Zürich, 31.10.2023

Grundlagen der Diagnostik und Therapie

Vom klinischen Symptom zur Diagnose

Jan Boegeholz
jan.boegeholz@usz.ch

Symptome

Gewichtsverlust

Fatigue

Oberbauchschmerzen

Schmerzloser Ikterus

Was ist häufig, was darf ich nicht übersehen, was muss ich schnell klären?

Symptome

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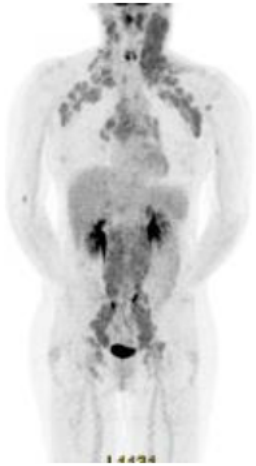
Gewichtsverlust

Wollten Sie Gewicht abnehmen?

Documented weight loss of 5% or more of usual body weight over 6 to 12 months



Major causes of unintentional weight loss
Malignancy (eg, gastrointestinal, lung, lymphoma, renal, and prostate cancers)
Nonmalignant gastrointestinal diseases (eg, peptic ulcer disease, celiac disease, inflammatory bowel disease)
Psychiatric disorders (particularly depression), also eating disorders, food-related delusional manifestations of other psychiatric disorders
Endocrinopathies (eg, hyperthyroidism, diabetes, adrenal insufficiency)
Infectious diseases (eg, HIV, viral hepatitis, tuberculosis, chronic fungal or bacterial disease, chronic helminth infection)
Advanced chronic disease (eg, cardiac cachexia from heart failure, pulmonary cachexia, renal failure)
Neurologic diseases (eg, stroke, dementia, Parkinson disease, amyotrophic lateral sclerosis)
Medications/substances
Rheumatologic diseases (eg, severe rheumatoid arthritis, giant cell vasculitis)
Chronic vigorous exercise (eg, distance running, ballet dancing, gymnastics)

Medikamente / Substanzen

Medication/substances associated with weight loss
Alcohol
Cocaine
Amphetamines
Drug withdrawal syndromes (withdrawal after chronic high-dose psychotropic medications or cannabis)
Tobacco
Adverse effects of prescription drugs (eg, anticonvulsants, diabetes medications, thyroid medication)*
Herbal and other nonprescription drugs (5-hydroxytryptophan, aloe, caffeine, cascara, chitosan, chromium, dandelion, ephedra, garcinia, glucomannan, guarana, guar gum, herbal diuretics, nicotine, pyruvate, St. John's wort)

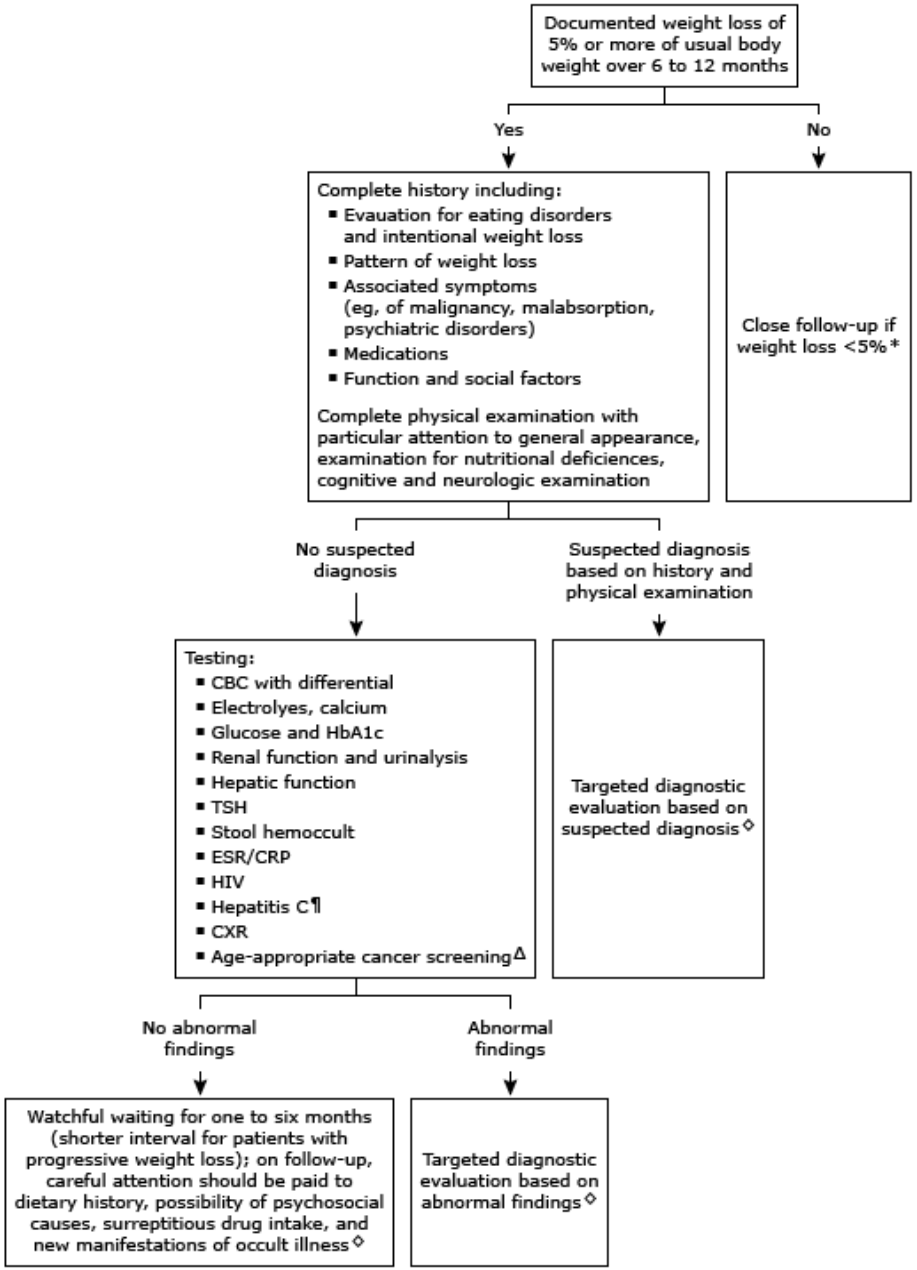
HIV: human immunodeficiency virus.

* Refer to the UpToDate topic on the approach to the patient with unintentional weight loss.

Causes of weight loss in older adults

Medications (eg, digoxin, theophylline, SSRIs, antibiotics)
Emotional (eg, depression, anxiety)
Alcoholism, older adult abuse
Late-life paranoia or bereavement
Swallowing problems
Oral factors (tooth loss, xerostomia)
Nosocomial infections (eg, tuberculosis, pneumonia)
Wandering and other dementia-related factors
Hyperthyroidism, hypercalcemia, hypoadrenalism
Enteral problems (eg, esophageal stricture, gluten enteropathy)
Eating problems
Low salt, low cholesterol, and other therapeutic diets
Social isolation, stones (chronic cholecystitis)

Stepwise approach to the patient with suspected unintentional weight loss

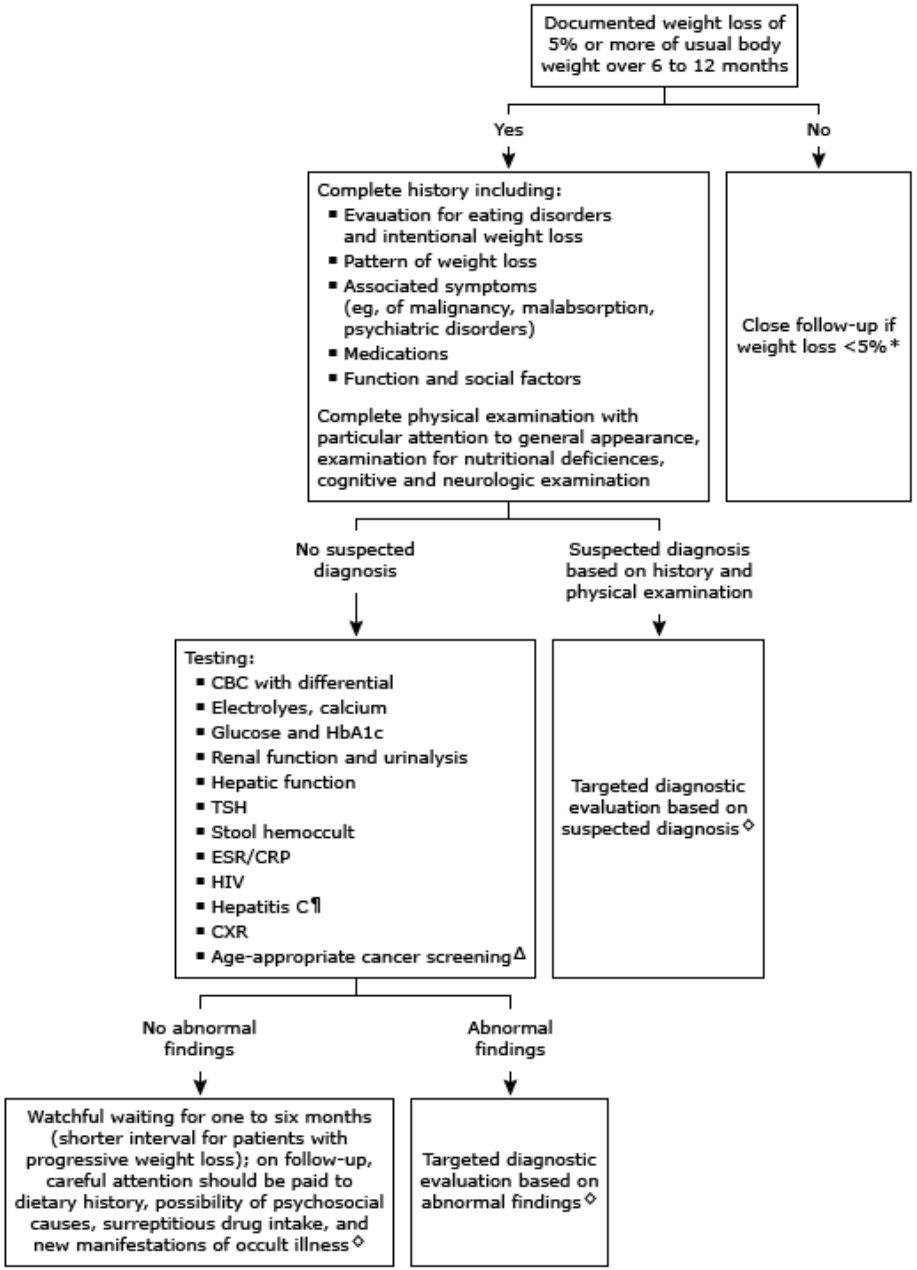


Physical examination

Physical examination focuses on evaluating for symptoms of the various etiologies of unintentional weight loss, including psychiatric disorders, hyperthyroidism, nutritional deficiencies, and chronic disease.

- **General appearance** – Patients may have a flat affect which can be a sign of psychiatric disease.
- **Head and neck** – Patients should be examined for ophthalmoplegia and stigmata of nutritional deficiencies (eg, cheilosis, glossitis). If appropriate, a dental examination should be done as poor dentition can lead to weight loss.
- **Cardiopulmonary examination** – Patients with chronic cardiac and pulmonary disease may have weight loss.
- **Abdominal examination** – Patients should be assessed for abdominal tenderness, ascites, hepatosplenomegaly, and abdominal masses.
- **Cognitive and neurologic exam** – We perform a neurologic exam to evaluate for deficits. Also, particularly in older patients, we assess for cognitive impairment and dementia as these can contribute to weight loss.
- **Other** – We also examine for lymphadenopathy.

Stepwise approach to the patient with suspected unintentional weight loss



Symptome

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DEFINITION

The term “fatigue” can be used to describe difficulty or inability to initiate activity (subjective sense of weakness); reduced capacity to maintain activity (easy fatigability); or difficulty with concentration, memory, and emotional stability (mental fatigue).

21 to 33 percent of patients seeking attention in primary care settings describe fatigue as an important problem (if not always the chief complaint)

The history should also determine the characteristics, severity, and temporal pattern of fatigue:

- Onset – Abrupt or gradual, relationship to illness or life event
- Course – Stable, improving, or worsening
- Duration and daily pattern
- Factors that alleviate or exacerbate it
- Impact on daily life – Ability to work, socialize, participate in usual activities
- Accommodations that the patient/loved ones have had to make to deal with symptoms

Causes of subacute and chronic fatigue

Condition	Symptoms	Physical findings	Supportive diagnostic studies
Cardiopulmonary			
Congestive heart failure	Dyspnea on exertion, orthopnea, leg swelling	S3 gallop, inspiratory rales, elevated jugular venous distension, peripheral edema	Chest radiograph, echocardiogram
Chronic obstructive pulmonary disease	Dyspnea, chronic cough, sputum production	Evidence of hyperinflation, wheezing, rales	Chest radiograph
Sleep apnea	Snoring, interrupted breathing during sleep	Obesity, hypertension	Sleep study
Endocrinologic/metabolic			
Hypothyroidism	Cold intolerance, weight gain, constipation, dry skin	Bradycardia, goiter, slow deep tendon reflex relaxation phase	Thyroid function tests
Hyperthyroidism	Heat intolerance, weight loss, diarrhea, moist skin	Tachycardia, goiter, ophthalmopathy	Thyroid function tests
Chronic renal disease	Nausea/vomiting, mental status changes, decreased urine	Hypertension, peripheral edema	Renal function tests/ serum electrolytes
Chronic hepatic disease	Abdominal distention, gastrointestinal bleeding	Jaundice, palmar erythema, gynecomastia, splenomegaly, evidence of ascites	Hepatic function tests
Adrenal insufficiency	Weight loss, salt craving, gastrointestinal complaints	Hypotension, hyperpigmentation, vitiligo	Morning cortisol/ACTH, ACTH stimulation test
Electrolyte abnormalities			
Hyponatremia	Nausea, malaise, cognitive dysfunction	Generally normal exam	Serum sodium level
Hypercalcemia	Anorexia, polydipsia/polyuria, nausea	Generally normal exam	Serum calcium/albumin levels

Hematologic/neoplastic			
Anemia	Dizziness, weakness, palpitations, dyspnea	Tachycardia, pallor	Complete blood count
Occult malignancy	Weight loss, localized symptoms may be present depending upon type	Variable	Variable depending upon type
Infectious diseases			
Mononucleosis syndrome	Fever, sore throat, tender lymph nodes	Fever, exudate pharyngitis, tender cervical adenopathy	Complete blood/differential count, monospot
Viral hepatitis	Fever, nausea/vomiting, abdominal discomfort	Fever, jaundice, tender hepatomegaly	Hepatic function tests, viral hepatitis serologies
HIV infection	Weight loss, variable localized complaints	Variable physical findings	HIV serology
Subacute bacterial endocarditis	Fever/chills, night sweats, myalgias	Fever, new (regurgitant) murmur, peripheral manifestations	Blood cultures, echocardiogram
Tuberculosis	Fever/chills, night sweats, fatigue, weight loss	Cough, chest pain, dyspnea, hemoptysis	PPD/gamma-interferon assay, chest radiograph
Rheumatologic			
Fibromyalgia	Chronic diffuse muscle pain	Multiple "tender points" on palpation	None
Polymyalgia rheumatica	Aching/morning stiffness of shoulders, neck, and hips	Decreased range of motion of shoulders, neck, and hips	Erythrocyte sedimentation rate
Psychological			
Depression	Sad mood, anhedonia, altered sleep, cognitive dysfunction	Generally normal exam	Screening test (eg, PHQ-2, PHQ-9)
Anxiety disorder	Generalized nervousness, panic attacks, phobias	Tachycardia, muscle tension	Screening test (eg, GAD-7)
Somatization disorder	Multiple chronic constitutional and localized complaints	Generally normal exam	Screening test (eg, SSS-8)
Medication toxicity*			
	Variable	Generally normal exam	None
Substance use¶			
	Variable	Generally normal exam	None

ACTH: adrenocorticotropic hormone; HIV: human immunodeficiency virus; PPD: purified protein derivative; PHQ-2: Patient Health Questionnaire-2; GAD-7: Generalized Anxiety Disorder-7; SSS-8: Somatic Symptom Scale-8.

* Benzodiazepines, antidepressants, muscle relaxants, first-generation antihistamines, beta-blockers, opioids, GABA analogues.

¶ Alcohol, marijuana, opioids, cocaine/other stimulants.

Laboratory and radiologic studies —

●Complete blood count with differential count
●Chemistries (including glucose, electrolytes, calcium, renal and hepatic function tests)
●Thyroid-stimulating hormone
●Creatine kinase (if muscle pain or weakness is present)

hepatitis C virus infection
HIV infection
testing for tuberculosis (eg, purified protein derivative [PPD] or gamma-interferon release assay, chest radiograph, sputum collection)

Erythrocyte sedimentation rate (ESR) and high-sensitivity C-reactive protein symptoms consistent with polymyalgia rheumatica or giant cell (temporal) arteritis.

Updating of cancer screening interventions

3 (zentrale) Fragen zur Anämieabklärung

Ist der Rest des Blutbildes normal?

Wie ist das MCV?

(Wie ist das “kinetische” Model?)

Blutwerte über eine Zeit anschauen

Blutstatus			
Hämoglobin	g/l	134-170	154
Hämatokrit	l/l	0.400-0.500	0.431
Erythrozyten	T/l	4.2-5.7	5.10
MCV	fl	80-100	84.5
MCH	pg	26-34	30.2
MCHC	g/l	310-360	357
RDW	%	11.0-14.8	12.9
Thrombozyten (automatisch)	G/l	143-400	221
Leukozyten	G/l	3.0-9.6	6.99

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Urgent/emergent evaluation and/or surgical abdomen —

Patients in whom there are concerns for life-threatening causes of abdominal pain should be referred to the emergency department.

These include those with:

●Unstable vital signs

●Signs of peritonitis on abdominal exam (eg, abdominal rigidity, rebound tenderness, and/or pain that worsens when the examiner lightly bumps the stretcher)

●Concern that the abdominal pain is from a life-threatening condition (**eg, acute bowel obstruction, acute mesenteric ischemia, perforation, acute myocardial infarction, ectopic pregnancy**)

DIAGNOSTIC APPROACH TO CHRONIC ABDOMINAL PAIN

Chronic abdominal pain is a common complaint, and the vast majority of patients will have a functional disorder, most commonly irritable bowel syndrome (IBS)

Initial workup — Initial workup is focused on differentiating benign functional illness from organic pathology. Features that suggest organic illness include weight loss, fever, hypovolemia, electrolyte abnormalities, symptoms or signs of gastrointestinal blood loss, anemia, or signs of malnutrition.

The following laboratory measurements should be performed in most patients with chronic abdominal pain:

- Complete blood count with differential
- Electrolytes, blood urea nitrogen (BUN), creatinine, and glucose
- Calcium
- Aminotransferases, alkaline phosphatase, and bilirubin
- Lipase and/or amylase
- Serum iron, total iron binding capacity, and ferritin
- Anti-tissue transglutaminase

Causes of epigastric abdominal pain

Epigastric	Clinical features	Comments
Acute myocardial infarction	May be associated with shortness of breath and exertional symptoms.	Consider particularly in patients with risk factors for coronary artery disease.
Acute pancreatitis	Acute-onset, persistent upper abdominal pain radiating to the back.	
Chronic pancreatitis	Epigastric pain radiating to the back.	Associated with pancreatic insufficiency.
Peptic ulcer disease	Epigastric pain or discomfort is the most prominent symptom.	Occasionally, discomfort localizes to one side.
Gastroesophageal reflux disease	Associated with heartburn, regurgitation, and dysphagia.	
Gastritis/gastropathy	Abdominal discomfort/pain, heartburn, nausea, vomiting, and hematemesis.	Variety of etiologies including alcohol and nonsteroidal antiinflammatory drugs (NSAIDs).
Functional dyspepsia	The presence of one or more of the following: postprandial fullness, early satiation, epigastric pain, or burning.	Patients have no evidence of structural disease.
Gastroparesis	Nausea, vomiting, abdominal pain, early satiety, postprandial fullness, and bloating.	Most causes are idiopathic, diabetic, or postsurgical.

Causes of left upper quadrant (LUQ) abdominal pain

LUQ	Clinical features	Comments
Splenomegaly	Pain or discomfort in LUQ, left shoulder pain, and/or early satiety.	Multiple etiologies.
Splenic infarct	Severe LUQ pain.	Atypical presentations common. Associated with a variety of underlying conditions (eg, hypercoagulable state, atrial fibrillation, and splenomegaly).
Splenic abscess	Associated with fever and LUQ tenderness.	Uncommon. May also be associated with splenic infarction.
Splenic rupture	May complain of LUQ, left chest wall, or left shoulder pain that is worse with inspiration.	Most often associated with trauma.

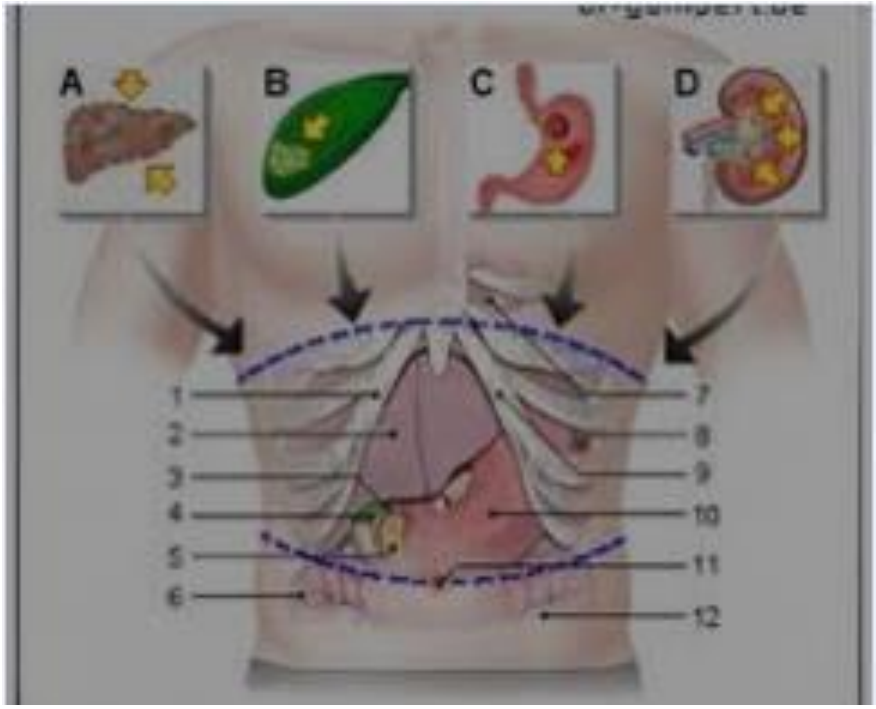
Causes of right upper quadrant (RUQ) abdominal pain

RUQ	Clinical features	Comments
Biliary		
Biliary colic	Intense, dull discomfort located in the RUQ or epigastrium. Associated with nausea, vomiting, and diaphoresis. Generally lasts at least 30 minutes, plateauing within one hour. Benign abdominal examination.	Patients are generally well-appearing.
Acute cholecystitis	Prolonged (>4 to 6 hours) RUQ or epigastric pain, fever. Patients will have abdominal guarding and Murphy's sign.	
Acute cholangitis	Fever, jaundice, RUQ pain.	May have atypical presentation in older adults or immunosuppressed patients.
Sphincter of Oddi dysfunction	RUQ pain similar to other biliary pain.	Biliary type pain without other apparent causes.
Hepatic		
Acute hepatitis	RUQ pain with fatigue, malaise, nausea, vomiting, and anorexia. Patients may also have jaundice, dark urine, and light-colored stools.	Variety of etiologies include hepatitis A, alcohol, and drug-induced.
Perihepatitis (Fitz-Hugh-Curtis syndrome)	RUQ pain with a pleuritic component, pain is sometimes referred to the right shoulder.	Aminotransferases are usually normal or only slightly elevated.
Liver abscess	Fever and abdominal pain are the most common symptoms.	Risk factors include diabetes, underlying hepatobiliary or pancreatic disease, or liver transplant.
Budd-Chiari syndrome	Symptoms include fever, abdominal pain, abdominal distention (from ascites), lower extremity edema, jaundice, gastrointestinal bleeding, and/or hepatic encephalopathy.	Variety of causes.
Portal vein thrombosis	Symptoms include abdominal pain, dyspepsia, or gastrointestinal bleeding.	Clinical manifestations depend on extent of obstruction and speed of development. Most commonly associated with cirrhosis.

Häufigste Ursachen Oberbauchschmerz

Magen: Gastritis, Ulkus
Dünndarm: Ulkus
Leber/Galle: Cholecystitis, Gallenkollik
Pankreas: Pankreatitis

Gastroskopie /
Ultraschall, ggfs CT



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Schmerzloser Ikterus

Herr B. – 75 Jahre alt

04/16 **Dunkelfärbung der Urins, Entfärbung Stuhl, Juckreiz;**

vegetativ: **kein Fieber, kein Nachtschweiß, Gewichtsverlust 6kg in 3 Monaten**

Vorerkrankungen: Hyperprolaktinämie ED 09/2015; Diabetes mellitus Typ 2, ED 2000; Arterielle Hypertonie

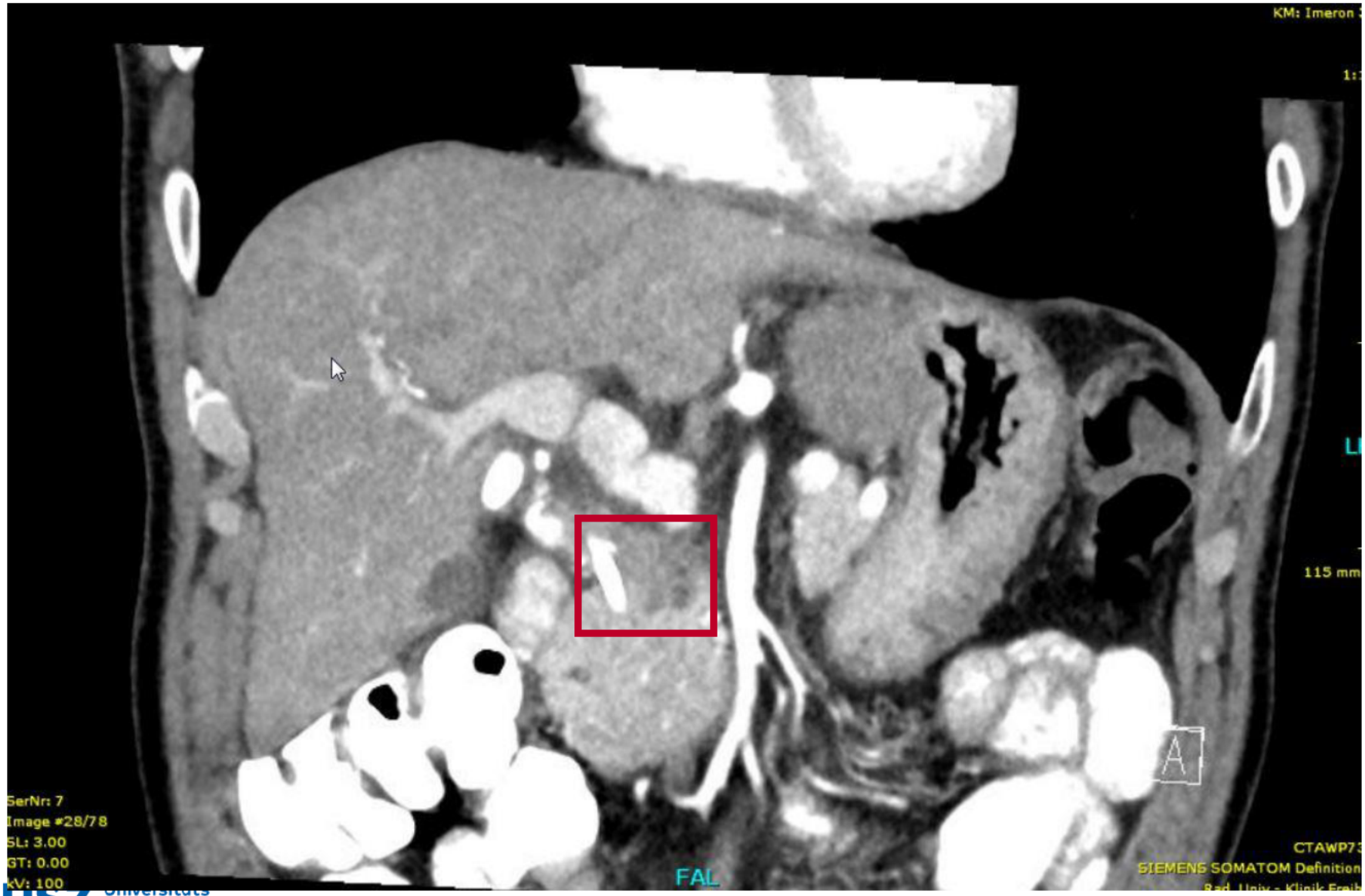
Diagnostik

	11.04.16 10:45
Quick [%]	111 ok
Intern. norm. Ratio	0,96 ok
PTT [sec]	23 ok
Hämolyse-Index (Serum)	1 ok
Natrium [mmol/l]	138 ok
Kalium [mmol/l]	3,8 ok
Calcium [mmol/l]	
Chlorid [mmol/l]	
Magnesium [mmol/L]	
Eisen [µg/dl]	
Transferrin immun. [mg/dl]	
Transferrinsättigung [%]	
Ferritin [ng/ml]	
Harnstoff [mg/dl]	32 ok
Kreatinin [mg/dl]	0,83 ok
GFR-Abschätzung(MDRD) [ml/min/1.73qm]	
CKD-EPI GFR geschätzt [ml/min/1.73qm]	
Harnsäure [mg/dl]	
Glukose [mg/dl]	132 ok
LDH [U/l]	179 ok
CK [U/l]	60 ok
proBNP [pg/ml]	
GOT (AST) [U/l]	96 ok
GPT (ALT) [U/l]	164 ok
Alk. Phosphatase [U/l]	305 ok
Gamma-GT [U/l]	807 ok*
Bilirubin gesamt [mg/dl]	6,9 ok
Bilirubin direkt [mg/dl]	5,9 ok*
Lipase [U/l]	41 ok
Pankreas-Amylase [U/l]	36 ok
C-reaktives Protein [mg/l]	4 ok
Eiweiß (gesamt) [g/dl]	
Albumin [g/dl]	4,4 ok
Vitamin B12 [pg/ml]	
Folsäure [ng/ml]	

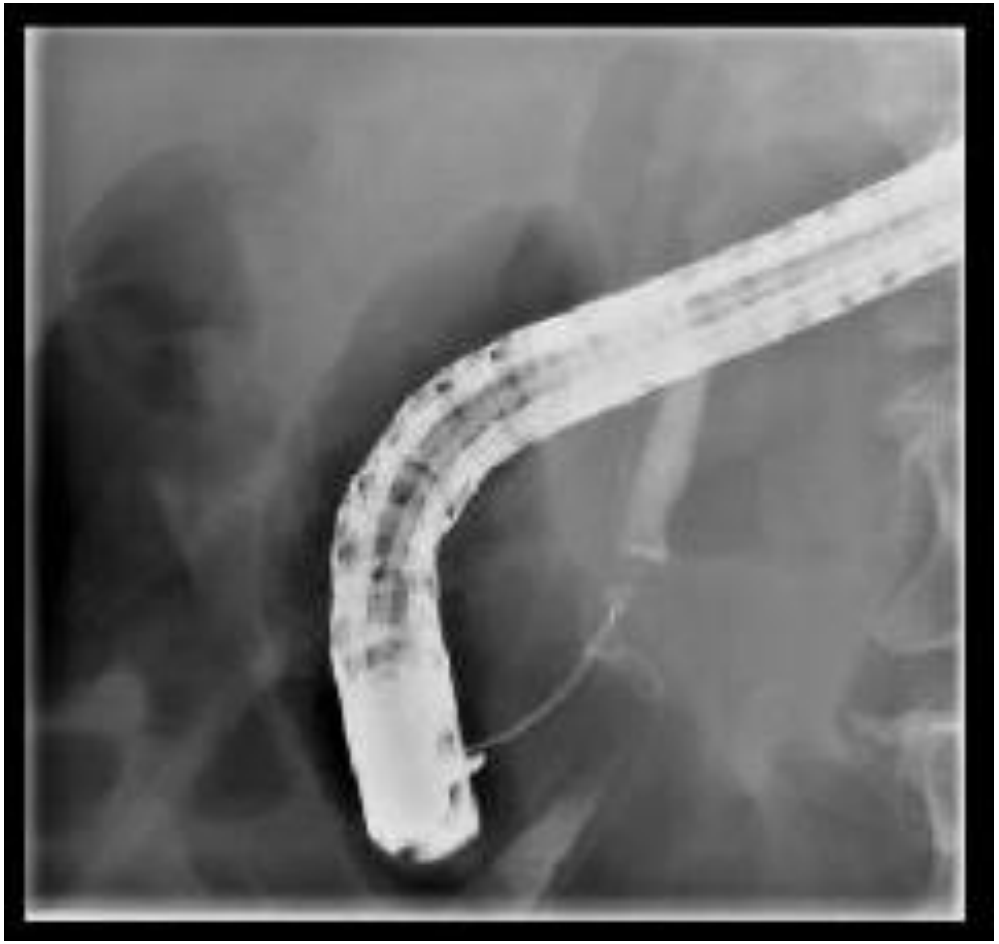
Ruhe-EKG vom 11.04.2016

normofrequenter Sinusrhythmus, keine ERBS

Diagnostik –CT Abdomen



Diagnostik - ERCP



Endoskopie: ERCP vom 12.04.16 08:02

Distale kurzstreckige DHC-Stenose mit intrahepatischer Cholestase

- Papillotomie + Endoprotheseneinlage (10F/6cm)

Herr B. – 75 Jahre alt

04/16 Dunkelfärbung der Urins, Entfärbung Stuhl, Juckreiz;

***vegetativ:* kein Fieber, kein Nachtschweiß, Gewichtsverlust 6kg in 3 Monaten**

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Distale kurzstreckige DHC-Stenose mit intrahepatischer Cholestase

- Papillotomie + Endoprotheseneinlage (10F/6cm)

CT-Thorax/Abdomen vom 13.04.2016:

1. Arteriell hypodense Raumforderung entlang des distalen DHC bis in den Pankreaskopf reichend DD CCC DD Pankreaskopfkarzinom.
2. Malignomsuspekte periportale Lymphknoten.
3. Kein Nachweis malignomsuspekter Herde pulmonal, hepatisch oder ossär.

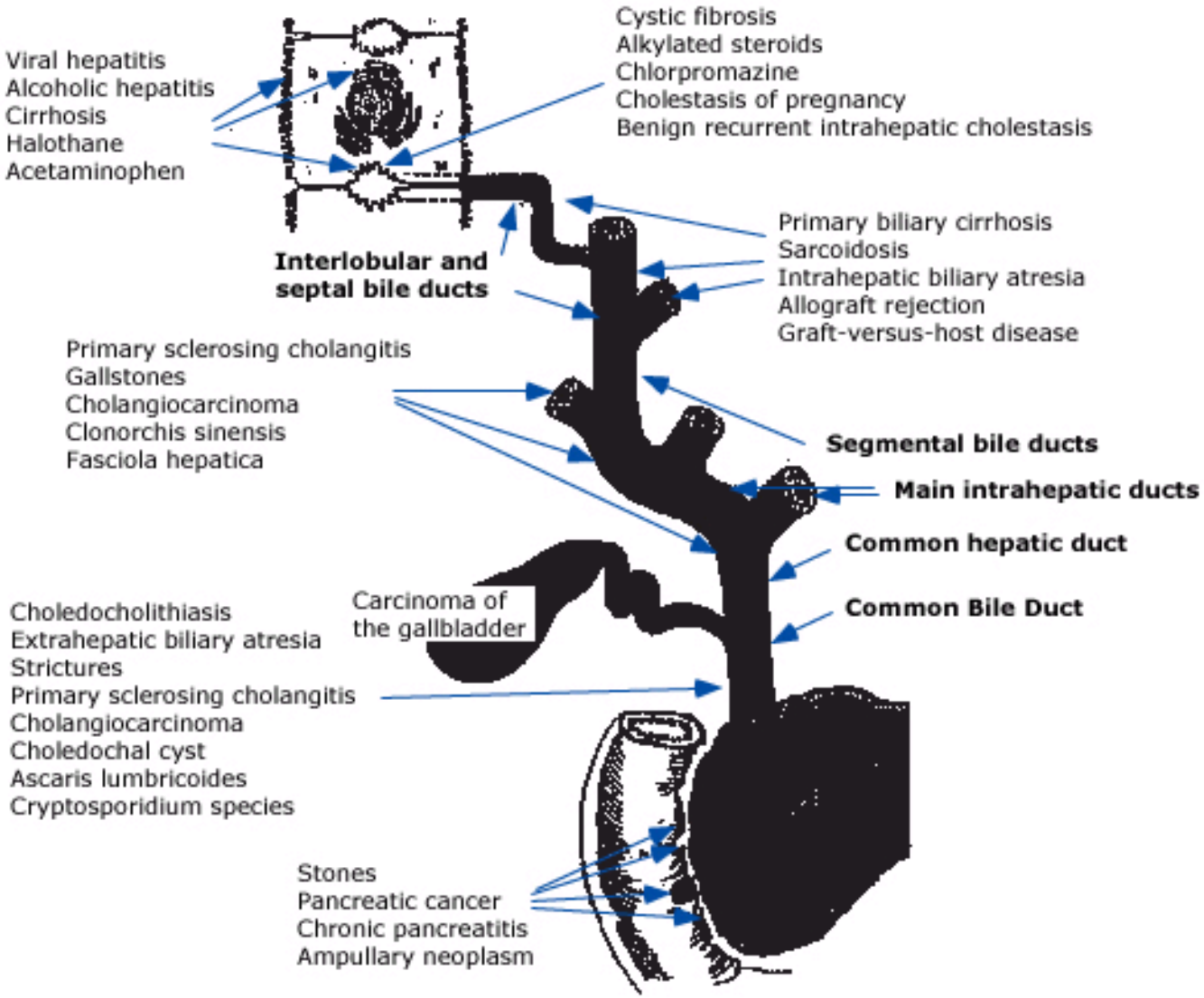
V.a. Pankreaskarzinom, DD: distales Cholangiokarzinom → TU-Board → technisch resektabel → OP-Empfehlung

Classification of jaundice according to type of bile pigment and mechanism

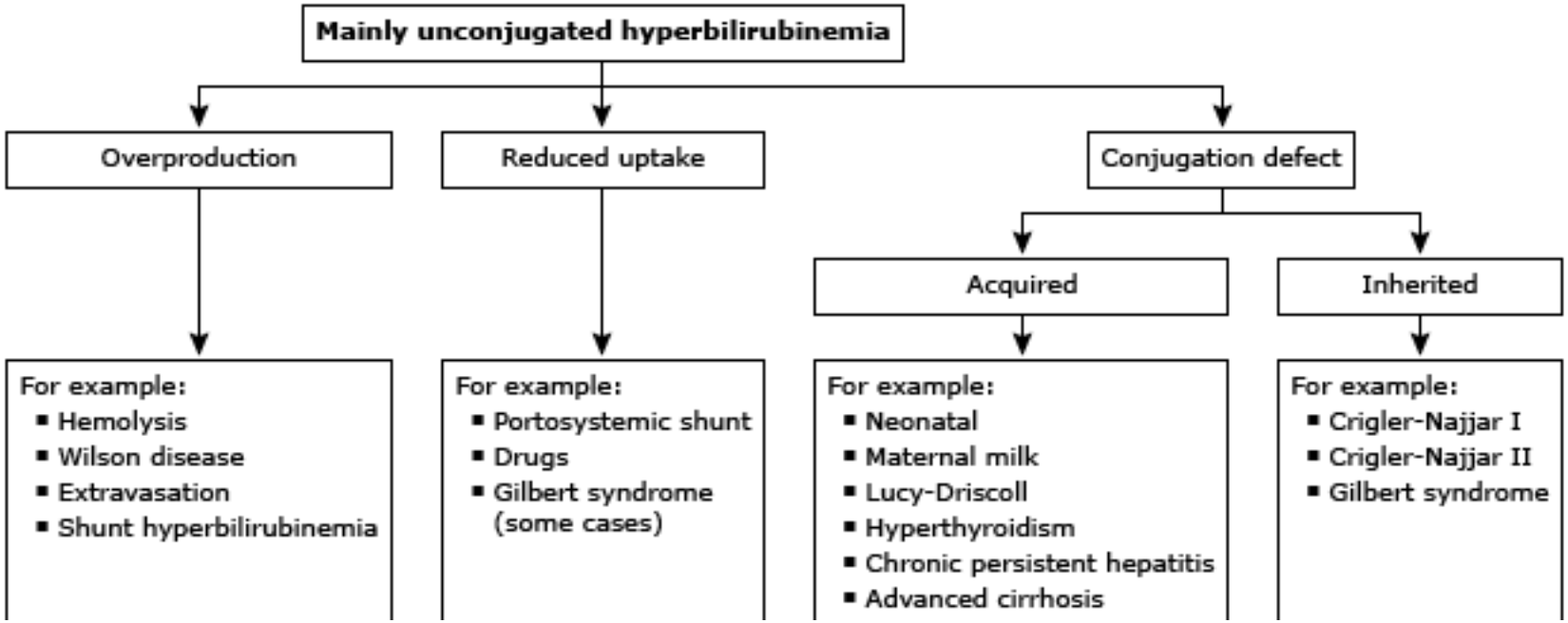
Unconjugated hyperbilirubinemia
Increased bilirubin production*
Extravascular hemolysis
Extravasation of blood into tissues
Intravascular hemolysis
Dyserythropoiesis
Wilson disease
Impaired hepatic bilirubin uptake
Heart failure
Portosystemic shunts
Some patients with Gilbert syndrome
Certain drugs¶ – Rifampin, probenecid, flavaspadic acid, bunamiodyl
Impaired bilirubin conjugation
Crigler-Najjar syndrome types I and II
Gilbert syndrome
Neonates
Hyperthyroidism
Ethinyl estradiol
Liver diseases – Chronic hepatitis, advanced cirrhosis
Conjugated hyperbilirubinemia
Defect of canalicular organic anion transport
Dubin-Johnson syndrome
Defect of sinusoidal reuptake of conjugated bilirubin
Rotor syndrome

Conjugated hyperbilirubinemia (continued)
Extrahepatic cholestasis (biliary obstruction)
Choledocholithiasis
Intrinsic and extrinsic tumors (eg, cholangiocarcinoma, pancreatic cancer)
Primary sclerosing cholangitis
AIDS cholangiopathy
Acute and chronic pancreatitis
Strictures after invasive procedures
Certain parasitic infections (eg, *Ascaris lumbricoides*, liver flukes)
Intrahepatic cholestasis
Viral hepatitis
Alcohol-associated hepatitis
Non-alcohol-associated steatohepatitis
Chronic hepatitis
Primary biliary cholangitis
Drugs and toxins (eg, alkylated steroids, chlorpromazine, herbal medications [eg, Jamaican bush tea], arsenic)
Sepsis and hypoperfusion states
Infiltrative diseases (eg, amyloidosis, lymphoma, sarcoidosis, tuberculosis)
Total parenteral nutrition
Postoperative cholestasis
Following organ transplantation
Hepatic crisis in sickle cell disease
Pregnancy
End-stage liver disease

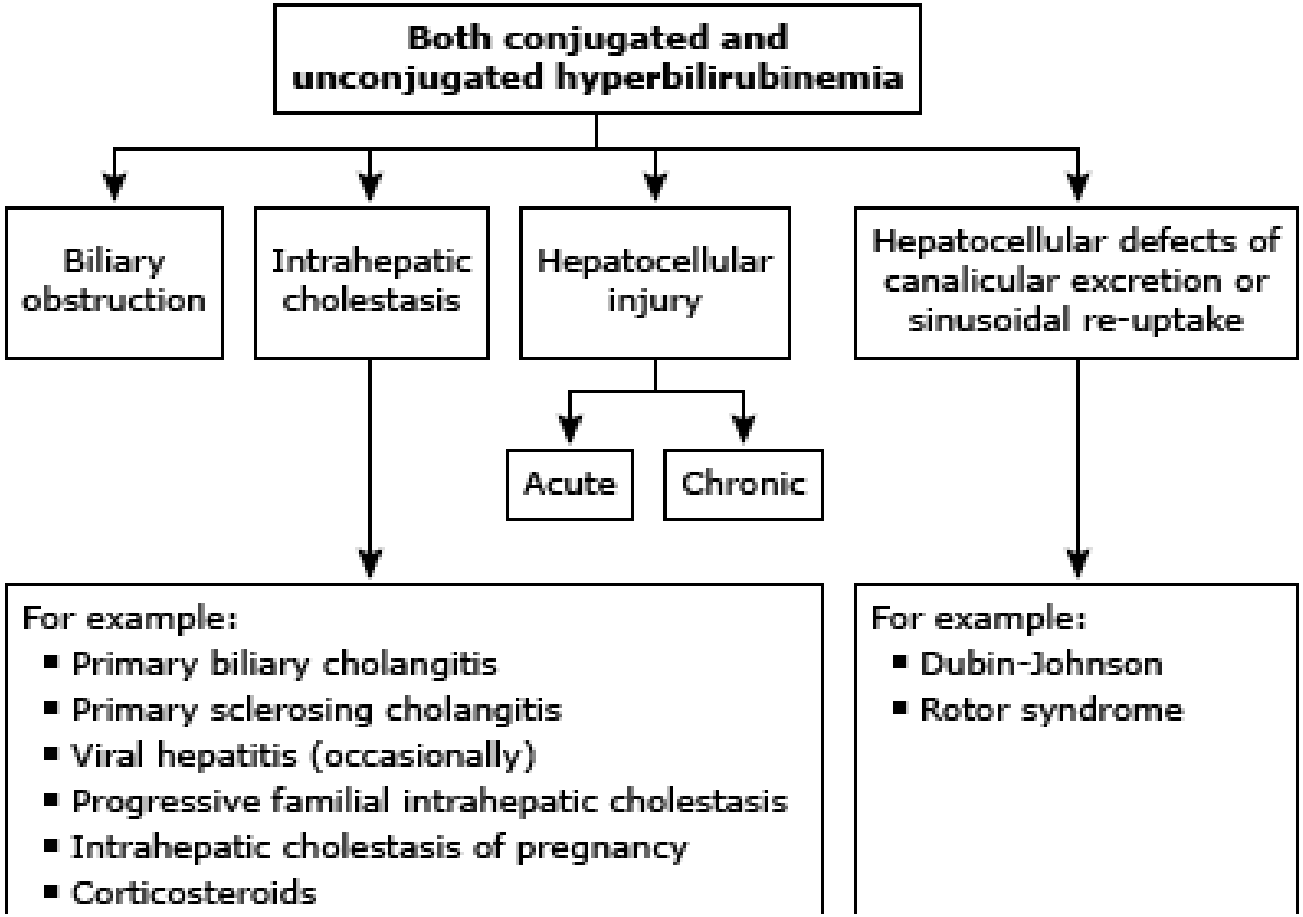
Diseases and their histopathologic sites of interference with hepatobiliary excretion of bilirubin



Classification of jaundice due to mainly unconjugated hyperbilirubinemia



Classification of jaundice due to both conjugated and unconjugated hyperbilirubinemia



Differential diagnosis of cholestatic jaundice: Extrahepatic

Cholangiopathies and other disorders involving bile ducts
Cholelithiasis
Biliary strictures after invasive procedure
Cholangiocellular carcinoma
Primary sclerosing cholangitis
AIDS cholangiopathy
CMV
Cryptosporidium sp
HIV
Choledochal cyst
Sphincter of Oddi dysfunction
Parasitic infections
Ascaris lumricoides
Histiocytosis X

Extrinsic causes
Pancreatitis (acute and chronic)
Pancreatic carcinoma
Portal adenopathy
Metastases
Tuberculosis
Periampullary carcinoma
Periampullary diverticulum
Mirizzi's syndrome

Differential diagnosis of cholestatic jaundice: Intrahepatic

Acute hepatocellular
Viral hepatitis
Alcoholic fatty liver and/or hepatitis
Non-alcoholic steatohepatitis
Drugs
Chronic hepatocellular
Primary sclerosing cholangitis
Primary biliary cholangitis
Drugs
Hepatitis (viral, alcohol, autoimmune)
Cirrhosis of any cause
Multifactorial
Total parental nutrition
Systemic infection
Postoperative
Sickle cell disease/crisis
Organ transplantation (rejection; graft-versus-host disease; venoocclusive disease)

Miscellaneous
Hypotension/hypoxemia/HF
Budd-Chiari syndrome
Parasitic infection (*Clonorchis sinensis*; *Fasciola hepatica*)
Inherited/endocrine
Benign recurrent intrahepatic cholestasis (BRIC)
Progressive familial intrahepatic cholestasis (PFIC)
Low phospholipid-associated cholestasis (LPAC)
Thyrotoxicosis
Alagille syndrome
Disorders of carbohydrate, lipid, or bile acid metabolism
Caroli's disease
Pregnancy
Protoporphyria
Infiltrative/granulomatous
Amyloidosis
Lymphoma*
Sarcoidosis
Tuberculosis

History and physical examination — Multiple clues to the etiology of a patients' hyperbilirubinemia can be obtained from the history, which should seek the following information

- Use of medications, herbal medications, dietary supplements, and recreational drugs
- Use of alcohol
- Hepatitis risk factors (eg, travel, possible parenteral exposures)
- History of abdominal operations, including gallbladder surgery
- History of inherited disorders, including liver diseases and hemolytic disorders
- HIV status
- Exposure to toxic substances
- Associated symptoms

Labor;
Ultraschall, CT; ERCP

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Schmerzloser Ikterus