulcer (GU)	Duodenal Ulcer (DU)
Population	Typically affects middle-aged/elderly male	Typically affects young-middle-aged male, although can affect any adult. M > F
Risk factors	*H pylori* (70-90%) NSAID use (increased risk x3-4) Delayed gastric emptying Reflux from the duodenum (increased by smoking)	*H pylori* (>90%) NSAID use Gastric hyperacidity Rapid gastric emptying Smoking Stress
Presentation	May be asymptomatic Epigastric pain worsened by food and helped by antacids or lying flat ± weight loss With complications	May be asymptomatic or spontaneously relapse and remit Epigastric pain typically relieved by food and worse at night ± weight increased ± waterbrash (saliva fills the mouth) With complications
Examination	In uncomplicated gastric ulceration, examination is usually normal, though there may be epigastric/left upper quadrant tenderness.	In uncomplicated duodenal ulceration, examination is usually normal, though there may be epigastric tenderness.
Investigation	As for dyspepsia	
Complications	***Bleeding:*** Acute GI bleeding, iron deficiency anaemia ***Perforated peptic ulcer:*** DU > GU; GUs may perforate posteriorly into the lesser sac; DUs usually perforate anteriorly into the peritoneal cavity. There may not be a past history of indigestion. Presents with sudden onset severe epigastric pain which rapidly becomes generalized. When a GU perforates into the lesser sac symptoms may remain localized or be confined to the right side of the abdomen. *Examination:* Generalized peritonism with 'board-like rigidity'. *Management:* acute surgical admission ***Pyloric stenosis in adults:*** duodenal stenosis secondary to scarring from a chronic DU. Characterized by copious vomiting of food l-2 days old. There may not be a past history of indigestion. *Examination:* if prolonged vomiting may be evidence of dehydration ± weight decreased. Succussion splash may be audible. *Management:* surgical referral for confirmation of diagnosis and surgical relief	

Management

*For patients not taking NSAIDs***want to big font*

- Eradicate H. pylori if present
- Speeds ulcer healing and decrease relapse; confirm eradication with a urea breath test (duodenal ulcer) or repeat endoscopy (gastric ulcer), and retreat if still present
- If H. pylori negative: Treat with full-dose PPI (e.g. omeprazole 20 mg od) for 1-2 month.
- If gastric ulcer, re-endoscope to check ulcer is healed

For patients taking NSAIDs

- Stop NSAIDs where possible. If not possible consider changing to a safer alternative (e.g. paracetamol, decreased dose of NSAID, COX2-selective NSAID) and adding gastric protection with a PPI or misoprostol
- Offer full-dose PPI or H2 receptor antagonist (H2RA) therapy for 2months
- Check eradication with repeat endoscopy (gastric ulcer) or urea breath test (duodenal ulcer).

Medical Management of NSAID Ulcers

- According to the ACG (American College of Gastroenterology) guideline, all patients who are beginning long-term NSAID therapy should first be tested for **H pylori**. NSAIDs should be immediately discontinued in patients with positive **H pylori** test results if clinically feasible.
- The 2017 ACG guidelines for the treatment of **H pylori** infection (HPI) have reaffirmed testing for HPI before initiating NSAID therapy.
- For patients who must continue with their NSAIDs, PPI maintenance is recommended to prevent recurrences even after eradication of **H pylori**. If NSAIDs must be continued, changing to a cyclooxygenase (COX)-2 selective inhibitor is an option.
- For patients with a known history of ulcer and in whom NSAID use is unavoidable, the lowest possible dose and duration of the NSAID and co-therapy with a PPI or misoprostol are recommended.
- Thus, the 2009 ACG guideline recommends that patients who are treated with NSAIDs and also require low-dose aspirin therapy for cardiovascular disease be treated with naproxen plus misoprostol or a PPI. Patients at moderate risk for gastrointestinal complications and at high risk for cardiovascular disease should avoid NSAIDs or COX-2 inhibitors entirely and receive alternative therapy.

For all patients

- Lifestyle measures
- Avoid foods (or alcohol) which exacerbate symptoms; eat little and often; avoid eating <3 hours before bed
- Stop smoking
- If symptoms recur following initial treatment, offer a PPI at lowest dose to control symptoms, with a limited number of repeat prescriptions. Discuss using the treatment on a pm basis
- Offer H2RA therapy If there is an inadequate response to a PPI
- In patients with unhealed ulcer or continuing symptoms despite adequate treatment, exclude non-adherence, malignancy, failure to detect H. pylori, inadvertent NSAID use, other ulcer-inducing medication, and rare causes, e.g. Zollinger-Ellison syndrome.

- Once symptoms are controlled, review at least annually to discuss symptom control, lifestyle advice, and medication.

Long-Term Monitoring

- Maintenance therapy with antisecretory medications (eg, H2 blockers, PPIs) for 1 year is indicated in high-risk patients. High-risk patients include those with recurrent ulcers and those with complicated or giant ulcers. If **H pylori** eradication is not achieved despite repeat treatment, maintenance antisecretory therapy should be recommended.
- Consider maintenance therapy with half of the standard doses of H2-receptor antagonists at bedtime in patients with recurrent, refractory, or complicated ulcers, particularly if cure of **H pylori** has not been documented or if an **H pylori** – negative ulcer is present.
- Patients with refractory ulcers may continue receiving once-daily PPI therapy indefinitely.
- In this setting, if **H pylori** is absent, consider a secondary cause of duodenal ulcer, such as Zollinger-Ellison syndrome

- Peptic ulcer rebleeding is extremely rare after **H pylori** eradication. The use of maintenance antisecretory therapy is not necessary if **H pylori** eradication has been achieved. However, NSAID use may cause rebleeding even in patients in
- **H pylori** has been eradicated.

Patient Education

- • Patients with peptic ulcer disease should be warned about known or potentially injurious drugs and agents.
- Some examples are as follows:
- Nonsteroidal anti-inflammatory drugs (NSAIDs)
- Aspirin
- Alcohol
- Tobacco
- Caffeine (eg, coffee, tea, colas)
- • Obesity has been shown to have an association with peptic ulcer disease, and patients should be counseled regarding benefits of weight loss. Stress reduction counseling might be helpful in individual cases but is not needed routinely.
- • A special diet is not indicated for patients with duodenal ulcers. It is a common-sense approach to avoid any food or beverages that may aggravate symptoms. Although the link between duodenal ulcers and alcohol is inconclusive, moderation of alcohol intake may be recommended for other health reasons.

Deterrence and prevention

- Primary prevention of NSAID-induced ulcers includes the following:
  - Avoid unnecessary use of NSAIDs
  - Use acetaminophen or nonacetylated salicylates when possible
  - Use the lowest effective dose of an NSAID and switch to less toxic NSAIDs, such as the newer NSAIDs or COX-2 inhibitors, in high-risk patients without cardiovascular disease
- Consider prophylactic or preventive therapy for the following patients:
  - Patients with NSAID-induced ulcers who require chronic, daily NSAID therapy
  - Patients older than 60 years
  - Patients with a history of peptic ulcer disease or a complication such as gastrointestinal bleeding

    - Patients taking concomitant steroids or anticoagulants or patients with significant comorbid medical illnesses.
- Prophylactic regimens that have been shown to dramatically reduce the risk of NSAID-induced gastric and duodenal ulcers include the use of a prostaglandin analog or a PPI according to the following regimens:
    - Misoprostol 100-200 mcg PO 4 times per day
    - Omeprazole 20-40 mg PO every day
    - Lansoprazole 15-30 mg PO every day

Refer

- If gastric ulcer fails to heal or if symptoms do not respond to medical treatment.
- Possible surgical procedures include: gastrectomy, vagotomy, and drainage procedure;highly selective vagotomy
- Alarm features that warrant prompt gastroenterology referral include the following:
    - Bleeding or anemia
    - Early satiety
    - Unexplained weight loss
    - Progressive dysphagia or odynophagia
    - Recurrent vomiting
    - Family history of gastrointestinal cancer

Reference

1. *Oxford Handbook of General Practice, 4th Edition*
2. *https://emedicine.medscape.com/article/181753-treatment*

DYSPEPSIA AND H.PYLORI

Definition

Functional dyspepsia (FD) is defined as the presence of one or more of the followings bothersome postprandial fullness, bothersome early satiation, bothersome epigastric burning and no evidence of structural disease (including at upper endoscopy) to explain symptoms. (Rome IV 3)

Causes

- Gastro-oesophageal reflux disease (GORD) 15-25%
- Peptic ulcer (PU)l5-25%
- Stomach cancer 2%
- The remaining 60% are classified as non-ulcer dyspepsia (NUD, 'functional' dyspepsia) manage as for uninvestigated dyspepsia
- Rarer causes: oesophagitis from swallowed corrosives, oesophageal infection (especially in the immunocompromised)

Differential diagnosis

- Cardiac pain (difficult to distinguish)
- Gallstone pain
- Pancreatitis
- Bile reflux

Presentation

- Clinical history taking in dyspepsia
- The patient should be asked about all possible upper gastrointestinal symptoms, including ‘red flags’,
- or alarm symptoms and signs.

Common symptoms

- Retrosternal or epigastric pain or burning, early satiation, postprandial fullness, heartburn, bloating, wind, heartburn, nausea, vomiting, belching, regurgitation, dysphagia, including the level at which food sticks, and rumination, ensuring the patient understands what he/she means.
- Weight loss is reported frequently by patients with FD. Depending on the patient’s age, this may be considered an alarm symptom, so attention should be paid to obtaining objective evidence of this.

Alarm – symptoms

- Anaemia
- Loss of weight
- Anorexia
- Recent onset of progressive symptoms
- Masses & Melaena/haematemesis
- Swallowing difficulty

Examination

- usually normal
- epigastric tenderness
- clinical anaemia, epigastric mass/hepatomegaly, and lymph nodes in the neck.

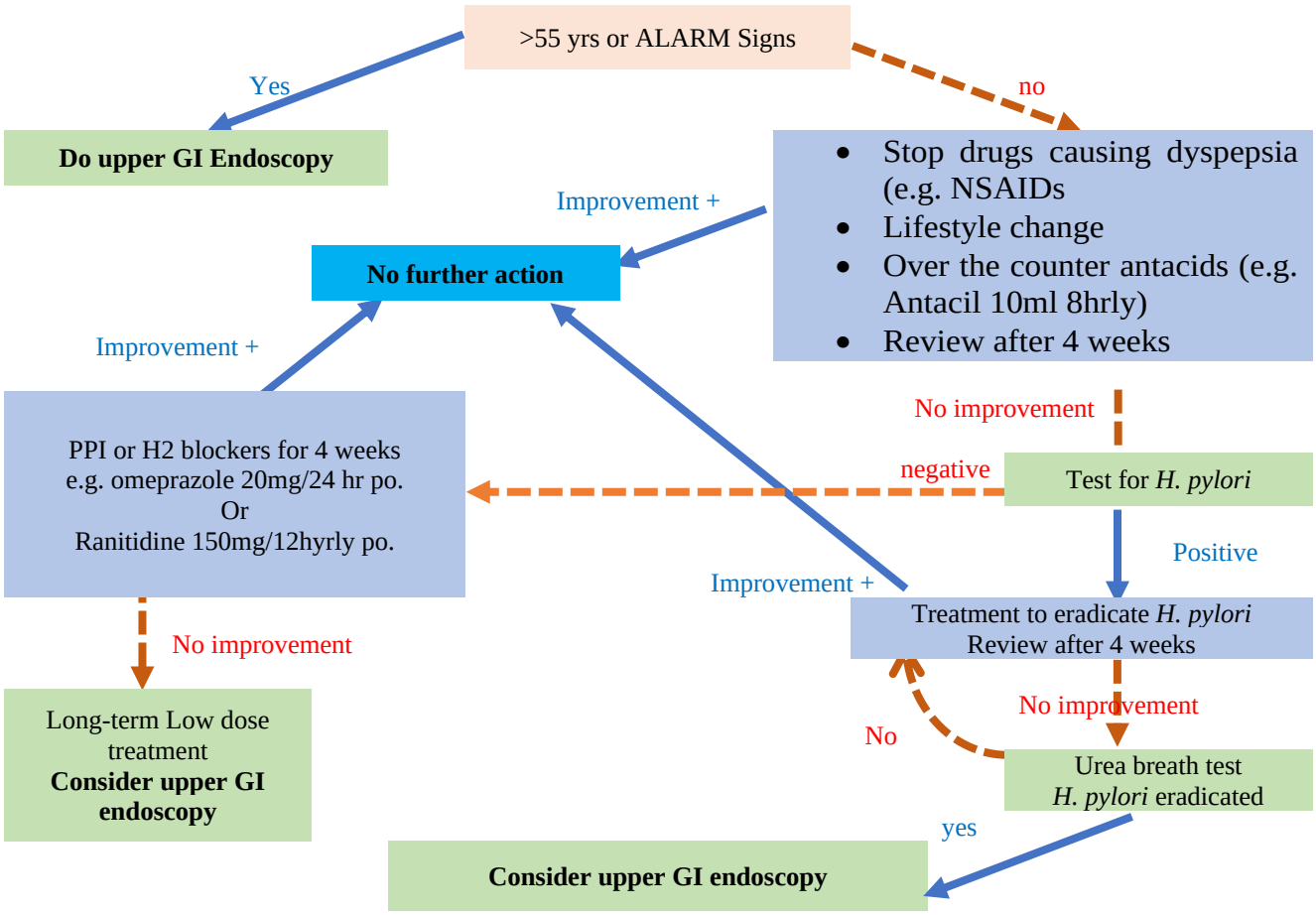
Investigation

- A full blood counts
- Testing for H. pylori and eradicating the bacterium in patients with dyspepsia in primary care who are found to be infected is logical. This is termed a 'test and treat' strategy and can be done via faecal antigen or carbon-urea breath testing, where available, which have a similar accuracy to rapid urease testing of biopsies obtained at endoscopy.

Endoscopy

- endoscopy only in patients aged ≥55 years with dyspepsia with evidence of weight loss. Non-urgent endoscopy can be considered in patients aged ≥55 years with treatment-resistant dyspepsia or dyspepsia with either a raised platelet count or nausea or vomiting.
- In patients from areas at high risk of gastric cancer, or those with a family history of gastrooesophageal malignancy, the age limit for endoscopy should be reduced to >40 years.
- In those with aged ≥60 years with abdominal pain and weight loss urgent CT scanning should be considered to exclude pancreatic cancer.
-
- • Definite referral criteria for urgent endoscopy to assess for gastro-oesophageal cancer
- People of any age with dysphagia
- People aged ≥55 years with weight loss and any of the following:
- Dyspepsia.
- Upper abdominal pain.
- Reflux.
- • Probable referral criteria for non-urgent endoscopy to assess for gastro-oesophageal cancer
- People with haematemesis.
- People aged ≥55 years with:
- Treatment-resistant dyspepsia.
- Dyspepsia with raised platelet count or nausea or vomiting.
- Upper abdominal pain with low haemoglobin, raised platelet count or nausea or vomiting.
- Reflux with raised platelet count, or nausea or vomiting.
- Nausea or vomiting with any of the following: weight loss, reflux, dyspepsia, or upper abdominal pain.

Managing New Dyspepsia



Management of dyspepsia in primary care

- It is important to build rapport and trust in the doctor–patient relationship by adopting the principles of empathic listening to optimise the consultation.

First-line treatment of FD

- All patients with FD are advised to take regular aerobic exercise (recommendation: strong, quality of evidence: very low).
- Insufficient evidence to recommend dietary therapies, including a diet low in fermentable oligosaccharides, disaccharides and monosaccharides, and polyols in FD (recommendation: weak; quality of evidence: very low).
- Eradication therapy is an efficacious treatment for H. pylori positive patients with FD.
- Adverse events are more common than with a control therapy (recommendation: strong; quality of evidence: high).
- Histamine-2 -receptor antagonists may be an efficacious treatment for FD. These drugs are well tolerated (recommendation: weak, quality of evidence: low).
- Proton pump inhibitors (PPIs) are an efficacious treatment for FD. There does not appear to be a dose response, so the lowest dose that controls symptoms should be used. These drugs are well tolerated (recommendation: strong, quality of evidence: high).
- Some prokinetics may be an efficacious treatment for FD. However, efficacy varies according to drug class, these drugs are well tolerated (recommendation: weak,

quality of evidence: low for acotiamide, itopride, and mosapride, recommendation: strong, quality of evidence: moderate for tegaserod).

Second-line treatment of FD

- Tricyclic antidepressants (TCAs) used as gut–brain neuromodulators are an efficacious second-line treatment for FD. They can be initiated in primary or secondary care, but careful explanation as to the rationale for their use is required, and patients should be counselled about their side effect profile.
- They should be commenced at a low dose (eg, 10 mg amitriptyline once daily) and titrated slowly to a maximum of 30–50 mg once daily (recommendation: strong, quality of evidence: moderate).
- Antipsychotics, such as sulpiride 100 mg four times a day or levosulpiride 25 mg three times a day, may be efficacious as a second-line treatment for FD. There should be careful explanation as to the rationale for be counselled on their side effect profile (recommendation: weak, quality of evidence: low).
- Pregabalin 75 mg once daily may be an efficacious second line treatment for FD but further randomised controlled trials (RCTs) are needed and given its controlled drug status we advise this drug is only used in specialist settings (recommendation: weak, quality of evidence: low).
- Mirtazapine 15 mg once daily may be an efficacious second line treatment for patients with FD with early satiation and weight loss, but further RCTs are needed (recommendation: weak, quality of evidence: very low)
- Hypnotherapy may be an efficacious treatment for global symptoms in FD (recommendation: weak, quality of evidence: very low).

Gut–brain behavioural therapies in FD

- Interpersonal psychodynamic informed psychotherapy may be an efficacious treatment for global symptoms in FD (recommendation: weak, quality of evidence: very low).
- Cognitive–behavioural therapy (CBT) and metacognitive therapy may be an efficacious treatment for global symptoms in FD (recommendation: weak, quality of evidence: very low).
- Stress management approaches may be an efficacious treatment for global symptoms in FD (recommendation: weak, quality of evidence: very low).

Management of severe or refractory FD

- A multidisciplinary support team should be involved for patients with severe or refractory FD (recommendation: strong, quality of evidence: low).
- Opioids and surgery should be avoided in patients with severe or refractory FD to minimize iatrogenic harm (recommendation: strong, quality of evidence: very low).
- Patients with severe or refractory FD presenting with weight loss and food restriction are assessed for eating disorders and disordered eating, including avoidant restrictive food intake disorder (ARFID) (recommendation: strong, quality of evidence: very low).
- Early dietitian involvement in patients with severe or refractory FD to avoid an overly restrictive diet (recommendation: strong, quality of evidence: very low)

Helicobacter pylori

Helicobacter pylori continues to be a major health problem worldwide, causing considerable morbidity and mortality due to peptic ulcer disease and gastric cancer. H. pylori infection usually persists for life, unless it is treated with antibiotics or autoeradication occurs when long-standing infection causes widespread gastric mucosal atrophy and metaplasia with achlorhydria. Transient infection may occur in some infants.

Infection is associated with:

- GI disease-peptic ulcer disease; gastric cancer; non-ulcer dyspepsia; oesophagitis
- Non-GI disease-ranging from cardiovascular disease and haematological malignancy to cot death
- Testing for H pylori
- 'Test and treat' all patients with dyspepsia who do not meet referral criteria.
- In practice choice of test is limited by availability, ease of access, and cost.
- Options in the community are: serology, urea breath test, and faecal antigen test.
- *Urea breath tests* (UBTs) are very useful and have higher diagnostic accuracy than other noninvasive tests for identifying H. pylori (in patients without a history of gastrectomy).
- Most commercial urease tests appear to be accurate to a sensitivity of about 95%.
- A 2 week wash out period following proton pump inhibitor (PPI) use is necessary before testing for H pylori with a breath test or a stool antigen test.
- Eradication: Clears 80-85% H pylori infections.

Options:

- PAC500 regimen:
- Full-dose PPI (e.g. omeprazole 20mg bd) +Amoxicillin lg bd +
- Clarithromycin 500 mg bd for 1week, or
- PMC250 regimen:
- Full-dose PPI (e.g. omeprazole 20mg bd) + Metronidazole 400mg bd +
- Clarithromycin 250mg bd for 1week
- Do not re-test even if dyspepsia remains unless there is a strong clinical need.
- Re-test if needed using a urea breath test.

Triple therapies and quadruple-therapy combinations—typical composition, dosage, and duration

Triple therapies	**1**	**2**	**3**	
All twice daily for 7–14 days	PPI PPI PPI	Amoxicillin 1 g Metronidazole 400 mg Amoxicillin 1 g	Clarithromycin 500 mg Clarithromycin 500 mg Metronidazole 400 mg	
All twice daily for 10–14 days	PPI	Amoxicillin 1 g	Levofloxacin 500 mg	
All twice daily for 7–10 days	PPI	Amoxicillin 1 g	Rifabutin 150 mg	
Quadruple therapies	**1**	**2**	**3**	**4**
For 7–14 days	PPI twice daily	Bismuth 120 mg four times daily	Metronidazole 400– 500 mg three times daily	Tetracycline 500 mg four times daily
	(Amoxicillin 500–1000 mg three times daily has been substituted for tetracycline)			
All twice daily for 7–14 days	Bismuth 240 mg	PPI	Amoxicillin 1 g	Clarithromycin 500mg

Treatment considerations when local resistance rates are not well defined, individual patient testing is not available, and there are low resource

First–line therapies		
PPI-AC	In regions where clarithromycin resistance rate is thought to be low or moderate (< 20%)	If prior clarithromycin use in monotherapy or combination, assume resistance and avoid in first-line therapy 7-day minimum duration, likely higher eradication success with 10–14 days (consider costs) Use quality generic drugs to minimize costs Encourage compliance with full course
Quadruple therapy	In regions where clarithromycin resistance rates are likely > 20%	Avoid PPI-AC first-line Quadruple therapy overcomes MR; unaffected by CR May be more difficult to take and "nuisance"; adverse effects are common Encourage compliance with full course Generic drugs may be less expensive than triple therapy
PPI-AC or quadruple therapies	In regions with unknown clarithromycin resistance rates	Avoid clarithromycin if past personal patient exposure PPI-AC otherwise a reasonable choice Quadruple therapy also a good option
Second–line therapies		
•Quadruple therapy •Levofloxacin triple therapy	After failure of clarithromycin containing regime	Avoid repeating the same treatment Avoid using clarithromycin again, as secondary resistance will be high and eradication success very low Levofloxacin triple therapy a good option if no prior personal exposure and resistance thought to be low or moderate
•Clarithromycin or levofloxacin triple therapy	After failure of quadruple therapy	Check compliance Levofloxacin preferred if likely high CR region or past personal exposure

A, amoxicillin; C, clarithromycin; CR, clarithromycin resistance; MR, metronidazole resistance; PPI, proton-pump inhibitor

Lifestyle advice

- Give advice on healthy eating, weight reduction, and smoking cessation.
- Advise patients to avoid precipitating factors, e.g. alcohol, coffee, chocolate, fatty foods.
- Raising the head of the bed and having a main meal well before going to bed may help some people.
- Promote continued use of antacids.

Reference

1. *Oxford Handbook of Clinical Medicine, 10th Edition*
2. *Oxford handbook of General Practice, 4th Edition*
3. *World Gastroenterology Organisation Global Guidelines Helicobacter pylori May 2021*

GASTRO- OESOPHAG EAL REFLUX

GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD)

Def: Retrograde flow of gastric contents into the esophagus through an incompetent gastro-oesophageal junction

Risk factors

- Smoking
- Alcohol
- Coffee
- Fatty food
- Big meals
- Obesity
- Hiatus hernia
- Tight clothes
- Pregnancy
- Systemic sclerosis

Conditions caused by GORD

- Oesophagitis (defined by mucosal breaks) ± oesophageal ulcer
- Benign oesophageal stricture
- Intestinal metaplasia: Barrett's oesophagus
- Oesophageal haemorrhage
- Anaemia

Presentation

- Heartburn:most common symptom.
- Burning retrosternal or epigastric pain which worsens on bending, stooping or lying, and with hot drinks. Relieved by antacids
- Other symptoms:
- Waterbrash-mouth fills with saliva
- Reflux of acid into the mouth especially on lying flat
- Nausea and vomiting
- Nocturnal cough/wheeze due to aspiration of refluxed stomach contents
- Examination:usually normal.
- Check for clinical anaemia, epigastric mass/hepatomegaly, and lymph-nodes in the neck

Complication

- Oesophagitis, ulcers, benign stricture, iron deficiency, metaplasia dysplasia neoplasia.
- GORD may lead to Barrett's oesophagus.

Investigation

Endoscopy if indicated

- Upper endoscopy is the most widely used objective test for evaluating the esophageal mucosa. For patients with GERD symptoms who also have alarm symptoms such as dysphagia, weight loss, bleeding, vomiting, and/or iron deficiency anemia, epigastric mass, endoscopy should be performed as soon as feasible. The endoscopic findings of EE and Barrett's esophagus are specific for the diagnosis of GERD.
- Symptoms are poorly correlated with endoscopic findings.
- Reflux may remain silent in patients with Barrett's oesophagus but heartburn can severely affect quality of life of patients with negative endoscopy results.

Esophageal manometry (HRM)

- HRM can be used to assess motility abnormalities associated with GERD, but HRM is not alone a diagnostic test for GERD. Weak lower esophageal sphincter (LES) pressure and ineffective esophageal motility often accompany severe GERD, but no manometric abnormality is specific for GERD.

Reflux monitoring

- Ambulatory reflux monitoring (pH or impedance-pH) allows for assessment of esophageal acid exposure to establish or refute a diagnosis of GERD and for correlating symptoms with reflux episodes using the symptom index (SI) or symptom association probability (SAP).
- The main methods of reflux testing include a wireless telemetry capsule (Bravo Reflux Capsule; Medtronic, Minneapolis, MN) attached to the esophageal mucosa during endoscopy and transnasal catheter-based testing, and there are strengths and weaknesses to each approach.

Diagnosis of GERD in pregnancy

- Heartburn is the only GERD symptom that has been studied in pregnancy, and the diagnosis of GERD is almost always symptom-based. Endoscopy and pH monitoring are rarely needed..

Initial management

- In all cases, give lifestyle advice (reduce weight, smoking cessation, small and regular meals, reduce hot drinks, alcohol, citrus fruit, tomatoes, onion, fizzy drinks, spicy food, caffeine, chocolate, avoid eating <3 hr before bed, raised the bed-head)
- If diagnosis is clinical (i.e. patient presents with 'reflux-like' symptoms), treat as for uninvestigated dyspepsia (see figure in dyspepsia)

Medications

- The backbone of pharmacologic therapy for GERD are medications that are directed at neutralization or reduction of gastric acid. Agents in this class include antacids, H2RA, and PPIs. Antacids are used exclusively for on-demand symptom relief.

- For patients with reflux confirmed on endoscopy, offer treatment with a PPI (e.g. omeprazole 20 mg od) for 1-2months.
- Optimization of PPI therapy includes verifying compliance, confirming that the PPI is taken 30–60 minutes before the first meal of the day for daily dosing and before the first and dinner meal for twice-daily dosing. Twice-daily PPI therapy is superior to once-daily double-dose PPI therapy in maintaining gastric pH above 4 during a 24-hour monitoring period.
- If oesophagitis at endoscopy and the patient remains symptomatic on PPI, double the dose of PPI for a further l month.
- If inadequate response to PPI, try an H2 receptor antagonist (e.g. ranitidine 150 mg bd) and/or add a prokinetic (e.g. domperidone 10 mg tds) for l month
- H2RA taken at bedtime
- Use of a bedtime H2RA may be beneficial if dosed on an as-needed basis for patients with nocturnal symptoms and for patients with objective evidence of nocturnal acid reflux on pH monitoring despite PPI treatment.

Baclofen

- Baclofen, a GABAB agonist, reduces the transient LES (Lower esophageal sphincter) relaxations that enable reflux episodes. Baclofen decreases the number of postprandial acid and nonacid reflux events, nocturnal reflux activity, and belching episodes. A trial of baclofen at a dosage of 5–20 mg 3 times a day can be considered in patients with objective documentation of continued symptomatic reflux despite optimal PPI therapy.
- Sucralfate is a mucosal protective agent, but few data document its efficacy in GERD.

Long-term management of endoscopically /barium-confirmed GORD

- Patients who have had dilatation of an oesophageal stricture should remain on long- term full-dose PPI therapy
- For all other patients, if symptoms recur following initial treatment, offer a PPI at the lowest dose possible to control symptoms, with a limited number of repeat prescriptions. Discuss using the treatment on an as-required basis to manage symptoms
- Refer for consideration of surgery if quality of life remains significantly impaired despite optimal treatment.
- Surgery of any type is >90% successful although results may deteriorate with time

Surgery

- Identifying patients with true refractory GERD is crucial because surgery (or endoscopic treatment) may truly be best in this group. GERD that fails to respond to medical therapy is another valid indication for antireflux procedures, but one that requires meticulous preprocedure evaluation to achieve good surgical outcomes.

Fundoplication

- Fundoplication especially Nissen fundoplication, is widely regarded as the "gold standard" among the antireflux procedures for its efficacy in improving the physiologic parameters of GERD such as LES pressure and esophageal acid exposure time. Fundoplication creates a barrier to the reflux of all gastric material (acidic and nonacidic) and therefore should be an effective treatment for any GERD symptom that is reflux-related.

Magnetic sphincter augmentation (MSA)

MSA with the LINX Reflux Management System, a necklace of titanium beads with magnetic cores that encircles the distal esophagus to bolster the LES and prevent reflux, was developed as a less invasive and more readily reversible GERD treatment than fundoplication.

Roux-en-Y gastric bypass (RYGB)

GERD is strongly associated with obesity. RYGB can control GERD in obese patients, presumably because the small gastric pouch fashioned during RYGB produces far less acid than an intact stomach, and because the accompanying long alimentary loop prevents the reflux of bile.

Endoscopic antireflux therapies

- Presently, the only endoscopic GERD treatments still widely available are radiofrequency antireflux treatment (Stretta; Restech, Houston, TX) and TIF (endogastric solutions).

Treatment of GERD during pregnancy

- Approximately two-thirds of pregnant women experience heartburn. It has been recommended that treatment of GERD during pregnancy should start with lifestyle modifications. When lifestyle modifications fail, antacids (aluminum-, calcium-, or magnesium-containing), alginates, and sucralfate are the first-line therapeutic agents. All histamine H2- blockers are FDA category B, and all PPIs are FDA category B except omeprazole, which is FDA category C.

HIATUS HERNIA

- Common (30% of over 50s); 50% have GORD.
- Obesity is a risk factor. The proximal stomach herniates through the diaphragmatic hiatus into the thorax
- 80% have a 'sliding' hiatus hernia where the gastro-oesophageal junction slides into the chest
- 20% have a 'rolling' hernia where a bulge of stomach herniates into the chest alongside the oesophagus. The gastro-oesophageal junction remains in the abdomen

Management

- Treat as for GORD.
- BARRETT'S OESOPHAGUS
- Usually found incidentally at endoscopy for symptoms of GORD and caused by chronic GORD. The squamous mucosa of the oesophagus undergoes metaplastic change, and the squamocolumnar junction appears to migrate away from the stomach.
- The length affected varies. It carries a 40 times increased risk of adenocarcinoma of the oesophagus, so regular endoscopy is essential.
- Treatment is with long-term PPIs (e.g. omeprazole 20-40mg od) ± laser therapy ±resection.

Reference

1. *Oxford handbook of General Practice, 4th Edition*
2. *ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease,Am J Gastroenterol 2022;117:27–56. https://doi.org/10.14309/ajg.0000000000001538; published online November 22, 2021*
3. *The American Journal of GASTROENTEROLOGY, VOLUME 117 | JANUARY 2022 www.amjgastro.com*

MALABSORPTION

Definition

- Malabsorption: defective mucosal uptake and transport of adequately digested nutrients including vitamins and trace elements.
- Presents with chronic diarrhoea, weight loss, steatorrhoea, vitamin/iron deficiencies, and/or oedema due to protein deficiency.

Causes

- Pancreatic
- Chronic pancreatitis Cancer of pancreas Cystic fibrosis
- Enteropathy Coeliac disease Tropical sprue Lymphoma
- Lymphangiectasia
- Blind loops, systemic sclerosis, and diverticula, where small intestinal bacterial overgrowth (SIBO) can occur. Intestinal bacteria may use up dietary vitamin B12 and other nutrients, perhaps interfere with enzyme systems, and cause mucosal injury.
- Cirrhosis and cholestasis reduce hepatic bile synthesis or delivery of bile salts to the duodenum, causing malabsorption.

Symptoms suggestive of malabsorption

- Pale and /or offensive stools
- Steatorrhoea-excess fat in faeces. The stool is pale-coloured and foul-smelling and floats ('difficult to flush')
- Severe vitamin and mineral deficiencies occur in advanced malabsorption; symptoms are related to the specific nutrient deficiency.
- Vitamin B12 deficiency may occur in blind loop syndrome or after extensive resection of the distal ileum or stomach.
- Iron deficiency may be the only symptom in a patient with mild malabsorption.
- Amenorrhea may result from undernutrition and is an important manifestation of celiac disease in young women.

Refer to gastroenterologist for investigation/treatment of the cause.

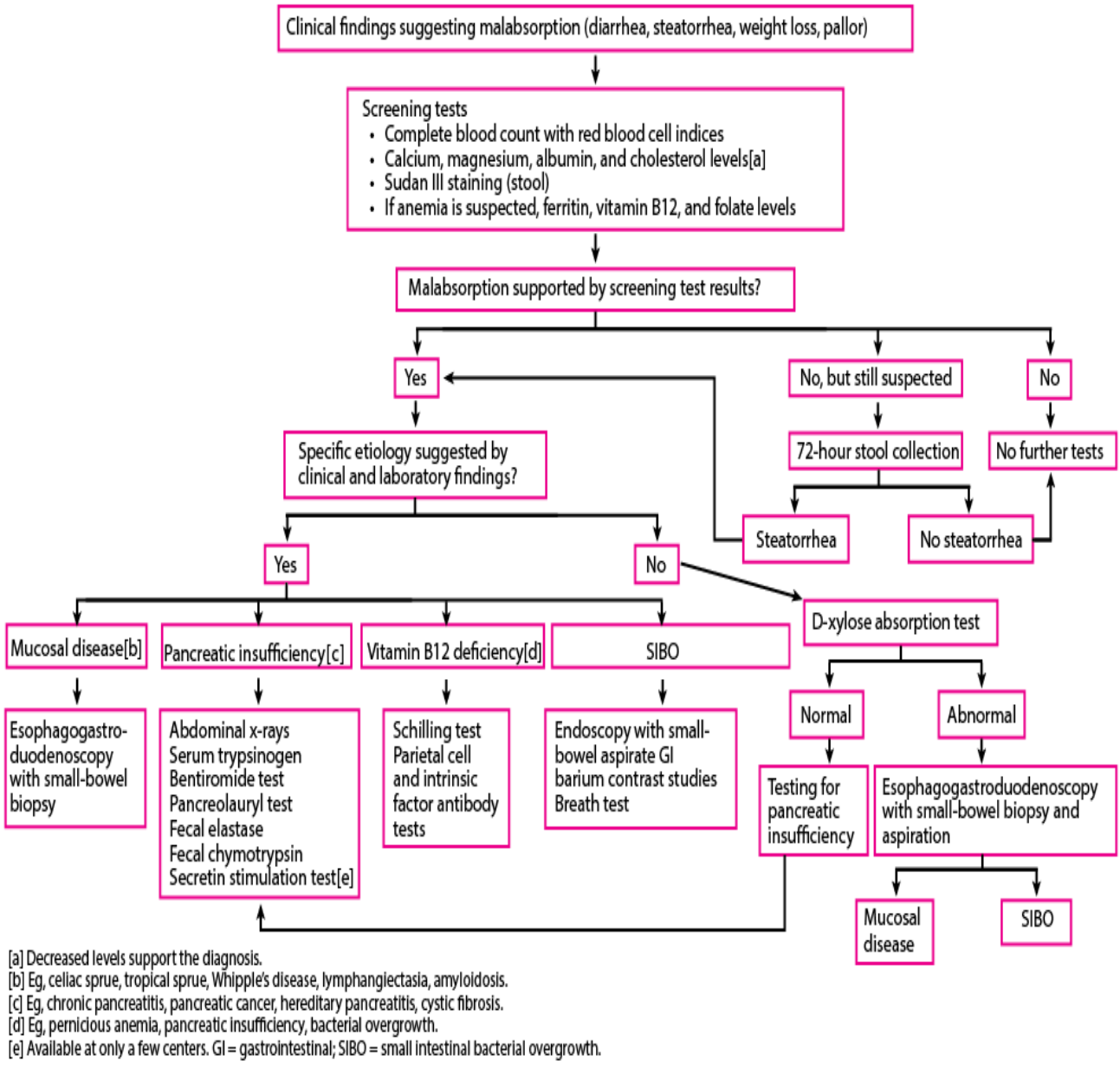
WHIPPLE'S DISEASE

- A cause of malabsorption which usually occurs in male >50 yr.
- Other features: arthralgia, pigmentation, weight loss, lymphadenopathy, ± cerebellar or cardiac signs.
- Cause: Tropheryma whippelii.
- Refer for gastroenterology assessment. Jejunal biopsy is characteristic.
- Treatment: long-term broad-spectrum antibiotics.

FACTITIOUS DIARRHOEA

- Responsible for 4% referrals to gastroenterology departments and 20% of tertiary referrals.
- Due to laxative abuse or adding of water or urine to stool samples.
- Difficult to spot-have a high index of suspicion especially in patients with history of eating disorder or somatization.

Suggested evaluation for malabsorption



Reference

1. *Gastroenterol Clin N Am 41 (2012) 629-637*
2. *https://www.msdmanuals.com/professional/gastrointestinal-disorders/malabsorption-syndromes/overview-of-malabsorption*

IRRITABLE BOWEL SYNDROME

Definition

- IBS is a chronic and sometimes disabling functional bowel disorder.
- IBS is diagnosed on the basis of recurrent abdominal pain related to defecation or in association with a change in stool frequency or form.

Rome (IV) criteria for IBS

- Recurrent abdominal pain, on average, at least 1 day/week in the last 3 months, associated with two or more of the following criteria:
- Related to defecation
- Associated with a change in frequency of stool
- Associated with a change in form (appearance)
- Criteria fulfilling for the last 3 months with symptoms onset at least 6 months before diagnosis.

Prevalence

- It is most common in women and young people.
- The diagnosing IBS accurately can minimize the invasive investigations and can recommend effective treatment to reduce the societal and economic effects of the disease.

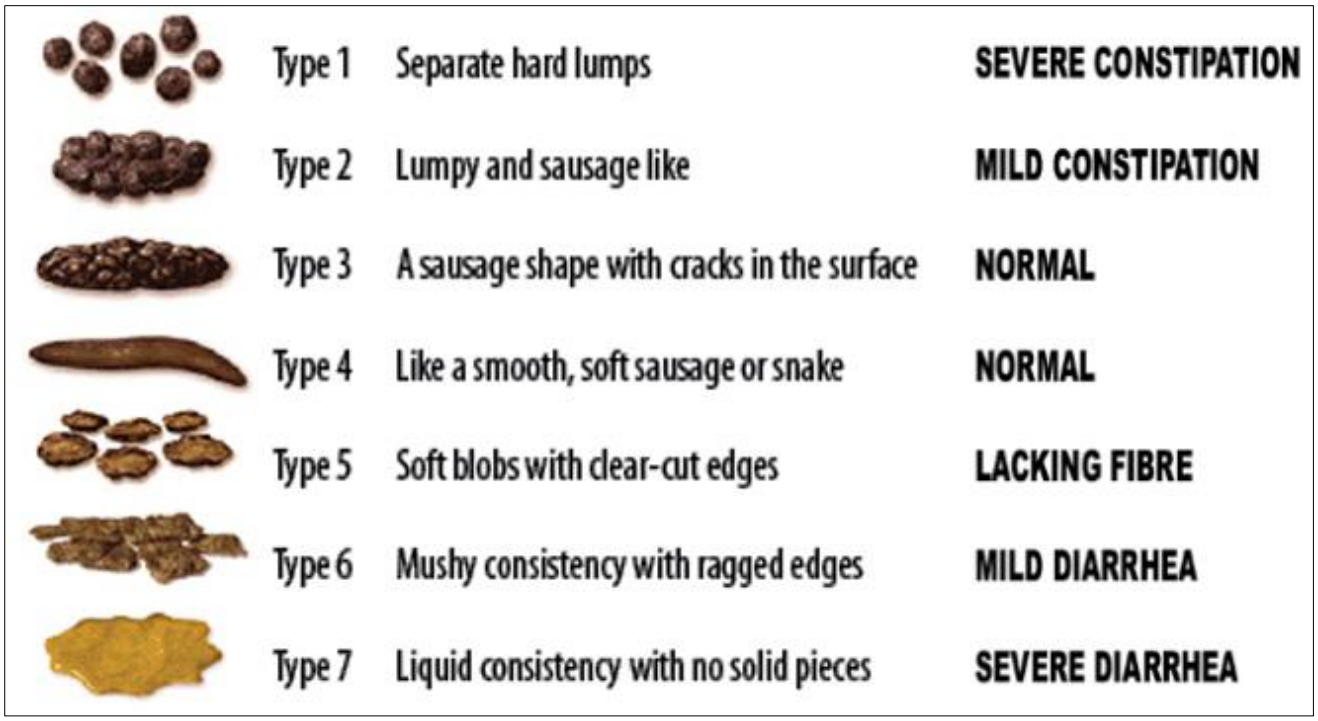
Classification

- On the basis of the Rome IV criteria, IBS is classified into four subtypes
- IBS with diarrhea (IBS-D)
- IBS with constipation (IBS-C)
- IBS with mixed symptoms of constipation and diarrhea (IBS-M)
- Undefined subtype (IBS-U) - unclassified; the symptoms cannot be categorized into one of the above three subtypes (IBS-U)

Diagnosis

- Patients with suspected IBS have symptoms of abdominal pam; the absence of abdominal pain precludes the diagnosis.
- Disordered bowel habits also need to be present. Abdominal bloating is not required but is frequently present and supports the diagnosis.
- A detailed history should be obtained to rule out disorders that can mimic IBS (e.g. carbohydrate malabsorption, celiac disease, ovarian cancer, and microscopic colitis).
- Physical examination in patients with IBS generally reveals no abnormalities other than lower abdominal tenderness.
- The presence of ascites, hepatosplenomegaly enlarged lymph nodes, or a mass → an alternative diagnosis.
- A digital rectal examination to exclude overlapping pelvic-floor dyssynergia.
- In the absence of warning signs, the Rome IV criteria should be applied to make a positive diagnosis.
- The clinician may order appropriate limited diagnostic testing to rule out other, less common, causes of similar symptoms.
- The Bristol Stool Form Scale can be used to accurately classify the patient.
- Treatment should be initiated as soon as the diagnosis is made and should focus on the predominant symptoms.

Bristol Stool Chart



Investigation

- Complete blood count to exclude IBD (Inflammatory Bowel Disease)
- C Reactive Protein (CRP)
- Thyroid Function Test (TFT),
- Serum Ca++ (for hyperparathyroidism)
- IBS-D
- Serology testing to exclude coeliac disease
- 23-seleno-25-homotaurocholicacid (75SeHCAT) testing
- serum 7a-hydroxy-4-cholesten-3-one [C4, a bile acid precursor] testing
- IBS- C
- Anorectal manometry-Pelvic floor dyssynergia
- USG (abdomen) (transvaginal) to exclude ovarian mass
- Fecal calprotectin testing- in IBS mixed, can reduce the use of colonoscopy novel biomarkers
- two serum biomarkers
- o (antibodies to a bacterial toxin produced by Campylobacter jejuni and vinculin),which distinguished IBS from IBD with good specificity (92% for C. jejuni and 84% for vinculin) but low sensitivity (44% for C. jejuni and 33% for vinculin).

TREATMENT

Therapy	Study outcome	Reported efficacy	Quality of evidence	Limitation of data	Side effect
Antispasmodic drugs (e.g. dicyclomine, 20-40 mg qid daily	Global symptoms, abdominal pain, diarrhoea	May be effective but class dependent	Low	No high-quality trials, only a small number of RCTs, assessing each drug and few trials with FDA-approved end points: none of the drugs identified as effective are available in the US	Abdominal pain, constipation, drug mouth, and dry eyes
Pepermint oil [e.g. colpermin (McNeil Products, two capsules tds daily)]	Global symptoms	Effective	Moderate	Few RCTs and no FDA-approved end points	Heartburn, dyspepsia, headache, and dry mouth
Rifaximin 550 mg tds	Global symptoms, abdominal pain, diarrhoea	Effective	Moderate	Few RCTs and only a modest benefit over placebo	Heartburn, nausea, abdominal pain, and diarrhoea
Soluble fibre (e.g. psyllium, one sachet tds daily)	Global symptoms,	Effective, start at a low dose and increase slowly	Moderate	Only one trial of high quality and no FDA-approved end point	Diarrhoea, constipation, bloating, and flatulence
Low fermentable oligo-dimono-saccharides and polylos (FODMAP) diet	Global symptoms, abdominal pain, bloating	May be effective; nutritionist's guidance helpful	Very low	Fre RCTs, may if cross over design with a small number of participants, and no FDA- approved end points	Potential effect on the colonic microbiome, with unknown long-term consequences

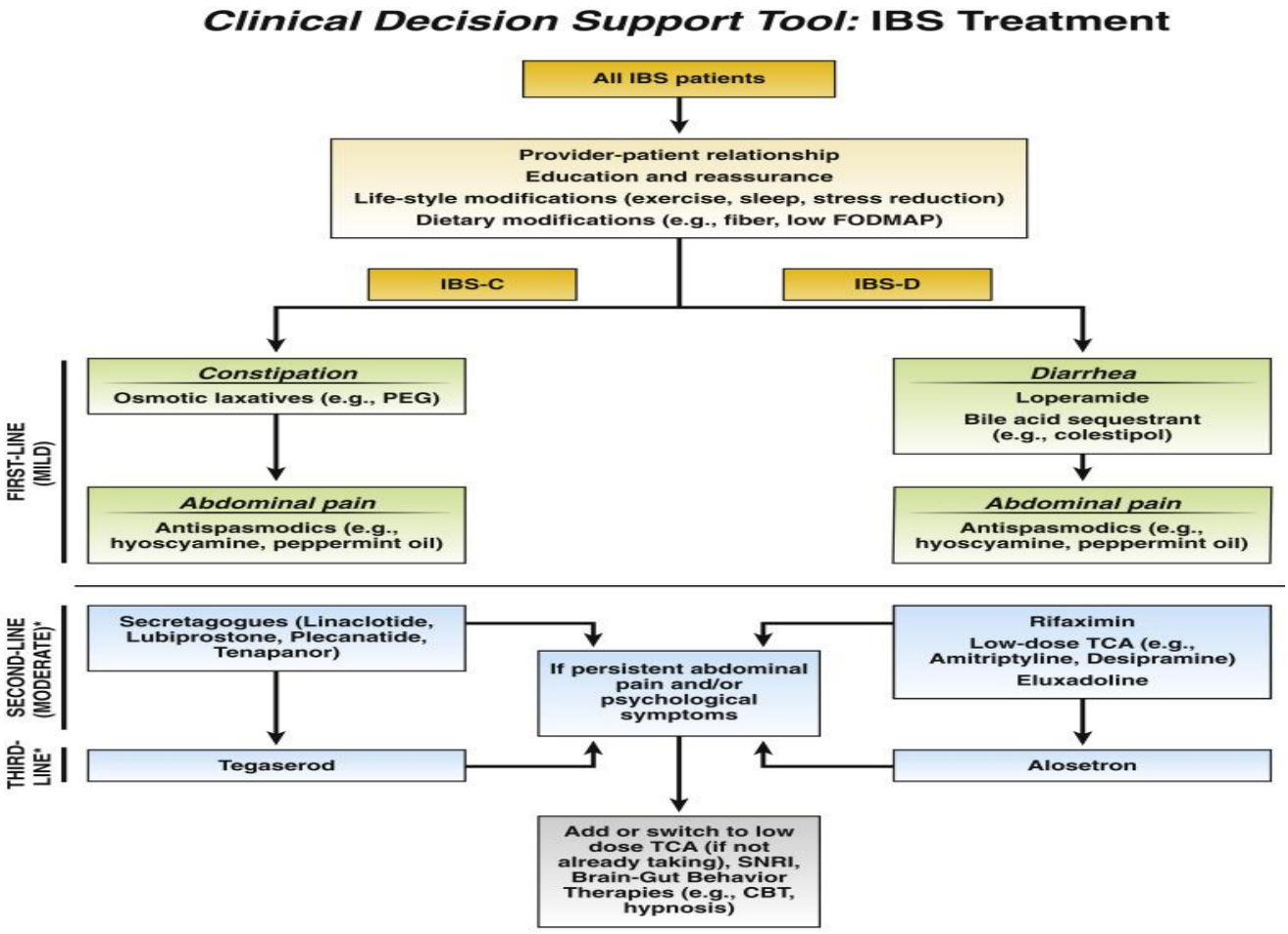
An individualized approach to management

- An effective doctor-patient relationship increases patient satisfaction and reduces the number of subsequent consultations.
- Reassurance, explanation, and a positive diagnosis are essential steps in management.
- Start with dietary modifications (slowly increasing soluble fiber if the patient has IBS with constipation or instituting a low-FODMAP diet temporarily if the patient has IBS with diarrhea or the mixed subtype of IBS).
- We also recommend increased exercise and stress reduction.
- A probiotic may be added, especially if bloating is prominent.
- Pain may be ameliorated with an antispasmodic agent or a tricyclic antidepressant, diarrhea with loperamide or a bile acid sequestrant (e.g., colestipol),

- constipation with polyethylene glycol
- 1-month trail of above Treatment
- Antihistamine-Ebastine is also effective
- Persistent and troublesome IBS-C symptoms, linaclotide or lubiprostone may help.
- IBS-D -alosetron, eluxadoline, or rifaximin
- Pain is often a predominant concern, and at least one psychiatric disorder is usually present.

Refractory IBS

- A multidisciplinary team approach to providing patient support is ideal.
- Opiates should be avoided, since their use increases the risk of the narcotic bowel syndrome.
- Patients with symptoms that are difficult to manage may request fecal microbial transfer.



*Selection of the medication should be based on the clinical features and needs of the patient.

TCA, tricyclic antidepressant; SNRI, serotonin-norepinephrine reuptake inhibitor; PEG, polyethylene glycol; CBT, cognitive behavioral therapy

Referral

- passing blood (except if from an anal fissure or haemorrhoid.
- Abdominal, rectal or pelvic mass
- Unintentional/unexplained weight loss
- Positive inflammatory markers and/or anorexia
- >40 years with new symptoms
- Change in symptoms especially if >40 years
- Atypical features
- Family history of bowel or ovarian cancer
- Patient is unhappy to accept a diagnosis of IBS despite explanation

Reference

1. *NEJM (June 29, 201 7)*
2. *Irritable Bowel Syndrome (IBS) Guidelines. Updated: Feb 15, 2022,Author: Jenifer K Lehrer, MD; Chief Editor: BS Anand, MD more...*

ACUTE HEPATITIS

Definition

- Acute inflammation of the liver that lasts less than six months, usually defined by features of acute liver insufficiency as well as by absence of features of chronic liver insufficiency and portal hypertension.

Causes

- Viral Hepatitis- Hepatitis A virus (HAV), Hepatitis B virus (HBV), Hepatitis C virus (HCV), Hepatitis E virus (HEV), Cytomegalovirus (CMV)
- Bacterial infection-Leptospirosis, Sepsis
- Alcoholic hepatitis
- Drugs induced hepatitis- Acetaminophen, Anti-Tuberculosis drugs (isoniazid, rifampicin and pyrazinamide), Antiepileptic drugs (phenytoin, carbamazepine, lamotrigine)

Clinical presentation

- Typical example of acute hepatitis is acute viral hepatitis. Onset is usually insidious but may be abrupt.
- Symptomatic acute viral hepatitis can present with three phases but more likely to be asymptomatic in children.

In the early phases:

- Tiredness, Fatigue, slight fever
- Nausea, poor appetite
- Pain in right hypochondrium
- Aching muscles and joints, headache, skin rash

In the jaundiced phase:

- Yellowish discoloration of sclerae, skin and mucous membranes
- Dark urine
- Light-coloured stools
- The symptoms in early phase subsided around this time.

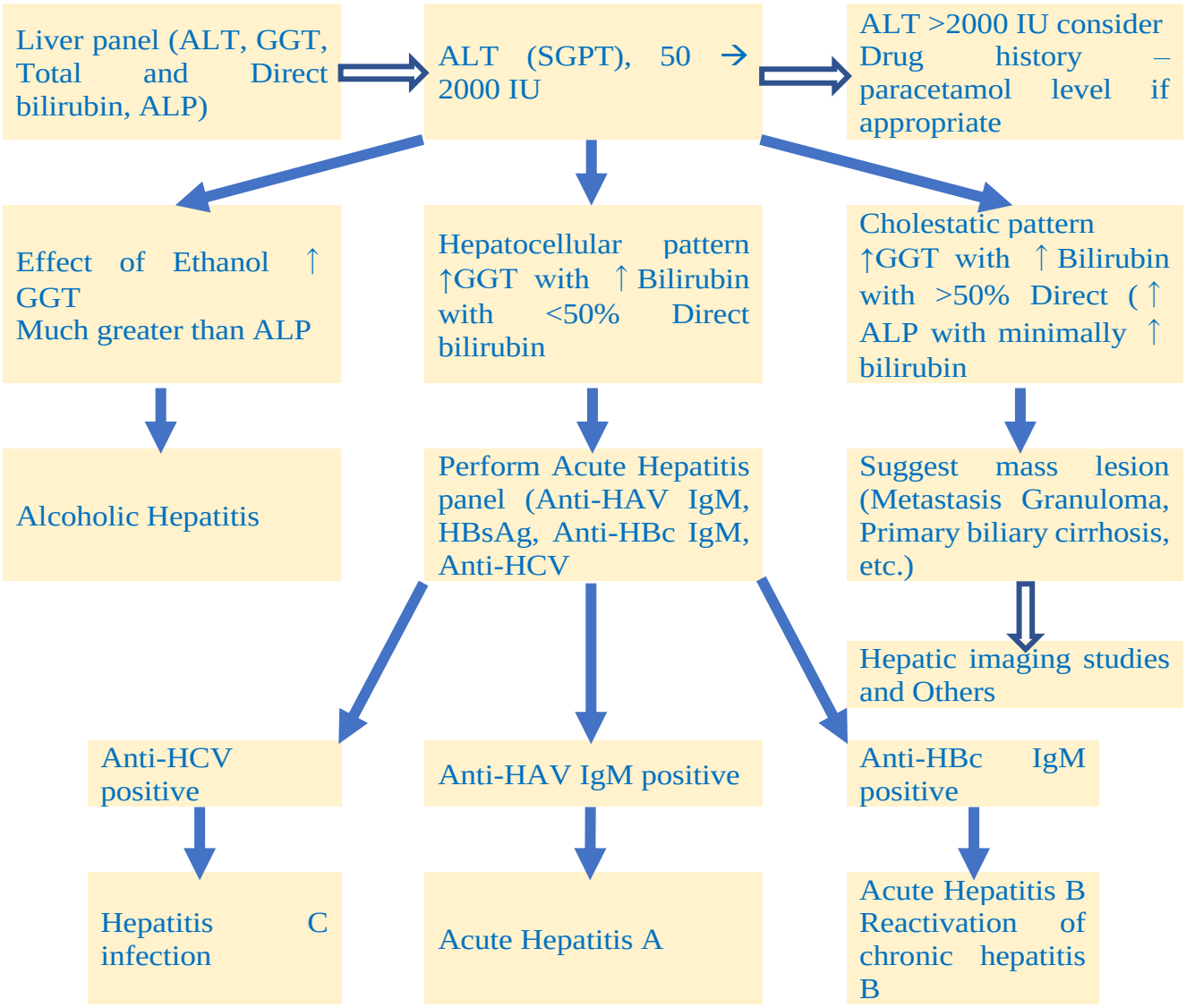
In the recovery phase:

- Tiredness that can last for weeks.
- The whole Illness typically lasts 2 to 4 weeks and ultimately resolves. In a very few, there is a potential of developing fulminant form (acute liver failure and death)
- In Fulminant forms- Signs of Hepatic Encephalopathy (personality change, aggressive behavior, sleep pattern changes and coma) can supervene rapidly. Widespread hemorrhage due to coagulopathy may develop.

Investigation

- In addition to History and physical examination, the following investigations should be done to arrive the diagnosis.
- Liver panel (ALT, GGT, Total & Direct bilirubin, ALP)
- Coagulopathy (prothrmbin time, INR)
- Viral serology (Anti-HAV IgM, HBsAg, Anti-HBc IgM, Anti- HCV)
- Ultrasound Abdomen

Diagnostic Algorithm for Acute Hepatitis



Treatment

General measure

- In most people, special treatment is not necessary.
- Bed rest, avoidance of alcohol and strenuous physical exertion is helpful.
- Stopping of causative drugs is also important.
- IV 10% glucose should be given if nausea, vomiting and reduced oral intake are pronounced.
- Regarding dietary management, palatable meals as tolerated, without overfeeding.
- Severe restrictions of diet or activity are unnecessary, and vitamin supplements may be helpful in malnourished patients.
- People with severe acute hepatitis (hepatic Encephalopathy, INR > 1.6) may require hospitalization.

Specific treatment

- There is no specific treatment for hepatitis A. Most cases of hepatitis A resolve themselves spontaneously.
- The only treatment for hepatitis B is rest, combined with a high protein/high carbohydrate diet to repair damaged liver cells and protect the liver. Spontaneous recovery occurs after acute infection with HBV occurs in 95-99% of previously healthy adults.

Follow up

- All patient with acute hepatitis will need regular follow up depend on severity and stage of hepatitis.

Prevention

- Personal hygiene and hand washing is important.
- 2 doses of Hepatitis A vaccine should be given within 6 to 12 months period before the age of 30 years.
- 3 doses of the hepatitis B vaccine should also be given to prevent hepatitis B infection.

Reference

1. *Therapeutic manual on internal medicine, 1st Edition, MMA*

HEPATITIS B (ENVELOPED DNA VIRUS)

- Common, Endemic in much of Asia and the Far East
- National -wide prevalence 6.5% (5/2015, Dept of Medical Research and Dept. of Public Health)
- The virus has 3 major structural antigens: HBsAg, HBcAg, HBeAg. Spread is via infected blood, sexual intercourse, from mother to newborn baby, or via human bites.
- Incubation period is 6- 23 weeks (average 17weeks)
- HBV infection can be either acute or chronic and the associated illness ranges in severity from asymptomic to symptomic, progressive disease (cirrhosis, HCC).
- Antiviral agents active against HBV are available, and have been shown to suppress HBV replication, prevent to progression cirrhosis and reduce the risk of HCC and liver related deaths.
- However, currently available treatments fail to eradicate the virus in most of those treated, necessitating potentially lifelong treatment.
- (In detail, please see in Infection and Infestation Chapter)

HEPATITIS C (RNA VIRUS)

- HCV is a major cause of acute and chronic hepatitis.
- National wide prevalence survey HCV -2.7% (Dept of Medical research and Dept of public health 5/2015)
- Should be tested anybody attending clinic for any illness or patient's desire.
- (In detail, please see in Infection and Infestation Chapter)

FATTY LIVER DISEASE (HEPATIC STEATOSIS)

Key highlight:

- Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease in the world.
- It is projected to become a leading indication for liver transplantation, superseding hepatitis C.
- The diagnosis of hepatic steatosis is based on exclusion of other etiologies, such as alcohol use along with histology.
- Associated with obesity and features of the metabolic syndrome in most cases. May progress to steatohepatitis and end-stage liver disease.
- There are no currently recommend drug treatment. Lifestyle modification remains the first line of the therapy.

Definition

- Non-alcoholic liver disease (NAFLD) is a clinicohistopathologic activity that includes a spectrum of condition characterized histologically by macrovesicular hepatic steatosis in those who do not consume alcohol in amounts generally considered harmful to liver.

Clinicopathological classification of NAFLD

- Steatosis
- Steatohepatitis (NASH-nonalcoholic steatohepatitis)
- NASH associated fibrosis
- NASH associated cirrhosis
- NASH associated end stage liver disease

High-Risk Groups

- Obesity (excessive body mass index [BMI] and visceral obesity) is the most common and well documented risk factor for NAFLD. In fact, the entire spectrum of obesity, ranging from overweight to obese and severely obese, is associated with NAFLD.
- Type 2 diabetes mellitus (T2DM): There is a very high prevalence of NAFLD in individuals with T2DM.
- Dyslipidemia: High serum triglyceride (TG) levels and low serum high-density lipoprotein (HDL) levels are also common in patients with NAFLD.
- Age and sex: both the prevalence of NAFLD and stage of liver disease appear to increase with age. The prevalence of NAFLD in men is 2 times higher than in women.
- Individuals with persistently abnormal aminotransferase levels in the absence of other causes of liver disease (eg, viral hepatitis and excessive alcohol use)
- Screen children and adolescents with type 2 diabetes for NAFLD using age appropriate liver enzyme tests.

Diagnosis of NAFLD in Adults

- Clinicians should consider persons with obesity and/or features of Metabolic Syndrome, those with prediabetes or T2D, and those with hepatic steatosis on any imaging study and/or persistently elevated plasma aminotransferase levels (over 6 months) to be “high risk” and screen for NAFLD and advanced fibrosis.

- Clinicians should use **liver fibrosis prediction calculations** to assess the risk of NAFLD with liver fibrosis. The preferred noninvasive initial test is the **fibrosis-4 index (FIB-4)*.**
- ***FIB-4- Fibrosis-4 index** An index to estimate the risk of hepatic cirrhosis calculated from the computation of age, plasma aminotransferases (AST and ALT), and platelet count. This noninvasive estimate of liver scarring is used to assess the need for biopsy. **The score is calculated using a person's age, AST level, platelet count (PLT), and ALT level**.
- **FIB-4 score** = age (years) x AST (U/L)/[PLT (10^9 /L) x ALT ½ (U/L).
- To stage the risk of fibrosis in persons with NAFLD, clinicians should prefer the use of VCTE as best validated to identify advanced disease and predict liver-related outcomes.
- (**VCTE - Vibration-controlled transient elastography**, A technique for liver stiffness measurement that is correlated with the severity of liver fibrosis on histology)
- The current "**gold standard"** for the diagnosis of steatohepatitis is a **liver biopsy.** Although safe, it is an **invasive procedure** associated with potential adverse effects, such as pain, bleeding, and infection. In addition, it has other limitations, including reduced acceptability, intraobserver and interobserver variability, sampling variability, and cost.
- Patients with **low-risk FIB-4** are managed with a focus on cardiometabolic disease prevention (weight management, diabetes, hypertension, lipids). High risk patients or indeterminate patients who need further evaluation are referred to the liver specialist."

Management of Non-alcoholic fatty liver disease

- Clinicians must manage persons with NAFLD for obesity, Metabolic Syndrome, prediabetes, diabetes mellitus, dyslipidemia, hypertension, and CVD based on the current standards of care.

Treatment options

- Non alcoholic fatty liver disease (NAFLD) with diabetes
- **First line:** Lifestyle modification (weight loss, diet, exercise) to lower fibrosis and hepatic steatosis
- **Weight loss in obese and overweight** patients through reduced caloric intake, increased exercise, or a combination of both.
- eight loss should be gradual, approximately 0.5 to 1.0 kg I week through dietary restrictions and regular exercise (30) minutes 3-5 times per week

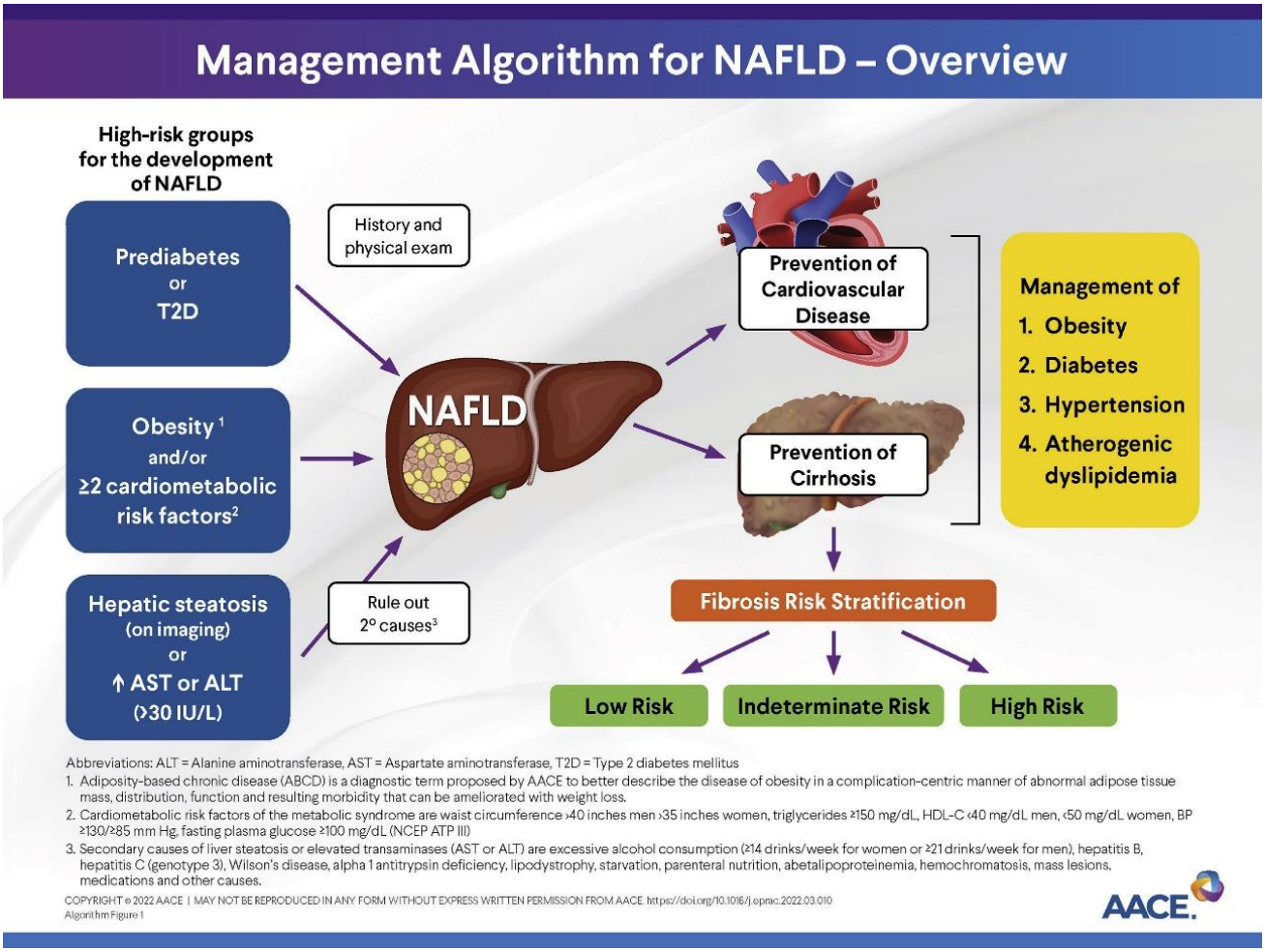
Adjunctive therapy

- Roux-en-Y gastric bypass.
- Morbidly obese patients (BMI >35kg/m^2) should be considered for more aggressive weight loss measures including bariatric surgery
- Weight loss pharmacotherapy
- ORLISTAT prevents the absorption of fats from the GI tract.
- Clinicians must consider treating diabetes with pioglitazone and/or GLP-1 RAs when there is an elevated probability of having NASH based on elevated plasma aminotransferase levels and noninvasive tests.
- To offer cardiometabolic benefit in persons with T2D and NAFLD, clinicians must consider treatment with GLP1 RAs, pioglitazone, or SGLT2 inhibitors; however, there is no evidence of benefit for treatment of steatohepatitis with SGLT2 inhibitors.

- Two antidiabetic agents have proven to be safe and effective to reverse NASH in persons with obesity, prediabetes, or T2D: pioglitazone and GLP-1 RA.
- For chronic weight management in individuals with a BMI of 27 kg/m2 and NAFLD or NASH, clinicians should give preference to semaglutide 2.4 mg/week (best evidence) or liraglutide 3 mg/day.

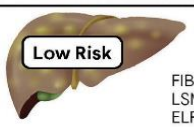
NAFLD with Dyslipidaemia

- First line
- Lifestyle modification
- Adjunctive therapy
- ORLISTAT
- Lipid lowering therapy
- Roux- en-Y gastric bypass



Diabetes Management in NAFLD

Fibrosis Risk Stratification

	 Low Risk FIB-4: <1.3 LSM <8 kPa ELF <7.7	 Indeterminate Risk FIB-4: 1.3 - 2.67 LSM 8 - 12 kPa ELF 7.7 - 9.8	 High Risk[1] FIB-4: >2.67 LSM >12 kPa ELF >9.8
General goal	Optimize glycemic control using preferred agents that reverse steatohepatitis, whenever possible. Prefer GLP-1 RA and SGLT2i in CVD. Prefer SGLT2i in CKD and HF.		
Dietary recommendations	Glycemic load reduction via emphasis on whole food carbohydrates (vegetables, legumes, fruit) versus sugar/processed carbohydrates.		
Individualize A1c target	≤6.5% for persons without concurrent serious illness and at low hypoglycemic risk (>6.5% otherwise).		In advanced cirrhosis[1], caution with risk of hypoglycemia and avoid oral agents[2]
Preferred diabetes pharmacotherapy	Consider agents that reduce liver fat (pioglitazone, GLP-1 RA, SGLT2i).	Strongly consider agents with efficacy in NASH: Pioglitazone and/or GLP-1 RA[3]. No evidence that SGLT2i improve steatohepatitis.	Strongly consider agents with efficacy in NASH: Pioglitazone and/or GLP-1 RA[3]. No efficacy data in cirrhosis.
Metformin, sulfonylurea, DPP-4i, acarbose and insulin	May continue but limited benefit on liver histology in NAFLD.	May continue but limited benefit on liver histology in NAFLD.	May continue (F2-F3) but avoid oral agents if advanced cirrhosis present. Cannot avoid insulin in patients with advanced liver cirrhosis – often only option

Abbreviations: CKD = Chronic kidney disease, CVD = Cardiovascular disease, DPP-4i = Dipeptidyl peptidase 4, GLP-1 RA = Glucagon-like peptide-1 receptor agonists, HF = Heart failure, NASH = Nonalcoholic steatohepatitis, SGLT2i = Sodium-glucose cotransporter-2 inhibitors.

1. Advanced cirrhosis is defined as persons with cirrhosis based on biopsy and Child class B or C with clinical evidence of comorbidities (varices, portal hypertension, ascites, etc.).
2. Limited data on oral diabetes medications and GLP-1 RA in persons with cirrhosis. Avoid metformin, GLP-1 RA appear safe, insulin preferred. Avoid oral agents in advanced cirrhosis.
3. Among GLP-1 RAs, semaglutide has the best evidence of benefit in persons with steatohepatitis and fibrosis.

Algorithm Figure 4

AACE.

Weight Management in NAFLD

Fibrosis Risk Stratification

	 Low Risk FIB-4: <1.3 LSM <8 kPa ELF <7.7	 Indeterminate Risk FIB-4: 1.3 - 2.67 LSM 8 - 12 kPa ELF 7.7 - 9.8	 High Risk FIB-4: >2.67 LSM >12 kPa ELF >9.8
General lifestyle changes	Decrease sedentary time and increase daily movement. Stress reduction through exercise and other methods.		
Dietary recommendations	Creating an energy deficit is the priority with reduction of saturated fat, starch, & added sugars. Persons with cirrhosis need an individualized nutritional assessment and treatment plan.		
Exercise	To improve cardiometabolic health, support weight loss and mitigate sarcopenia. Aerobic exercise for 30-60 min (3-5 days/week) + resistance training 20-30 min (2-3 times/week).		
Alcohol intake	Minimize	Minimize	Avoid if F3 or cirrhosis (F4)[1]
Weight loss goal to treat NAFLD (if overweight or obesity)[2]	Greater weight loss associated with greater liver and cardiometabolic benefit.		
Weight loss tools	Behavioral modification counseling. In person or remote programs.	Greater intensity of weight loss to reverse steatohepatitis and fibrosis.	Specialized obesity management, with a structured program, anti-obesity medications, bariatric surgery.
Medical therapy to treat obesity	Phentermine, phentermine/topiramate ER, naltrexone/bupropion, orlistat, liragluitde 3 mg/d, semaglutide 2.4 mg/wk	GLP-1 RA preferred for NASH.[3,4]	GLP-1 RA preferred for NASH.[3,4]
Bariatric surgery	Consider to treat obesity and comorbidities.	Strong consideration to treat steatohepatitis and fibrosis.	Stronger consideration to treat steatohepatitis and fibrosis. Avoid in decompensated cirrhosis.

Abbreviations: GLP-1 RA = Glucagon-like peptide-1 receptor agonists, HCC = Hepatocellular carcinoma, NASH = Nonalcoholic steatohepatitis

1. Persons with confirmed cirrhosis based on biopsy or high likelihood based on LSM >13.6kPa from vibration controlled transient elastography (FibroScan®), ELF ≥9.8 or >5.0 kPa on MRE) should undergo HCC surveillance. Varices screening is recommended if LSM >20 kPa or platelet count of <150,000/mm^3.
2. These goals should only be taken as a broad guidance. NAFLD/NASH may also improve by changes in macronutrient content, exercise and other factors beyond magnitude of weight loss. All high-quality studies available limited to a maximum of 12 month duration.
3. No high-quality evidence for pharmacotherapy in persons with NASH cirrhosis. Treatment should be individualized and used with caution only by liver specialists.
4. Among GLP-1 RAs, semaglutide has the best evidence of benefit in persons with steatohepatitis and fibrosis.

Algorithm Figure 3

AACE.

Atherogenic Dyslipidemia Management in NAFLD

Lipid risk levels are similar in the presence of NAFLD or NASH

General goal	Early intensive management of dyslipidemia needed to reduce cardiovascular risk. Intensify therapy until lipid goal is reached.		
Dietary recommendations	Increase fiber intake (>25 g/d), prioritize vegetables, fruits whole grains, nuts, reduce saturated fat & added sugars (e.g., Mediterranean diet).		
Lipid risk levels	**High CV Risk[1]** ≥2 risk factors and 10-year risk 10-20% Diabetes or CKD ≥3 with no other risk factors	**Very high CV Risk[1]** Established CVD or 10-year risk >20% Diabetes with >1 risk factor, CKD ≥3, HeFH	**Extreme CV Risk[1]** Progressive CVD CVD + diabetes or CKD ≥3 or HeFH FHx premature CVD (<55 yrs male <65 yrs female)
LDL-C goal (mg/dL)	<100	<70	<55
Non-HDL-C goal (mg/dL)	<130	<100	<80
Triglycerides goal (mg/dL)	<150	<150	<150
Apo B goal (mg/dL)	<90	<80	<70
First line pharmacotherapy: Statins	Use a moderate-to-high intensity statin[2], unless contraindicated. Statins are safe in NAFLD or NASH but do not use in decompensated cirrhosis (Child C).		
If LDL-C not at goal[3]: Intensify statin therapy	Use higher dose or higher potency statin.		
If LDL-C not at goal (or statin intolerant)[4]: add 2nd agent, then add 3rd agent	Ezetemibe, PCSK9 inhibitor, bempedoic acid, colesevelam, inclisiran.		
If triglycerides > 500 mg/dL	Fibrates, Rx grade omega 3 FA, icosapent ethyl (if diabetes, optimize glycemic control and consider pioglitazone).[5]		
If TG 135-499 mg/dL on max statin dose	Emphasize diet (as above).	Add icosapent ethyl.[6]	Add icosapent ethyl.[6]

Adapted from Handelsman Y, et al. Endocr Pract. 2020;26:1196-1224.

Abbreviations: CKD = Chronic kidney disease, CVD = cardiovascular disease, FA = Fatty acids, HeFH = Heterozygous familial hypercholesterolemia, HTN = Hypertension, Rx = Prescription
1. Major risk factors: age >40, DM, HTN, FHx of early CVD, low HDL C, elevated LDL, Smoking, CKD 3,4
2. High intensity statin therapy: rosuvastatin 20, 40 mg/d, atorvastatin 40, 80 mg/d.
3. Other lipid modifying agents should be used in combination with maximally tolerated statins if goals not reached: ezetimibe, PCSK9 inhibitor, bempedoic acid, colesevelam, or inclisiran.
4. Assess adequacy and tolerance of therapy with focused laboratory evaluations and patient follow up.
5. Niacin may lower triglycerides but does not reduce CVD and worsens insulin resistance. It may promote hyperglycemia in a population at high-risk of diabetes.
6. Icosapent ethyl 4g/d is recommended as an adjunct to maximally tolerated statin therapy to reduce risk of cardiovascular disease in high-risk persons.

Algorithm Figure 6

AACE.

Hypertension Management in NAFLD

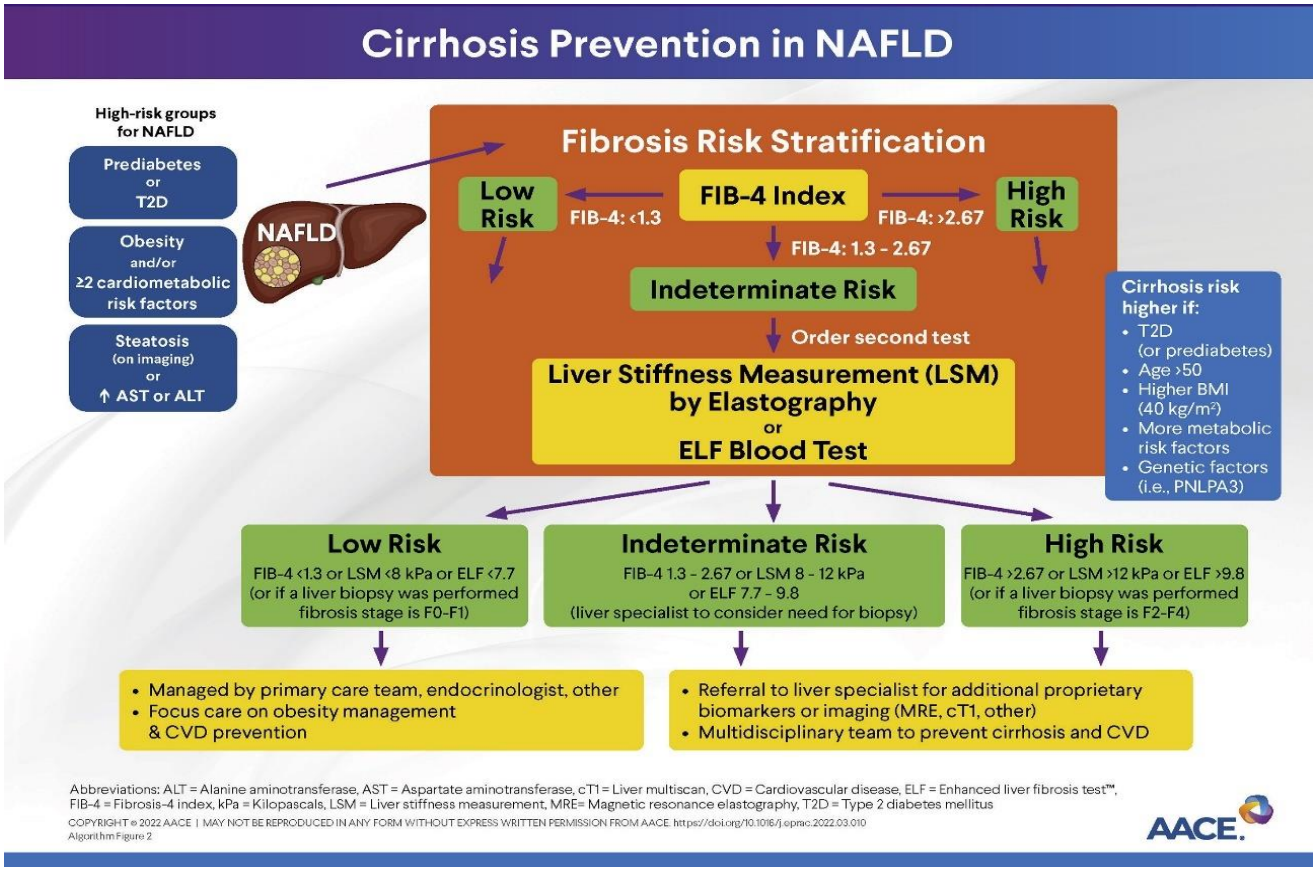
Fibrosis Risk Stratification

	 FIB-4: <1.3 LSM <8 kPa ELF <7.7	 FIB-4: 1.3 - 2.67 LSM 8 - 12 kPa ELF 7.7 - 9.8	 FIB-4: >2.67 LSM >12 kPa ELF >9.8
General goal	Optimize BP control and improve cardiovascular health using preferred agents, whenever possible. Assess every 3 months and intensify therapy until goal achieved.		
Goal (individualize)[2,3,4]	Systolic < 130 mm Hg / Diastolic < 80 mm Hg	Systolic < 130 mm Hg / Diastolic < 80 mm Hg	Systolic < 130 mm Hg / Diastolic < 80 mm Hg; individualize if decompensated cirrhosis
Dietary recommendations	In addition to general dietary recommendations, reduce sodium & increase high potassium foods (e.g., DASH diet).		
Pharmacotherapy for hypertension[5]	First-line therapy: ACEIs and ARBs.	First-line therapy: ACEIs and ARBs.	Same but avoid ACEI or ARB if decompensated cirrhosis.
Intensification of therapy	Second agent: CCB, BB[6] or thiazide diuretic (as additional agents as needed).		Same but individualize if decompensated cirrhosis. Use diuretics with caution (risk of excessive diuresis).
Additional options	Additional BP medication choices: alpha blockers, central agents, vasodilators, aldosterone antagonist.		Same but individualize if decompensated cirrhosis.

Abbreviations: ACEIs = Angiotensin-converting enzyme inhibitors, ARBs = angiotensin II receptor blockers, BB = beta blockers, CCB = calcium channel blockers.
1. Advanced cirrhosis defined as persons with cirrhosis based on biopsy and Child class B or C and clinical evidence of comorbidities (varices, portal hypertension, ascitis, etc.).
2. AACE recommends that BP control be individualized, but that a target of <130/80 mm Hg is appropriate for most persons.
3. Less-stringent goals may be considered for frail persons with complicated comorbidities or those who have adverse medication effects.
4. A more intensive goal (e.g., <120/80 mm Hg) should be considered for some persons if this target can be reached safely without adverse effects from medication.
5. If initial BP > 150/100 mm Hg start with dual therapy. (ACEI or ARB + CCB, BB or thiazide diuretic).
6. Prefer weight neutral beta-blockers: carvedilol, nebivolol.

Algorithm Figure 5

AACE.



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- Vitamin E can be considered for the treatment of NASH in persons without T2D, but there is not enough evidence at this time to recommend for persons with T2D or advanced fibrosis.

Drugs used in NAFLD

Drug	Benefits	Avoid Use	Recommend Use
Pioglitazone	• Improves insulin sensitivity • Anti-atherosclerotic and anti-inflammatory properties • Decreases liver steatosis and fibrosis	Patient without diabetes	• Biopsy proven nonalcoholic steatohepatitis (NASH) • Patients with diabetes
GLIP-1 agonists • *Liraglutide* • *Semaglutide*	• Cardiometabolic benefit • Weight management • Decreases liver steatosis • Normalizes aminotransferases levels	• Patient without diabetes • BMI <27 kg/m2	Obesity (≥27 kg/m^2) • *Semaglutide 2.4 mg weekly* • *Liraglutide 3 mg daily* Type 2 diabetes • *Semaglutide 2 mg weekly* • *Liraglutide 1.8 mg daily*
SGLT-2	Cardiometabolic benefit	Patient without diabetes Steatohepatitis	Patients with diabetes
Statin	• Anti-oxidant • Antithrombotic • Anti-inflammatory effect • Reduce cardiovascular mortality	• Significant liver disease • Unexplained elevated serum transaminase	• NASH • High ASCVD risk or clinical ASCVD
Vitamin E	Improvement in liver histology	Patient with diabetes	NASH

NASH associated end stage liver disease

Liver transplant and transjugular intrahepatic portosystemic shunt (TIPS)

Reference:

1. *Ludwig J et al. Non-alcoholic steatohepatitis: Mayo ClinProc.1980;55:434-438*
2. *Epocrates, Athena gp. 2018*
3. *Clinical Practice Guidelines American Association of Clinical Endocrinology Clinical Practice Guideline for the Diagnosis and Management of Nonalcoholic Fatty Liver Disease in Primary Care and Endocrinology Clinical Settings Co-Sponsored by the American Association for the Study of Liver Diseases (AASLD)2022*
4. *https://www.sciencedirect.com/science/article/pii/S1530891X22000908*

LIVER CIRRHOSIS

- A pathological condition of liver fibrosis generated by continuous scar formation and recovery due to chronic liver injury, eventually leading to the development of regenerative nodules around the fibrotic scar.

Common aetiology

- Viral hepatitis (B and C)
- Alcohol
- NASH
- Metabolic (e.g. haemochromatosis, Wilson's disease)
- Primary biliary cirrhosis
- Autoimmune hepatitis
- Toxins and drugs (e.g. methotrexate, amiodarone)

Diagnosis

- Clinically classified as compensated and decompensated (cases with ascites, variceal bleeding, hepatic encephalopathy or jaundice)

Imaging

- Abdominal ultrasound (coarse echo pattern by fibrosis and regeneration)
- CT
- MRI

Evaluation of the cause, severity, and staging

- History taking (drug use, blood transfusion, alcohol use, history suggestive of chronic liver disease)
- Physical examination (jaundice, ascites, spider angioma, hepatomegaly or splenomegaly)
- Laboratory tests (whole blood count including platelet count, liver function test including albumin, prothrombin time)
- Endoscopy should be carried out to confirm the presence or absence of esophageal varices which are indicator of portal hypertension.
- Tests for hepatitis B or C virus infection
- The Child-Pug score to assess the severity
- alpha fetoprotein
- Presence of one condition of following findings suggest the diagnosis of liver cirrhosis
- nodularity of the liver surface,
- a platelet count of less than 100,000/mm3,
- albumin less than 3.5 g/dL
- an international normalized ratio of ≥ 1.3
- Pathological diagnosis of liver cirrhosis
- liver biopsy--- gold standard for confirming the diagnosis, invasive and not
- routinely used

Child-Turcotte-Pugh Classification for Severity of Cirrhosis			
Clinical and Lab Criteria	Point		
	1	**2**	**3**
Encephalopathy	None	Mild to moderate (grade 1 or 2)	Severe (grade 3 or 4)
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin (mg/dl)	<2	2-3	>3
Albumin (g/dl)	>3.5	2.8-3.5	<2.8
Prothrombin time			
Seconds prolonged	<4	4-6	>6
International normalized ratio	<1.7	1.7-2.3	>2.3
+Child-Turcotte-Pugh Class obtained adding score for each parameter (total points) Class A = 5 to 6 points (least severe liver disease) Class B = 7 to 9 points (moderately severe liver disease) Class C = 10 to 15 points (most severe liver disease)			

Management

- Treatment of the underlying disease
- (antiviral therapy for chronic hepatitis B to reduce liver fibrosis from virus proliferation, DAA treatment for chronic hepatitis C, abstinence of alcohol in alcoholic cirrhosis, improving insulin resistance, removing risk factors of metabolic syndrome, lifestyle modifications, drug therapy for nonalcoholic fatty liver disease, prednisolone and azathioprine for autoimmune hepatitis, phlebotomy for haemochromatosis)
- Treatment of complications
- Give flu and pneumococcal vaccination

Treatment of the underlying disease

Recommendations

- The cause of cirrhosis should be treated to improve liver fibrosis.
- In patients with liver cirrhosis due to chronic hepatitis B, antiviral therapy with sustained suppression of viral replication is needed.
- In patients with liver cirrhosis due to chronic hepatitis C, antiviral therapy with DAA and ribavirin should be considered.
- In patients with alcoholic liver cirrhosis, strict abstinence is recommended to prevent worsening of disease.
- In patients with nonalcoholic fatty liver disease, losing weight, diet therapy and exercise can be recommended.
- In patients with primary biliary cirrhosis, high dose ursodeoxycholic acid is recommended.
- Trientine and zinc for Wilson disease

Treatment of complications

Variceal bleeding

Recommendations for screening

- It is recommended that all patients undergo endoscopy when they are at first diagnosed of liver cirrhosis.

- For patients with compensated liver cirrhosis, endoscopy every 2 to 3 years should be considered and for patients with decompensated liver cirrhosis endoscopy every 1 to 2 years should be considered.
- Patients with compensated liver cirrhosis with small varices not using nonselective beta-blocker,endoscopy every 2 years is recommended.
- The frequency of endoscopy can be adjusted according to the cause and progression of liver cirrhosis.

Recommendations for acute variceal bleeding

- Initially be administered vasoconstrictor (e.g. Somatostatin, octreotide) and antibiotic treatment.
- Endoscopic treatment is recommended for patients with acute variceal bleeding.
- Balloon tamponade can be used as a rescue therapy if active variceal bleeding cannot be controlled.

Recommendations for prevention of variceal bleeding

- Nonselective beta-blockers should be considered for patients with varices.
- In patients with large varices in which bleeding has never been observed, nonselective beta-blockers and endoscopic variceal ligation (EVL) are recommended.

Ascites

Recommendations for ascites

- Paracentesis should be performed when Grade 2 or 3 ascites occurs.
- When the initial paracentesis is performed, a total cell count and differential, albumin, and total protein tests should be performed. A culture of ascitic fluid in blood culture bottles at the bedside is recommended.
- If serum-ascites albumin gradient is greater than or equal to 1.1 g/dL, it indicates ascites by portal hypertension.
- Patients with cirrhotic ascites should be advised to take in less than 5 g of salt a day.
- When the serum sodium is normal, restriction of water intake is not necessary.
- Bed rest is not recommended for the treatment of ascites.
- The first-choice diuretic for patients with cirrhotic ascites is aldosterone antagonist. Loop diuretics can be used along with aldosterone antagonist.
- Spironolactone can be used with a starting dose of 50-100 mg/day up to400 mg/day.
- To increase the diuretic effects and maintain a normal serum potassium level, 20-40 mg of furosemide should be used with spironolactone (40:100) at the initial stage.
- The rate of weight loss should be up to 1 kg/day for patient with peripheral edema and 0.5 kg/day for patients without edema.
- In cases of severe hyponatremia, kidney dysfunction, encephalopathy, or severe muscle spasms, diuretics should be stopped.
- In cases of hypokalemia, loop diuretic should be reduced or stopped, and if hyperkalemia occurs, the dose of aldosterone antagonist should be adjusted.
- Therapeutic large volume paracentesis is recommended as the first-line treatment for tension-type ascites.
- Patients with refractory ascites should be referred to specialist center.
- Serial therapeutic paracenteses are a treatment option for patients with refractory ascites.
- Post-paracentesis albumin infusion may not be necessary for a single paracentesis of less than 4 to 5 L.
- For large-volume paracenteses, an albumin infusion of 6-8 g per liter of fluid removed is recommended.

The older system
1+ is minimal and barely detectable
2+ is moderate
3+ is massive but not tense
4+ is massive and tense
The International Ascites Club grading (2003)
Grade 1: mild ascites detectable only by US
Grade 2: moderate ascites manifested by moderate symmetrical abdominal distension
Grade 3: large or gross ascites with marked abdominal distension

Spontaneous bacterial peritonitis (SBP)

The diagnosis is made in the presence of an elevated ascitic fluid neutrophil count (>250 cells/mm3) without an evident intra-abdominal, surgically treatable source of infection.

Recommendations for SBP

- Empirical antibiotics should be started immediately following the diagnosis of SBP.
- The first line antibiotic treatment is third-generation cephalosporins for 7 days.
- Alternative options include amoxycillin/clavulanic acid and quinolones for 7 days.
- Patients who have recovered from an episode of SBP should be considered for treatment with norfloxacin (400 mg once daily), ciprofloxacin (500 mg once daily, orally) or co-trimoxazole (800 mg sulfamethoxazole and 160 mg trimethoprim daily, orally) to prevent further episode of SBP. (Quality of evidence: low; Recommendation: weak)
- Patients who recover from an episode of SBP have a high risk of developing recurrent SBP.
- The prophylactic antibiotics reduce the risk of recurrent SBP.
- Ciprofloxacin (500 mg/day, orally) is the treatment of choice. Norfloxacin 400 mg once a day also as secondary prophylaxis,
- Patients presenting with gastrointestinal bleeding and underlying ascites due to cirrhosis should receive prophylactic antibiotic treatment (cefotaxime has been widely studied but the antibiotic should be chosen based on local data) to prevent the development of SBP. (Quality of evidence: strong, Recommendation: strong)
- Primary prophylaxis should be offered to patients considered at high risk, as defined by an ascitic protein count <1.5 g/dL. However, it is important that the potential risks and benefits and existing uncertainties are communicated to patients. (Quality of evidence: low; Recommendation: weak)
- Give prophylaxis for high-risk patients (↓ albumin, ↑PT/INR, low ascetic albumin) or those who have had a previous episode: ciprofloxacin 500 mg po daily.

Hepatic encephalopathy

- A broad range of neurologic and neuropsychiatric impairments seen m patients with significant underlying liver disease

West-Haven criteria for hepatic encephalopathy

Grade	Consciousness	Intellect and behavior	Neurologic finding
0	Normal	Normal	Normal examination: if impaired psychomotor testing then MHE
1	Mild lack of awareness	Shortened attention span: impaired addition or subtraction	Mild asterixis or tremor
2	Lethargic	Discontented: inappropriate behavior	Obvious asterixis: slurred speech

3	Somnolent but arousable	Gross disorientation: bizarre behavior	Muscular rigidity and clonus; hyperreflexia
4	Coma	Coma	Decerebrate posturing

- Precipitating factors of hepatic encephalopathy are gastrointestinal bleeding, infection, constipation, excessive intake of protein, dehydration, renal function disorder, electrolyte imbalance, psychoactive medication,and acute hepatic injury.

Recommendations for treatment

- Nonabsorbent disaccharides (e.g., lactulose, lactitol and rifaximin) are recommended.
- Nonabsorbable disaccharides can be used to adjust the bowel movement-loose stool (2-3 times/day).
- L-omithine-L-aspartate (LOLA) 20 g can be injected daily for 1-2 weeks or LOLA of 6 g can be given orally 3 times per day for 1-2 weeks.
- In patients with a history of hepatic encephalopathy, nonabsorbable disaccharide can be used until patients have loose stools 2-3 times a day.

Renal failure

- Reduced hepatic clearance of immune complex leads to trapping in kidneys (:.IgA nephropathy ± hepatic glomerulosclerosis).
- Renal dysfunction worsens the prognosis of patients with Liver cirrhosis
- Presently, the combined administration of noradrenaline and albumin has been suggested. (Recommendation: weak, 73% agreed, evidence level B)
- In appropriately selected patients, transjugular intrahepatic portosystemic shunts (TIPS) improves renal function, reduces ascites, and can be expected to improve prognosis.
- Liver transplantation (LT) improves the prognosis for liver and kidney syndrome.

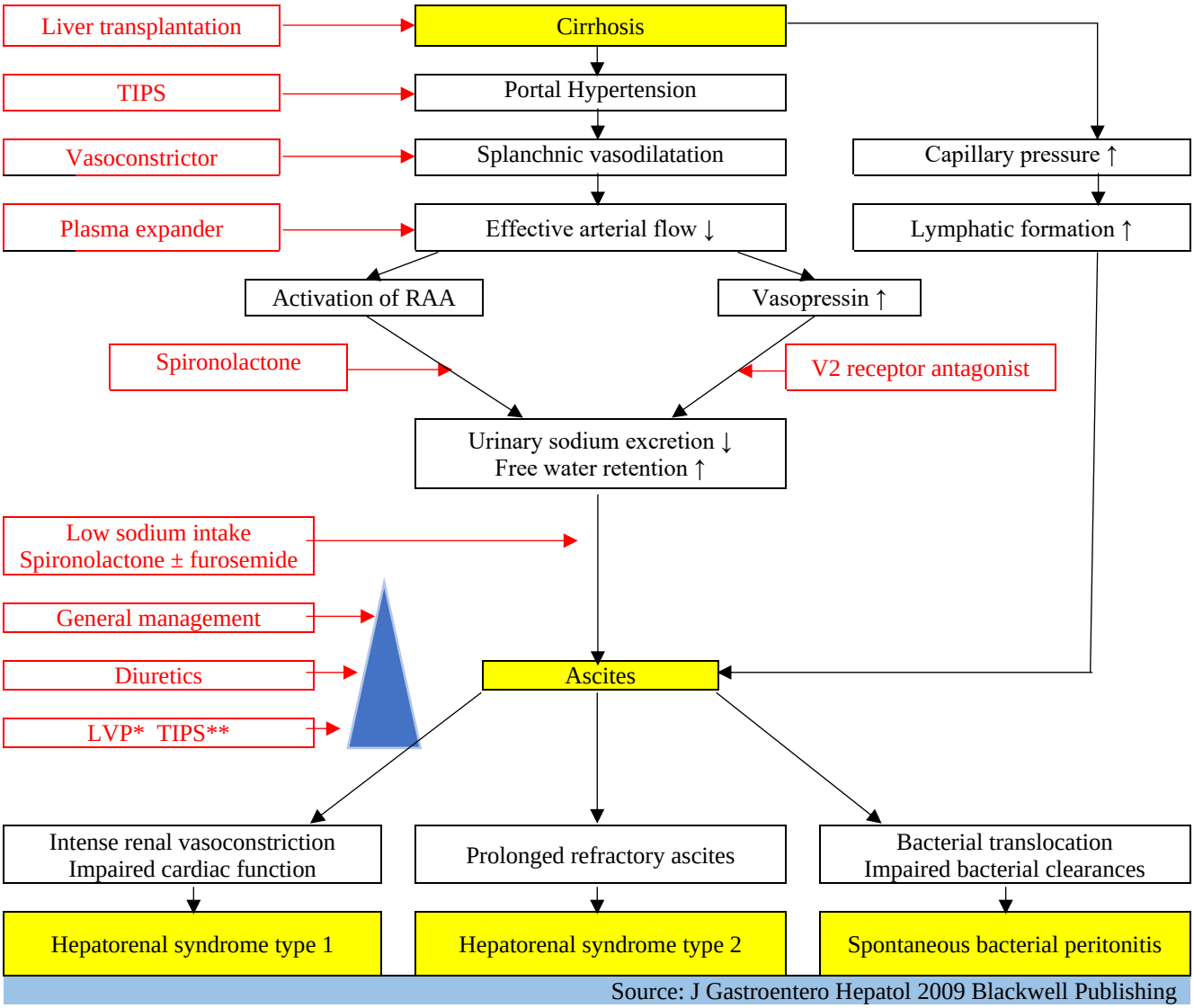
Follow up

- Patient with liver cirrhosis needs regular follow up depending on stage and severity of disease (maximum interval of four months).
- Hepatocellular carcinoma surveillance is needed for every patient with liver cirrhosis.

Reference

1. *Aithal GP, et al. Gut 2020;0:1–21. doi:10.1136/gutjnl-2020-321790*
2. *Evidence-based clinical practice guidelines for Liver Cirrhosis 2022, J Gastroenterol (2021) 56:593–619 https://doi.org/10.1007/s00535-021-01788-x, J Gastroenterol (2021) 56:593–619*

Algorithm for management of cirrhosis



Source: J Gastroentero Hepatol 2009 Blackwell Publishing

**Large volume paracentesis, ** Transjugular intrahepatic porto systemic shunt*

CHOLELITHIASIS (GALL STONES)

- Gallstones are increasingly common. 9% of 60 years old have them and prevalence increase with age.

Risk factors

- Gender (F > M)
- Body weight-prevalence increase with weight; also associated with rapid decreased weight
- Affluency
- Pregnancy (and possibly HRT but not COC pill)
- Diet-vegetarian diet is protective
- Associated conditions like:
- Haemolysis
- DM
- Hypertriglyceridaemia
- Cirrhosis
- Crohn's disease
- Partial gastrectomy

Drugs which cause gallstones: Clofibrate (and other fibric acid derivatives); octreotide (somatostatin analogue).

Pathophysiology

- Gallstones are conveniently classified into cholesterol or pigment stones, although the majority are of mixed composition.
- Cholesterol stones are most common in developed countries, whereas pigment stones are more frequent in developing countries.

Presentation

- Gallstones are blamed for many digestive symptoms. They are probably innocent in most cases. 70% of stones in the gall bladder do not cause symptoms. Common presentations as follows:

Table 13.19 Presentation and management of gallstone disease

	Presentation	Management
Biliary colic	• Clear-cut attacks of severe upper abdominal pain which may radiate back/shoulder tip, lasting ≥:30min and causing restlessness ± jaundice ± nausea or vomiting • *Examination:* tenderness ± guarding in the right upper quadrant (increase on deep inspiration - Murphy's sign)	• Treat acute attacks with pethidine (50mg IM/po) or naproxen (500mg po) + prochlorperazine 12.5 mg IM or domperidone 10mg po/PR for nausea • Admit if: uncertain of diagnosis, inadequate social support, persistent symptoms despite analgesia, suspicion of complications, and/or concomitant • medical problems (e.g. dehydration, pregnant, DM, Addison's) • Investigate: for gallstones with abdominal USS to prove diagnosis when the episode has settled. • Differential diagnosis: any cause of acute abdomen • Treat gallstones to prevent recurrence

Acute cholecystitis/ cholangitis	• Pain and tenderness in the right upper quadrant/epigastrium ± vomiting • Examination: tenderness ± guarding in the right upper quadrant ± fever ± jaundice	• Treatment: broad-spectrum antibiotic (e.g. ciprofloxacin) and analgesia as for biliary colic • Admit if: generalized peritonism, diagnosis uncertain, very toxic, concomitant medical problems (e.g. dehydration, DM, Addison's, pregnancy), inadequate social support, or not responding to medication • Empyema occurs when the obstructed gall bladder fills with pus. Presents with persistent swinging fever and pain. Usually requires cholecystectomy ± surgical drainage • Investigate and follow up to prevent recurrence as for biliary colic
Pancreatitis	• Poorly localized, continuous, boring epigastric pain which increase over l hour, often worse lying down ± radiation to the back • (50%) Nausea ± vomiting	• Admit as an acute surgical emergency. Prior to transfer, give analgesia with pethidine.
Gallstone ileus	• Occurs usually after an attack of cholecystitis. • A stone perforates from the gall bladder into the duodenum and impacts in the terminal ileum causing bowel obstruction	• Admit as surgical emergency.
Chronic cholecystitis	• Vague intermittent abdominal discomfort, nausea, flatulence, and intolerance of fats	• Investigate for gallstones with abdominal USS to prove the diagnosis • Differential diagnosis: reflux, IBS, upper GI tumour, PU • Refer for treatment of gallstones
Jaundice	• Obstructive jaundice ± right upper quadrant pain	• Refer for same day or urgent specialist surgical assessment (depending on clinical state)

Ultrasound is the primary modality for diagnosing gallstones.

Complications

- Pancreatitis
- Bile duct stones
- Acute cholecystitis
- Gallbladder empyema, necrosis
- Gallbladder cancer
- Cholecystoenteric fistula

Management

- The management of gallstones depends on patient symptoms. Only 50% of patients with stones will develop symptoms. Asymptomatic patients should be educated on a low-fat diet, exercise, and weight loss.
- Advise the patient to stick to a low-fat diet
- The primary clinicians should educate the patient that weight loss and regular exercise also lead to a much-lowered risk of gallstones.
- Definitive treatment for symptomatic stones is cholecystectomy
- Refer for surgical review ± further evaluation (e.g. ERCP-endoscopic retrograde cholangiopancreatography)

- Gallstones can be removed by cholecystectomy (laparoscopic or open) or ERCP or may be dissolved with ursodeoxycholic acid (stones <5mm diameter---40% recur in <5years) or shattered with lithotripsy for non-calcified gallstones is another option.
- (1:3 develop biliary colic afterwards)
- Persistent digestive symptoms after surgery are common (50% after cholecystectomy) and difficult to treat.

References:

1. *Oxford Handbook of General Practice, 4th Edition*
2. *Davidson's Principles and Practice of Medicine, 22"dEdition 22nEdition*
3. *https://www.ncbi.nlm.nih.gov/books/NBK470440/*

PANCREATITIS

ACUTE PANCREATITIS

- Premature activation of pancreatic enzymes results in autodigestion and tissue damage. Most episodes are mild and self-limiting but 1:5 patients have a severe attack. Overall mortality is 5-10%. It may be recurrent.

Causes

- In 10% patients no cause is identified.
- Common causes (80%): gallstones, alcohol
- Rarer causes:
- Drugs (e.g. azathioprine)
- Trauma
- Pancreatic tumours
- Post-ERCP
- Viral infection (mumps, HIV, Coxsackie B)
- Mycoplasma infection
- Hypercalcaemia
- Hyperlipidaemia
- Pancreas divisum (normal variant in 7-8% of the white population)
- Familial pancreatitis
- Vasculitis
- Ischaemia or embolism
- Pregnancy
- End-stage renal failure

Presentation

- Poorly localized, continuous, boring epigastric pain which increase over 1 hr, often worse on lying down ± radiation to the back (50%)
- Nausea ± vomiting

Examination

- General: Tachycardia, fever, shock, jaundice
- Abdominal: Localized epigastric tenderness or generalized abdominal tenderness; abdominal distension ± decreased bowel sounds; evidence of retroperitoneal haemorrhage (periumbilical and flank bruising-rare)
- The diagnosis of AP is most often established by the presence of two of the three following criteria:
  (i) abdominal pain consistent with the disease
  (ii) serum amylase and/or lipase greater than three times the upper limit of normal, and/or
  (iii) characteristic findings from abdominal imaging.
- (Strong "We recommend", Moderate)
- Transabdominal ultrasound should be performed in all patients with acute pancreatitis.
- (Strong "We recommend", Low)
- In the absence of gallstones and/or history of significant history of alcohol use, a serum triglyceride should be obtained and considered the etiology if >1,000 mg/dl. (Conditional (weak) "We suggest", Moderate)

- In a patient older than 40 years, a pancreatic tumor should be considered as a possible cause of acute pancreatitis. (Conditional (weak) “We suggest”, Low)
- Endoscopic investigation in patients with acute idiopathic pancreatitis should be limited, as the risks and benefits of investigation in these patients are unclear. (Conditional (weak) “We suggest”, Low)

Management

- Admit as an acute surgical emergency. Prior to transfer, give analgesia with pethidine (morphine may induce spasm of the sphincter of Oddi).

Initial assessment and risk stratification

- Hemodynamic status should be assessed immediately upon presentation and resuscitative measures begun as needed. (Strong “We recommend”, Moderate)
- Risk assessment should be performed to stratify patients into higher- and lower-risk categories to assist triage, such as admission to an intensive care setting. (Conditional (weak) “We suggest”, Moderate)

Initial management

- Aggressive hydration, defined as 250-500 ml per hour of isotonic crystalloid solution should be provided to all patients, unless cardiovascular and/or renal comorbidities exist.
- Early aggressive intravenous hydration is most beneficial the first 12–24 h, and may have little benefit beyond. (Strong “We recommend”, Moderate)

The role of antibiotics in acute pancreatitis

- Antibiotics should be given for an extrapancreatic infection, such as cholangitis, catheter-acquired infections, bacteremia, urinary tract infections, pneumonia. (Strong “We recommend”, High)
- Routine use of prophylactic antibiotics in patients with severe acute pancreatitis is not recommended. (Strong “We recommend”, Moderate)

The role of surgery in acute pancreatitis

- In patients with mild AP, found to have gallstones in the gallbladder, a cholecystectomy should be performed before discharge to prevent a recurrence of AP. (Strong “We recommend”, Moderate)
- In a patient with necrotizing biliary AP, in order to prevent infection, cholecystectomy is to be deferred until active inflammation subsides and fluid collections resolve or stabilize. (Strong “We recommend”, Moderate)
- The presence of asymptomatic pseudocysts and pancreatic and/or extrapancreatic necrosis do not warrant intervention, regardless of size, location, and/or extension. (Strong “We recommend”, Moderate)

Complications

- Delayed complications may present in general practice- suspect if persistent pain or failure to regain weight or appetite.Complications include:
- Pancreatic necrosis
- Pseudocyst-localized collection of pancreatic secretions
- Fistula/abscess formation
- Bleeding or thrombosis

Prevention of further attacks

- Avoid factors that may have caused pancreatitis, e.g. alcohol, drugs
- Advise patients to follow a low-fat diet
- Treat reversible causes, e.g. hyperlipidaemia, gallstones

CHRONIC PANCREATITIS

- Chronic inflammation of the pancreas results in gradual destruction and fibrosis of the gland ± loss of pancreatic function causing malabsorption and DM.

Causes

- Alcohol is responsible for most cases.
- More rarely: familial; CF; haemochromatosis; pancreatic duct obstruction (gallstones/ pancreatic cancer); hyperparathyroidism.

Presentation

Constant or episodic epigastric pain, radiating to the back and relieved by sitting forwards

- Vomiting
- Weakness
- Jaundice
- Steatorrhoea
- Weight loss
- DM
- Chronic poor health
- Natural History and Clinical Symptoms of Chronic Pancreatitis (CP)
- Alcohol and smoking cessation are recommended for all patients with CP.
- Progression to CP can be predicted by the identification of disorders of underlying pancreatic inflammation, such as acute pancreatitis and recurrent acute pancreatitis.
- The risk for development of diabetes mellitus (DM) due to pancreatic enzyme failure is thought to be related to the duration of CP disease.
- Other risks for DM development include a high body mass index (BMI) and tobacco use.
- There is no evidence to support the routine screening of CP patients for malignancy.

Investigation

- Ultrasound +/- CT (pancreatic calcifications confirm the diagnosis)
- MRCP (magnetic resonance cholangio-pancreatography + ERCP(endoscopic retrograde cholangio-pancreatography) (risks acute attack),
- Abdominal XR: speckled calcification

Management

Refer to gastroenterologist Treatment:

- Diet Low-fat, high-protein,high-calorie diet with fat-soluble vitamin supplements.
- Pancreatic enzyme supplementation (e.g. Creon (pancrelipase) capsules pre-meals) may improve diarrhoea
- Alcohol abstinence
- Smoking cessation.
- Pain control: Provide analgesia-beware of opioid abuse.
- Diabetes management
- Surgery -Pancreatectomy or pancreatico-jejunostomy for pancreatic duct stricture,
- obstructive jaundice, unremitting pain, or weight loss.
- Management of Exocrine Pancreatic Insufficiency in Chronic Pancreatitis

- To improve associated nutritional complications, pancreatic enzyme replacement therapy (PERT) is recommended for individuals with CP and Exocrine Pancreatic Insufficiency.
- Periodic evaluation for malnutrition and related complications, such as osteoporosis and fat-soluble vitamin deficiency, is recommended

PANCREATIC INSUFFICIENCY

- Global decreased function of the pancreas.

Causes:

- Child- Cystic fibrosis
- Adult - Chronic pancreatitis, pancreatic tumour, pancreatectomy, total gastrectomy

Presentation

- Malabsorption (frequent loose, odorous stools ± abdominal pain), weight loss or failure to thrive,
- DM.

Management

- Take specialist advice.
- Treat the underlying cause.
- Treat associated DM.
- Supplement digestive enzymes

Reference

1. *Oxford handbook of General Practice, 4th Edition*
2. *https://www.guidelinecentral.com/summaries/american-college-of-gastroenterology-guideline-management-of-acute-pancreatitis/*
3. *Gardner, T. B., Adler, D. G., Forsmark, C. E., Sauer, B. G., Taylor, J. R., & Whitcomb, D. C. (2020). ACG Clinical Guideline: Chronic Pancreatitis. The American journal of gastroenterology, 115(3), 322–339.*

ROUTINE LIVER BIOCH EMICAL TESTS AND CLINICAL USEFULNESS

Biochemical tests can be used to detect acute and chronic diseases of the liver before development of symptoms.
Single laboratory test is generally not useful in evaluating the severity of acute or chronic liver diseases.
A combination of tests such as serum bilirubin, aminotransferases, alkaline phosphatase, albumin and prothrombin time is referred to "liver function tests" or a "liver panel." These tests can provide an initial characterization of the etiology and severity of liver disease.
Traditionally liver diseases have been characterized as primarily hepatocellular or cholestatic based on the predominance of elevated aminotransferases or alkaline phosphatase.

Routine liver function tests

1.SERUM BILIRUBIN
- Unconjugated (Indirect) bilirubin Conjugated (Direct) bilirubin

2.SERUM AMINOTRANSFERASES
- Aspartate aminotransferase (AST, SGOT [serum glutamic oxaloacetic transaminase]) Alanine aminotransferase (ALT, SGPT [serum glutamic pyruvic transaminase])

3.SERUM ALKALINE PHOSPHATASE
4.GAMMA GLUTAMYL TRANSFERASE (GGT)
5.SERUM PROTEINS
- Albumin
- Prothrombin time (PT)/ INR

Serum bilirubin

- With the van den Bergh method, the normal serum bilirubin concentration is usually
- <1mg/dL (18 mmol/L).
- As much as 30% or 0.3 mg/dL (5.1 mmol/L) of the total is direct bilirubin.
- Jaundice clinically apparent when serum bilirubin exceeds 3 mg/dL; often the first evidence of liver disease.

Causes of hyperbilirubinemia

a.Unconjugated (Isolated hyperbilirubinemia, nearly always <7 mg/dL)
Overproduction → hemolysis, ineffective erythropoiesis, resorption of hematoma
Defective uptake and storage of bilirubin → Gilbert's syndrome
b.Conjugated
Hereditary → Dubin-Johnson and Rotor's syndromes, bile transport protein defects
Cholestasis
Intrahepatic → cirrhosis, hepatitis,primary biliary cirrhosis, drug-induced
Extrahepatic → biliary obstruction: choledocholithiasis,stricture, neoplasm, biliary atresia, sclerosing cholangitis
Serum enzyme tests can be grouped into two categories:
enzymes whose elevation in serum reflects generalized damage to hepatocytes; and
enzymes whose elevation in serum primarily reflects cholestasis

Serum aminotransferases

- Aspartate aminotransferase (AST, SGOT [serum glutamic oxaloacetic transaminase])
- Found in liver as well as skeletal muscle, heart, kidney, brain, and pancreas
- Alanine aminotransferase (ALT, SGPT [serum glutamic pyruvic transaminase])
- Highest concentration in liver (more sensitive and specific than AST)
- These intracellular enzymes are the most useful marker of hepatic injury (inflammation or cell necrosis).
- Normal levels of ALT are up to 30 U/L in men and up to 19 U/L in women.
- Aminotransferase → mainly viral, alcoholic, autoimmune, or drug-induced hepatitis.
- In alcoholic hepatitis, the serum AST is usually no more than 2 - 10 times the upper limit of normal, and the ALT is normal or nearly normal with an AST:ALT >2.
- In nonalcoholic fatty liver disease, ALT is typically higher than AST until cirrhosis develops.
- Aminotransferase <500 U/L 7 in obstructive jaundice.

Causes of elevated serum aminotransferase levels

Mild elevation (<5 × normal) ALT predominant	**Marked elevation (>15× normal)**
Chronic viral hepatitis (B,C)	Acute viral hepatitis (A–E, herpes)
Acute viral hepatitis (A–E, Epstein-Barr virus, cytomegalovirus)	DILI
NAFLD(nonalcoholic fatty liver disease)	Ischemic hepatitis
Haemochromatosis	Autoimmune hepatitis
DILI (drug-induced liver injury)	Wilson disease
Autoimmune hepatitis	Acute bile duct obstruction
Alpha-1 antitrypsin deficiency	Acute Budd–Chiari syndrome
Wilson disease	Hepatic artery ligation
Celiac disease	

Serum alkaline phosphatase

- This test is sensitive for detection of biliary tract obstruction; may be intrahepatic or extrahepatic.

Isolated elevation of alkaline phosphatase

- This may indicate infiltrative liver disease: tumor, abscess, granulomas, or amyloidosis.
- High levels → biliary obstruction, sclerosing cholangitis, primary biliary cirrhosis, sepsis, acquired immunodeficiency syndrome, cholestatic drug reactions, and other causes of vanishing bile duct syndrome.
- Non-hepatic sources of alkaline phosphatase are bone, intestine, kidney, and placenta and also elevated in → Paget' s disease of the bone, osteoblastic bone metastases, small bowel obstruction, growing children and normal pregnancy.
- Hepatic origin of an elevated alkaline phosphatase level is suggested by simultaneous elevation of serum gamma glutamyl transferase (GGT).

Gamma glutamyl transferase (GGT)

- It is a very sensitive indicator of hepatobiliary disease but is not specific.
- Elevated levels → renal failure, myocardial infarction, pancreatic disease, diabetes mellitus, phenytoin or alcohol in the absence of other clinical evidence of liver disease.

- Many patients with isolated serum GGT elevation have no other evidence of liver disease; an extensive evaluation is usually not warranted. Patients should be retested after avoiding alcohol and other hepatotoxins for several weeks.

Serum proteins

- reflect the synthetic capability of the liver.

Albumin

- Normal in acute viral hepatitis, drug related hepatoxicity, and obstructive jaundice.
- Hypoalbuminemia (<3 g/dL) is common in chronic liver disease (an indicator of severity).
- It is not specific for liver disease and may also reflect glomerular or gastrointes- tinal losses.

Prothrombin time (PT)/International normalized ratio (INR)

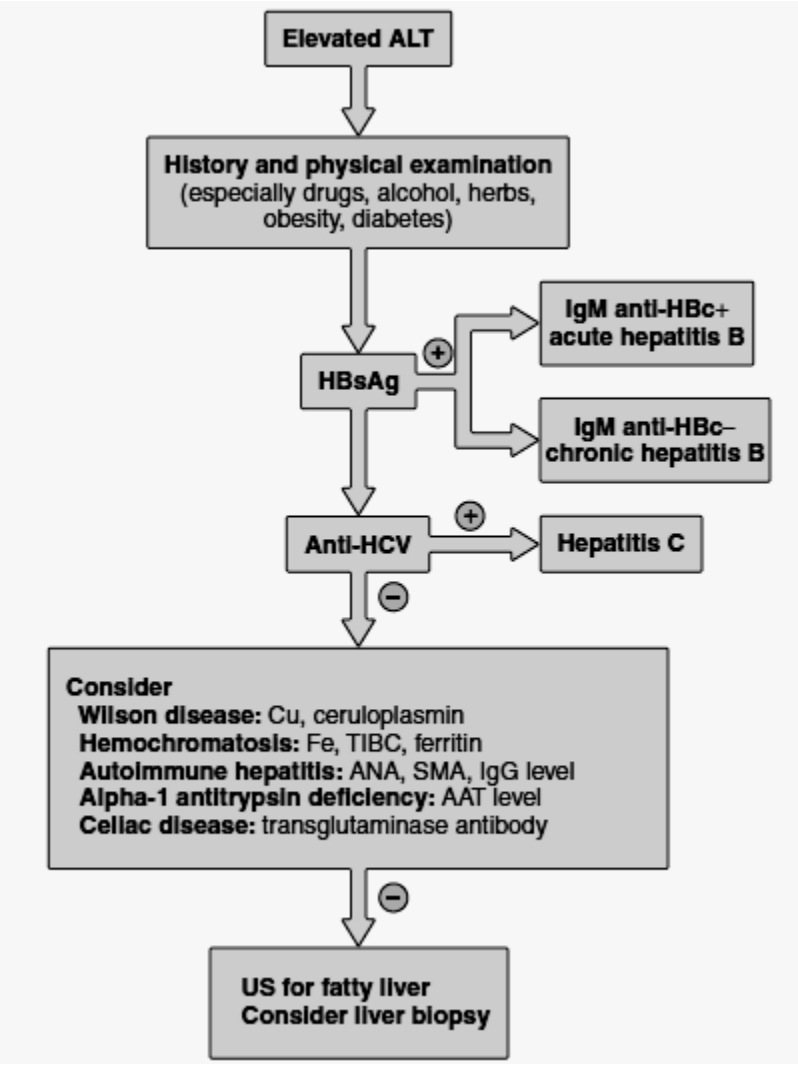
- Prothrombin time is useful in assessing the severity and prognosis of acute liver disease.
- Deficiency of one or more of liver-produced coagulation factors results in a prolonged prothrombin time.
- Prolongation of the prothrombin time in cholestatic liver disease may result from vitamin K deficiency.
- The international normalized ratio (INR) is used to standardize prothrombin time determinations performed in different laboratories.

Distinguishing different types of jaundice

Types of jaundice	Pre-hepatic	Hepatic	Post-hepatic
Type of bilirubin elevated	Unconjugated bilirubin	Both conjugated & unconjugated bilirubin	Conjugated bilirubin
Serum bilirubin Van den Bergh test	Indirect positive	Biphasic	Direct positive
Urine Conjugated bilirubin	Absent	++	+++
Urobilinogen	+++	+ early, obst, -dee	Absent
Bile salt	Absent	+	++
Urine colour	Normal-Acholuric	Dark-Cho luric	Dark-Choluric
Stool colour	Dark brown colour	N/decreased	Clay coloured stools
AST & ALT	Normal	Very high	increased
ALP level	Normal	2-3 times increased	10-12 times increased

The followings are the common stepwise approach to the patients with abnormal LFT.

1. Approach to the patient with an elevated ALT



In young patients, check for Acute Hepatitis A (Anti HAV IgM).

Fig. Approach to patients with an elevated serum alanine aminotransferase (ALT) level. AAT, alpha- I antitrypsin; ANA, antinuclear antibodies; anti-HBc, antibody to hepatitis B core antigen; anti-HCV, antibody to hepatitis C virus; CT, computed tomography; HBsAg, hepatitis B surface antigen; IgG, immunoglobulin; SMA, smooth muscle antibodies; TIBC, total iron binding capacity; US, ultrasonography.

2. Approach to the patient with mild diffuse liver test abnormalities

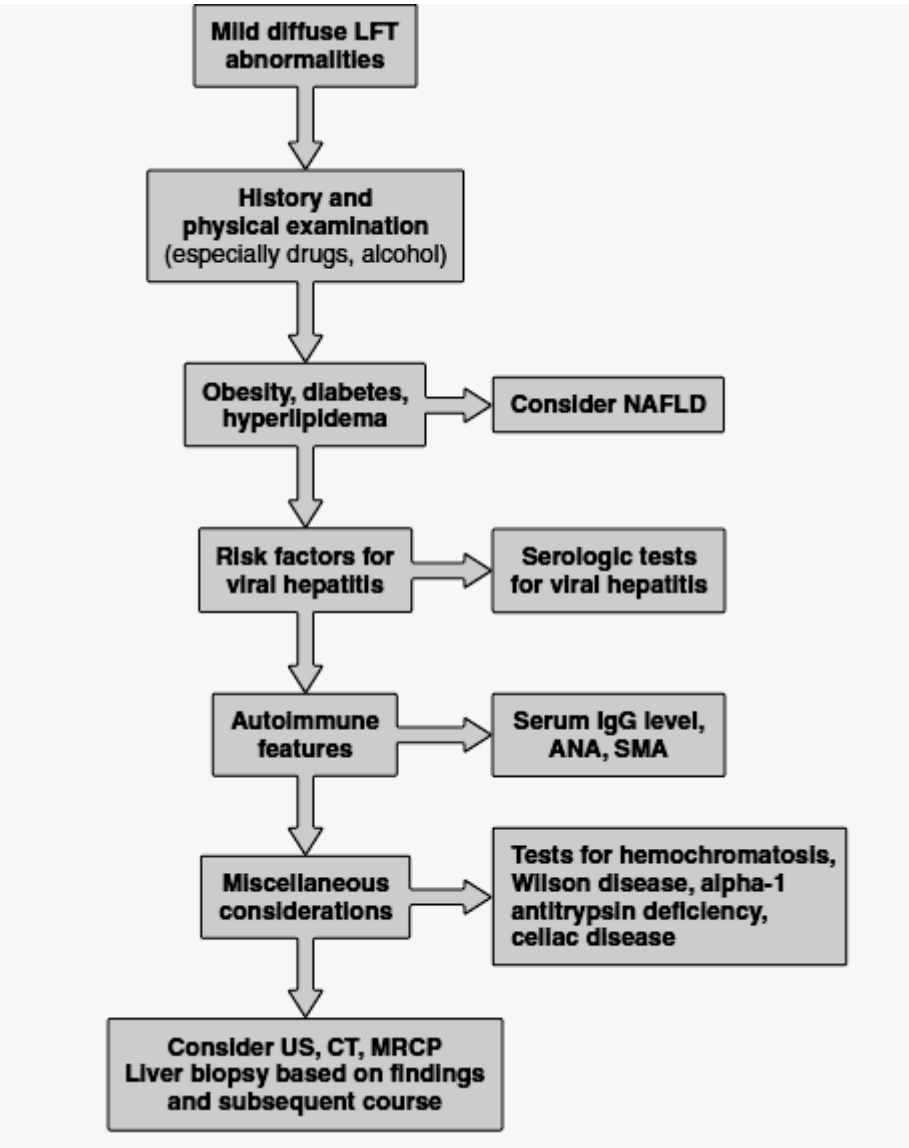


Fig. Approach to a patient with mild diffuse liver biochemical test abnormalities. ANA, antinuclear antibodies; CT, computed tomography; LFT, liver function test; IgG, immunoglobulin; MRCP, magnetic resonance cholangiopancreatography; NAFLD, nonalcoholic fatty liver disease; SMA, smooth muscle antibodies; US, ultrasonography.

3. Approach to a patient with isolated serum alkaline phosphatase elevation

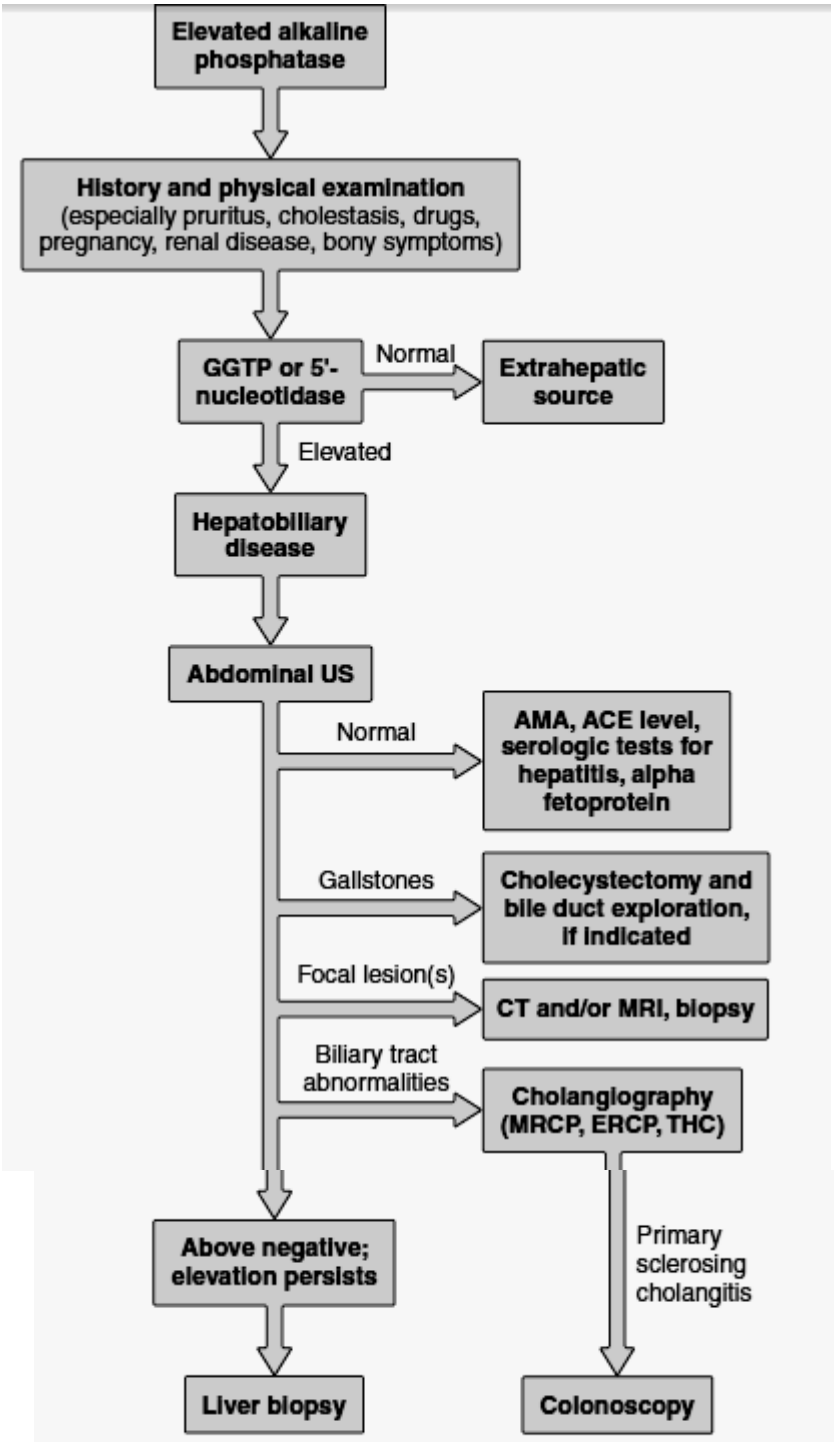


Fig. Approach to a patient with isolated serum alkaline phosphatase elevation. ACE, angiotensin- converting enzyme; AMA, antimitochondrial antibodies; ERCP, endoscopic retrograde cholangiopancreatography; MRCP, magnetic resonance cholangiopancreatography; MRI, magnetic resonance imaging; THC, transhepatic cholangiography; US, ultrasonography.

Reference

1. *Therapeutic Manual (Internal Medicine) 1st Edition 2016*

COLORECTAL CANCER (CRC) SCREENING:

Introduction and relevance to GP:

- Colorectal cancer is the third most common cancer and the second most common cause of cancer related death in US. Most CRC arise from preexisting adenomatous polyps. Adenomatous polyps occur in 30% of adults 50 years and older and the incidence increases with advancing age. The goal of CRC screening is to identify early cancers and adenomatous polyps by mass screening of all average -risk adults 50 years and older up to 75 years of age (USPSTF recommendation)
- CRC screening in overview and recommendations:
- AAFP: strongly recommends that adults 50 years and older be screened for CRC.
- CRC screening is cost-effective, regardless of the screening method, and it has been estimated that routine screening could save 18,800 lives per year.

Methods of screening:

1.Fecal occult blood test (FOBT)

- It should be performed using testing cards sent home with the patient. Office testing of stool samples obtained by DRE has not been shown to reduce mortality. Single FOBT performed by DRE will miss 95% of CRC and is not recommended for screening. Rather, patients should take home three cards with two testing windows on each card, and be instructed to use one card a day for three consecutive days. Rehydration of stool cards with water before development may improve sensitivity, but is also lead to increased false-positive results.
- A Cochrane systematic review showed a reduction in CRC mortality of 16% with FOBT.
- Fecal immunochemical testing is a newer way to detect occult blood in stool. Unlike FOBT, fecal immunochemical testing does not require dietary restriction before testing.
- A positive test should be followed up with a colonoscopy.

2.Flexible sigmoidoscopy

- Flexible sigmoidoscopy every five years is an accepted modality for CRC screening by most recommending organizations. USPSTF recommends combining sigmoidosopy every 5 years with high sensitivity FOBT every 3 years.

3.Colonoscopy

- Several organizations recommend colonoscopy every 10 years for CRC screening in average risk persons. Colonoscopy carries a greater risk of perforation and other serious complications than sigmoidoscopy.

4.Double-contrast barium enema

- This method is still used as a screening tool, particularly in the right side of the colon following an incomplete colonoscopy.

5.CT colonography

- Studies of this method have reported sensitivities 55-100% and specificities of 86-98% for detection of polyps larger than 10mm

6.Fecal DNA testing

- In a large prospective study, it was four times more sensitive than FOBT for detecting invasive cancer. Also, patients have been shown to prefer fecal DNA testing to FOBT and colonoscopy.

7.Pillcam colon

- It involves ingestion of a capsule that wirelessly acquires colonic images for later viewing. The sensitivity and specificity of Pillcam Colon was inferior to that of colonoscopy.

Primary and secondary prevention

- Following risk factors should be reduced for prevention of CRC.

Obesity

- A large cohort study showed that an association between increasing BMI and relative risk of CRC mortality.

Fat intake

- There is evidence that high fat intake increases the risk of developing adenomatous polyps.

Red meat

- There is conflicting evidence about red meat and CRC risk.

Fiber

- A systematic review failed to show any benefit of increased dietary fibre intake for reducing incidence or recurrence of adenomatous polyps.

Aspirin, NSAIDs, and COX21

- Although there is poor evidence of reducing CRC mortality, risk of GI bleeding and other harms outweighs the benefit. So the USPSTF recommends against using them for chemoprevention.

Calcium

- There was insufficient evidence to recommend the general use of calcium supplementation to prevent CRC.

Vitamin D

- Vitamin D alone or combined with Calcium may reduce the risk of CRC. However, little evidence to support Vitamin D as chemo prevention was seen in analysis of cohort and case-control studies.

HRT

- There is contradictory evidence regarding whether HRT reduces the risk of CRC.

Anti-oxidants

- There was no benefit of anti-oxidants in decreasing CRC. Vitamin E was found to increase of adenomatous polyps.

Statins

- A population-based case-control study found that CRC was less likely to occur in patients who took a statin for at least 5 years.

Key recommendation for practice (summary)		
Clinical recommendation	Evidence ratio!!	Comments
CRC screening		
1. All adults 50 yrs and older should be screened	A	Most CRCs arise from adenomatous polyps
2. Routine screening for CRC should continue until 75 yrs of age	A	The USPSTF recommends against continued routine screening in previous screened adults 75-85 yrs of age and against any screening in adults older than 85 yrs
3. Options for screening:		
a. Annual FOBT	A	Decreased mortality from CRC, but not all-cause mortality
b. 5 yrs flexible sigmoidoscopy (with or without FOBT)	A	Decreased mortality from CRC, effect on all-cause mortality unknown.
c. 10 yrly colonoscopy	B	Mortality benefit not proven. Greater single test-accuracy than FOBT or sigmoidoscopy, but higher risk of serious complucations.
Primary prevention of CRC		
1. Fibre supplementation should not be recommended to decrease the risk of CRC.	A	Not recommended for chemoprevention, no evidence of benefit.
2. Aspirin and NSAID should not be routinely used for chemoprevention of CRC.	A	Increased harms, such as GI bleeding and renal impairment, limit routine use.
3. Risks and benefits should be considered when recommending hormone therapy for women to decrease risk for CRC.	B	Good evidence of benefit to decrease the risk of colon cancer, inconsistent evidence of rectal cancer. Increased risk of more advanced colon cancers with oestrogen use; and associated with VTE and breast cancer.
4. Antioxidants should not be recommended to decrease the risk of CRC.	A	Not recommneded for chemoprevention; vitamin E associated with increased risk of adenomatous polyps.