

Anaesthesia for Obstructive Jaundice





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- Obstructive Jaundice in Major surgery!
- What is Major Surgery?



Medical definition - Major surgery

- Surgery involving a risk to the life of the patient; specifically: an operation upon an organ within a cavity - the cranium, chest, abdomen or pelvic cavity

Implications:

- Almost always require GA
- Involves major fluid shifts
- Can have significant blood loss
- Involves multiple drugs administration

In this presentation

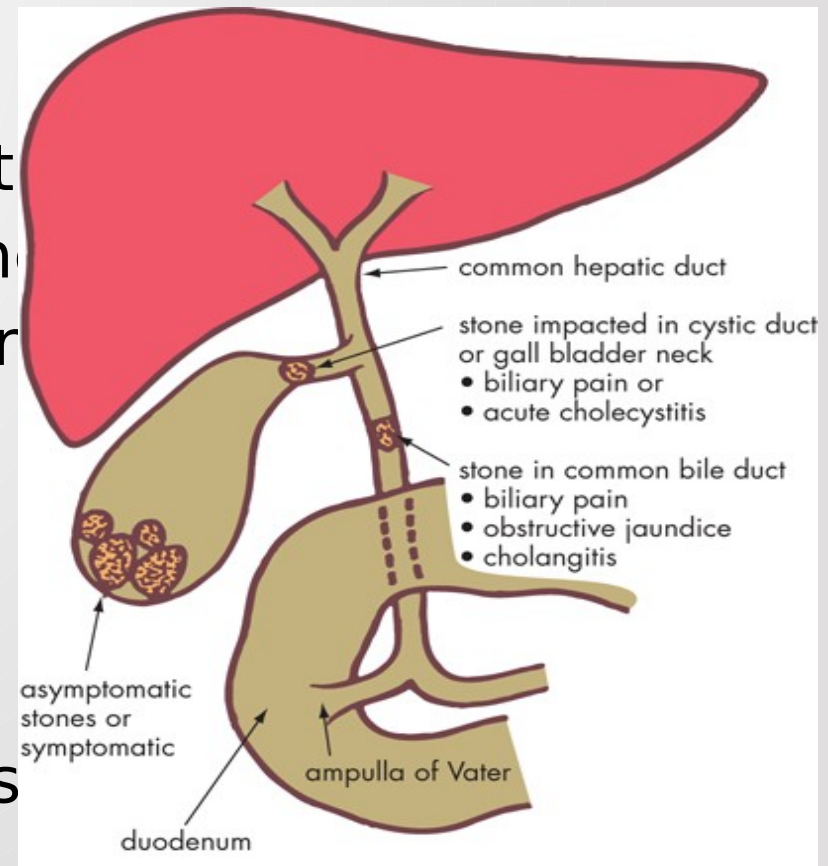
“Perioperative Anaesthetic concerns in a patient with Obstructive Jaundice scheduled for major abdominal surgery”

Perioperative concerns:

- Obstructive Jaundice per se
- Associated hepatic dysfunction

Obstructive Jaundice : Causes

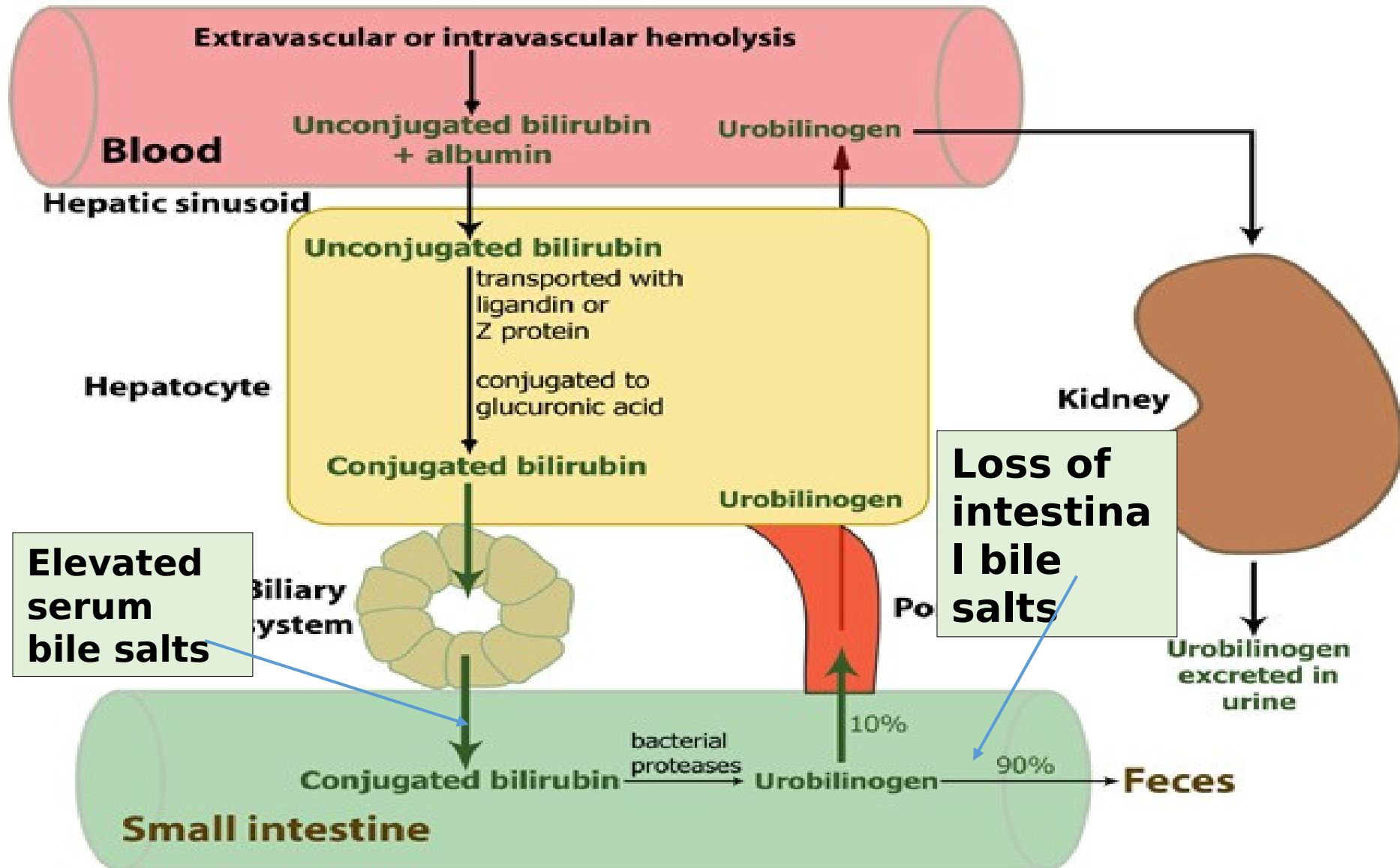
- Choledocholithiasis
- Benign strictures of biliary tract
- Pancreaticobiliary malignancy
- Iatrogenic injury of biliary tract
 - cholangitis
- Parasites
- Metastatic disease
 - PBS/PSC associated autoimmune pathologies



Perioperative Implications

- Higher incidence of complications, mortality
- Postoperative morbidity 20- 30%

Bilirubin formation & excretion



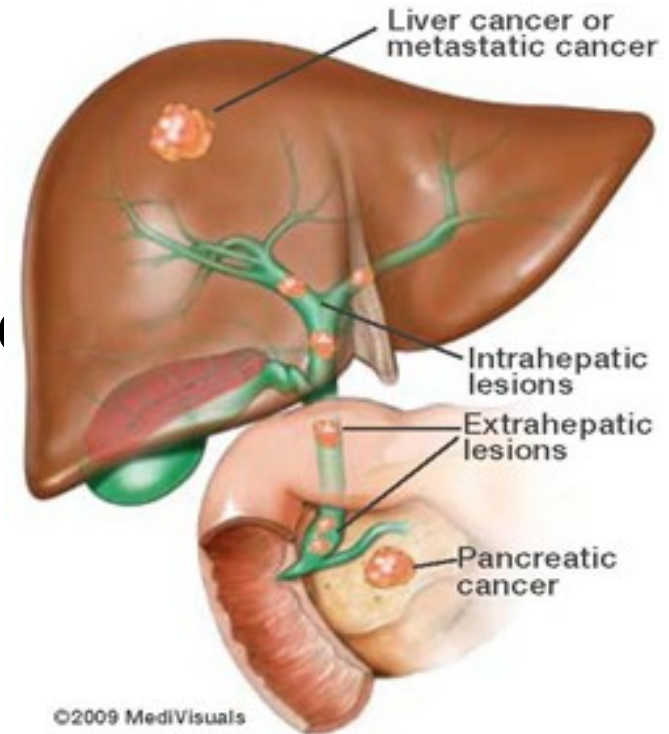
Biliary Obstruction

- **Increase in Bile duct pressure**

- **Normal - 10-15 cm H₂O**

- **> 15 cmH₂O - bile flow decreases**

- **> 30 cm H₂O - bile flow stops**



Pathophysiology

Obstructive
Jaundice

Concerns of
associated hepatic
dysfunction

GI tract

Malnutrition

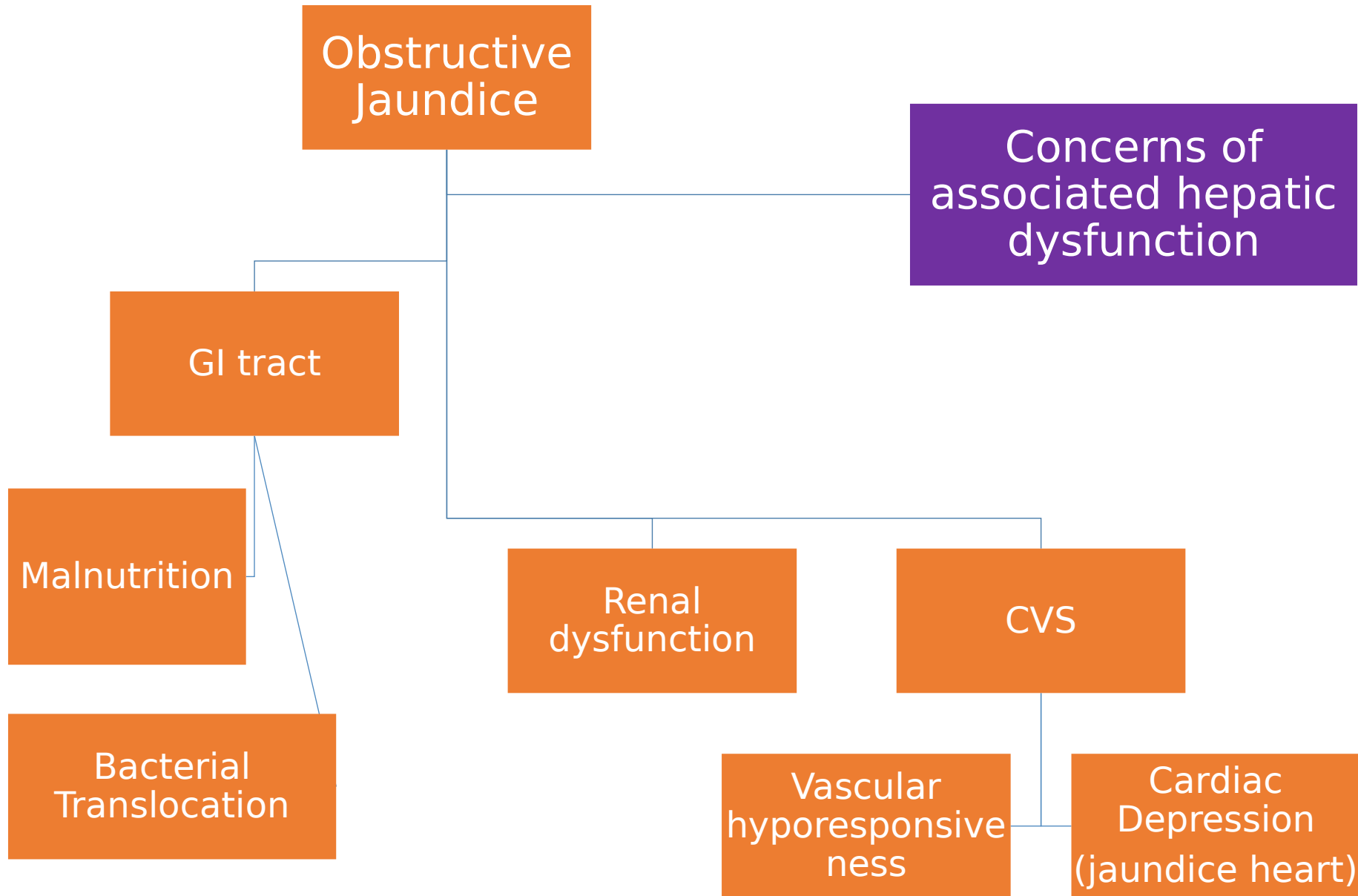
Bacterial
Translocation

Renal
dysfunction

CVS

Vascular
hyporesponse-
ness

Cardiac
Depression
(jaundice heart)



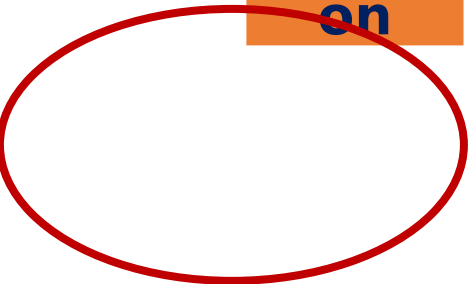
Obstructive Jaundice

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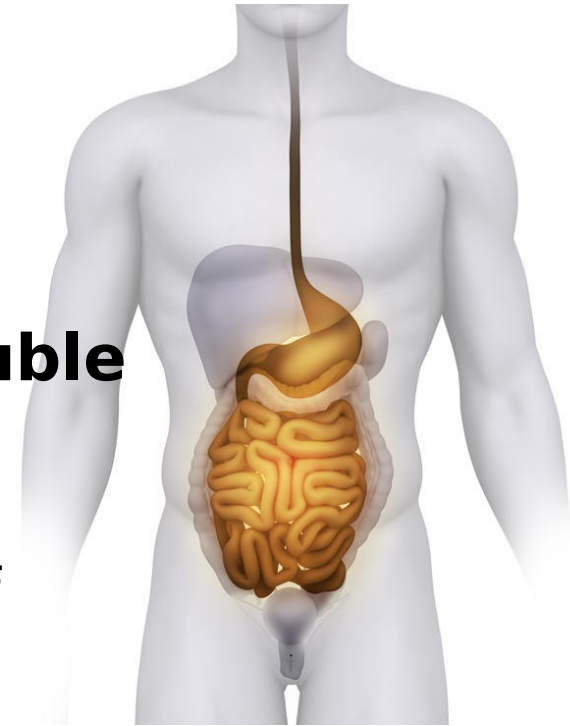
Pathophysiology ...Malabsorption

- **Malnutrition**

- Decreased appetite

- **Malabsorption of fats, fat-soluble vitamins**

- Steatorrhea
- Night blindness - vitamin A def
- Hepatico-steopathy- Vit D def
- Neuromuscular weakness- Vit E def
- Prolong PT- Vit K def



Pathophysiology....

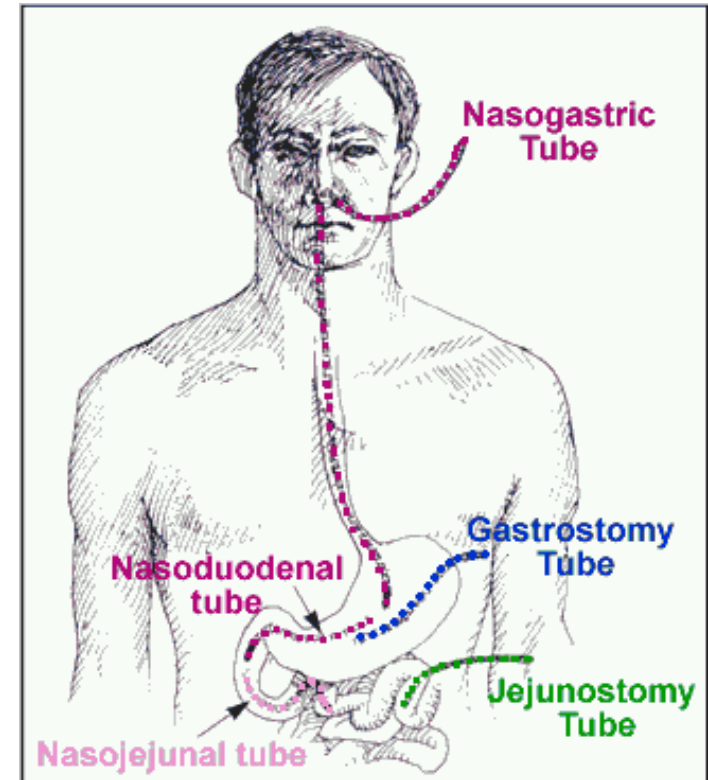
Malabsorption

- **Associated Hepatocellular dysfunction**
 - Insufficient protein synthesis
 - Gluconeogenesis
 - Ketogenesis
- **Malnutrition** - stubborn to correct if obstructive jaundice not relieved promptly
- **Preoperative biliary drainage important**

Pathophysiology ... Malabsorption...Management

Preoperative malnutrition
correction:

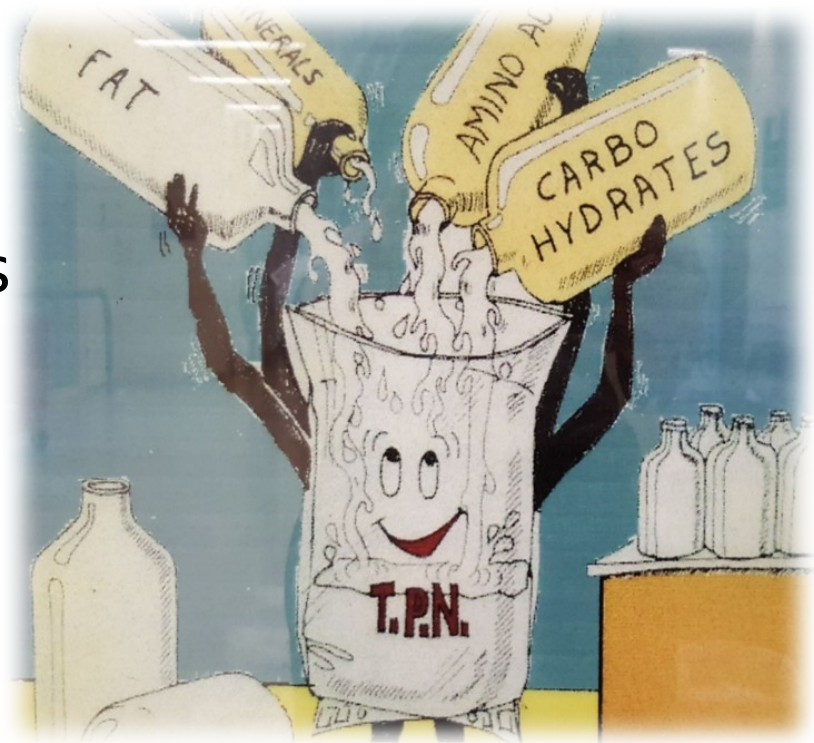
- **Replenish nutrients**
- **Enteral route preferred**
 - In case of gastric dilatation- consider naso-jejunal tube feeding



Pathophysiology ... Malabsorption...Management...

Parenteral nutrition

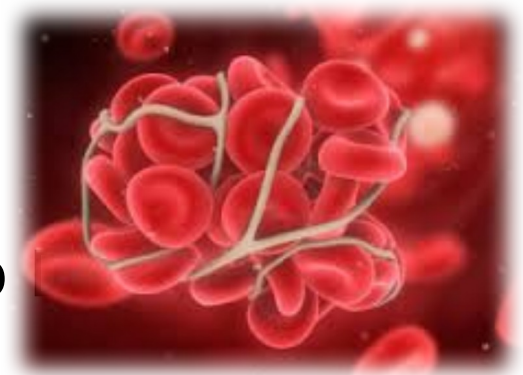
- If enteral nutrition not possible
- Severe malnutrition exists
 - recent weight loss, >10-15%
 - Actual body weight, <90% of ideal body weight
- Start PN - 5 to 7 days preoperative, continue till postop



Pathophysiology ...

Coagulopathy

- Prolonged partial thromboplastin time
 - **Vit K def- fat malabsorption**
 - Lack of Vit K dependent clotting factors
 - prothrombin, factor VII (FVII), FXI, FX
 - Protein C, and protein S
 - **Accompanying liver disease**
 - Natural anticoagulants - AT-III, heparin cofactor-II, TFPI-1, TFPI-2
- **Aggravated** by
 - Periop bleeding
 - Associated sepsis, can lead to
- Serious prognosis



Pathophysiology...

Coagulopathy

- Tm cells □ inc platelet adhesiveness & aggregation in situ
 - Activation of angiogenesis pathway
- Circulating **carcinoma mucins** (e.g. Ca 19-9) induce formation of circulating microthrombi (without the participation of thrombin)
- Tm cells produce **procoagulant factors**
 - TF & prothrombin
- Elevated levels of decarboxylated prothrombin
- Increased activity of **fetal enzyme sialyl-transferase**
 - abnormally polymerized fibrin

Pathophysiology ...Coagulopathy...

Management

- **Reversal of coagulopathy**

- Prevention of intraoperative bleeding
- Epidural catheter insertion preoperatively

- **IM Vit K (10 mg) x 3 days**

- When advanced liver dysfunction with subsequent reduction in the liver synthetic functions, benefit remains questionable.

- In presence of liver failure- **FFP**

- 10-20 ml/kg body wt □ PT inc < 3sec
- Correction lasts 12-24 h (T/2 FVII 4-6 h)
- If not corrected - dysfibrinogenemia or FDPs

- Low platelet count □ low TT/BT

- 0.3 µg/kg of DDVAP

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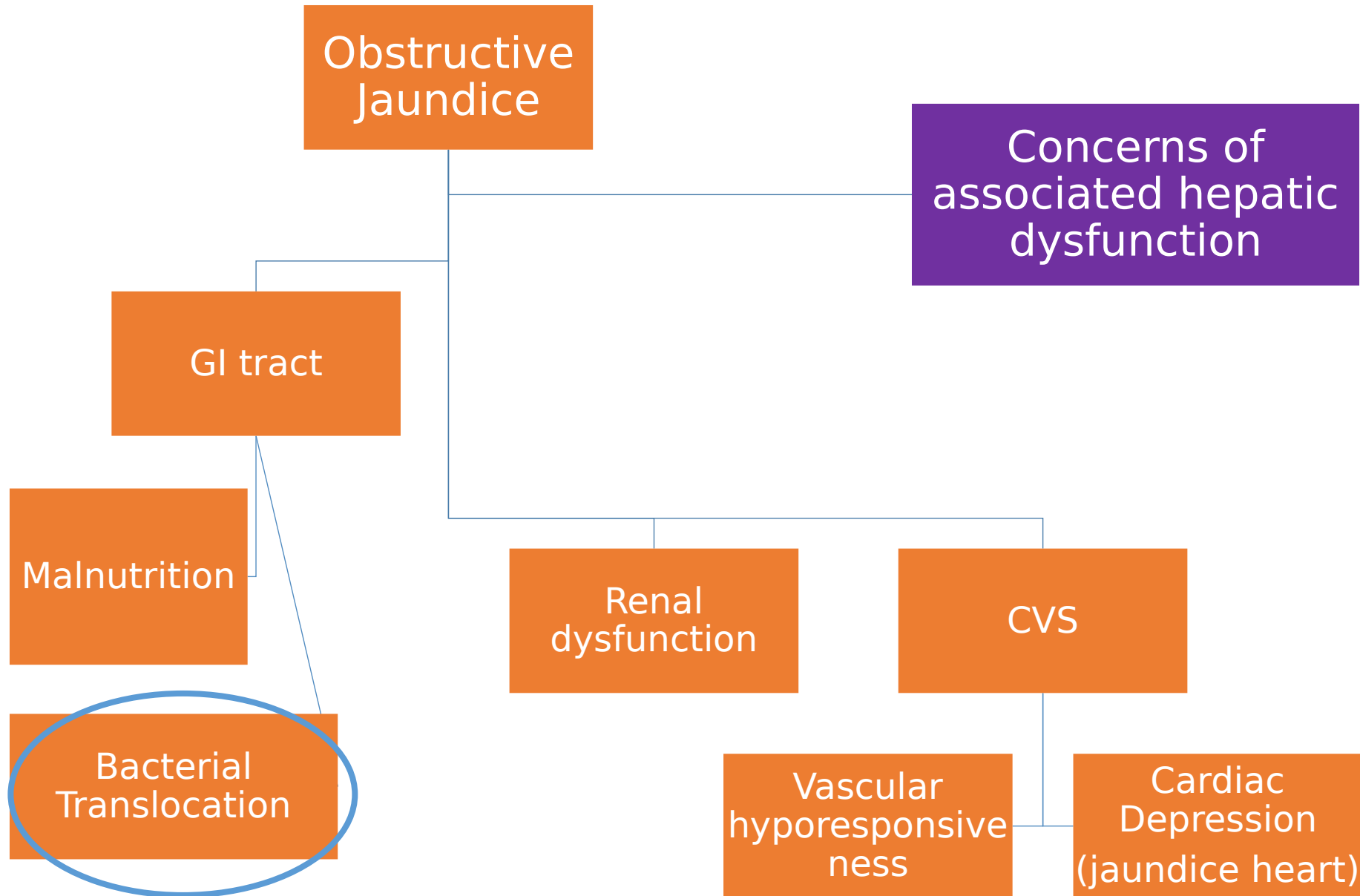
Bacterial
Translocation

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dysfunction

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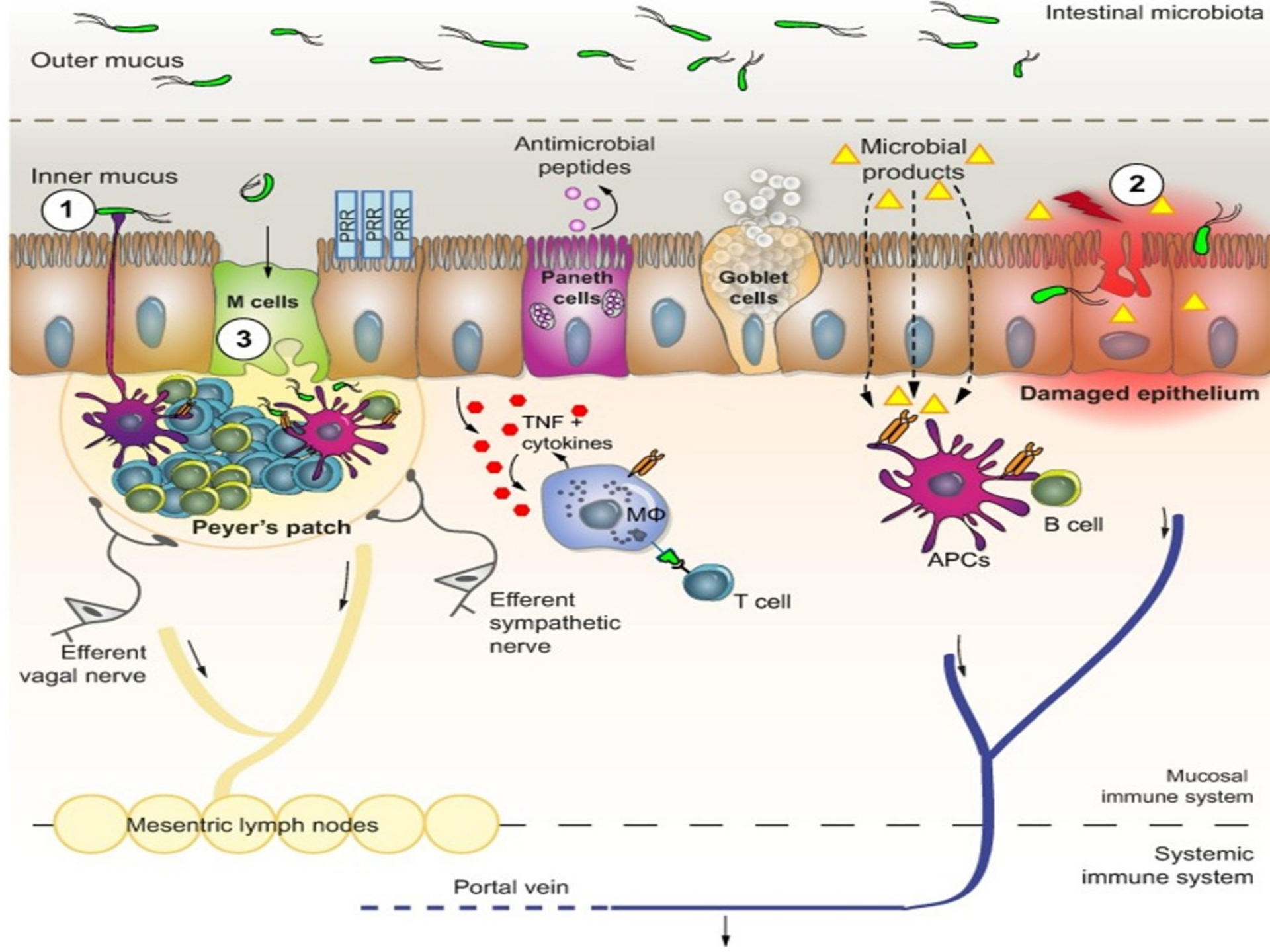
Cardiac
Depression
(jaundice heart)



Pathophysiology ...

Bacterial translocation

- Bacteria routinely regress into the biliary tract from intestines
- Prevented by
 - **Sphincter of Oddi** - prevents retrograde translocation of bacteria
 - **Bile salts** - limits proliferation of bacteria
 - Eliminated from bile by **RE system**
 - Bile excretion from the bile tract into the intestine also clear bacteria



Pathophysiology ...

Bacterial translocation

- Reflux of bile into liver sinusoids
 - It may also communicate with the vascular system
- Rise in serum bilirubin, bile salts, Alk PH3ase
- Repeated reflux of bacteria and endotoxin into the vascular system □ SIRS & sepsis

Pathophysiology ...

Bacterial translocation...

Bacteria isolated from bile of patients with cholangitis

- **Gram negative organisms**
 - Escherichia coli, Klebsiella, Proteus, Pseudomonas
- **Gram positive organisms**
 - Strepto, Enterobacter sps
- **Empiric antibiotic therapy**
 - β -lactamase inhibitors (clavulanate, sulbactam, tazobactam) + β -lactams (amoxicillin, ampicillin, piperacillin, ticarcillin)
 - Aminoglycosides
- Antibiotics **alone not so effective**, until effective biliary drainage done

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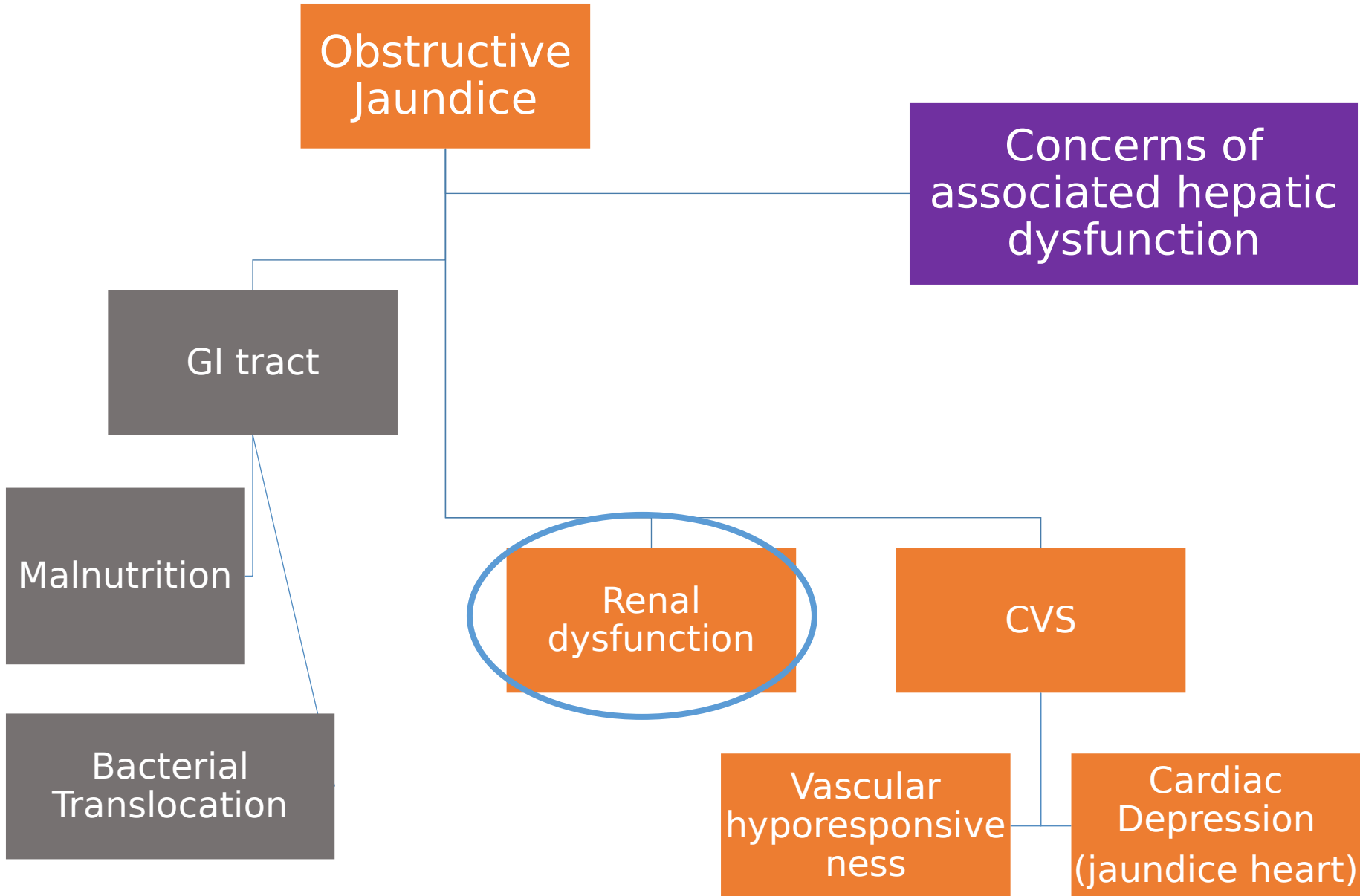
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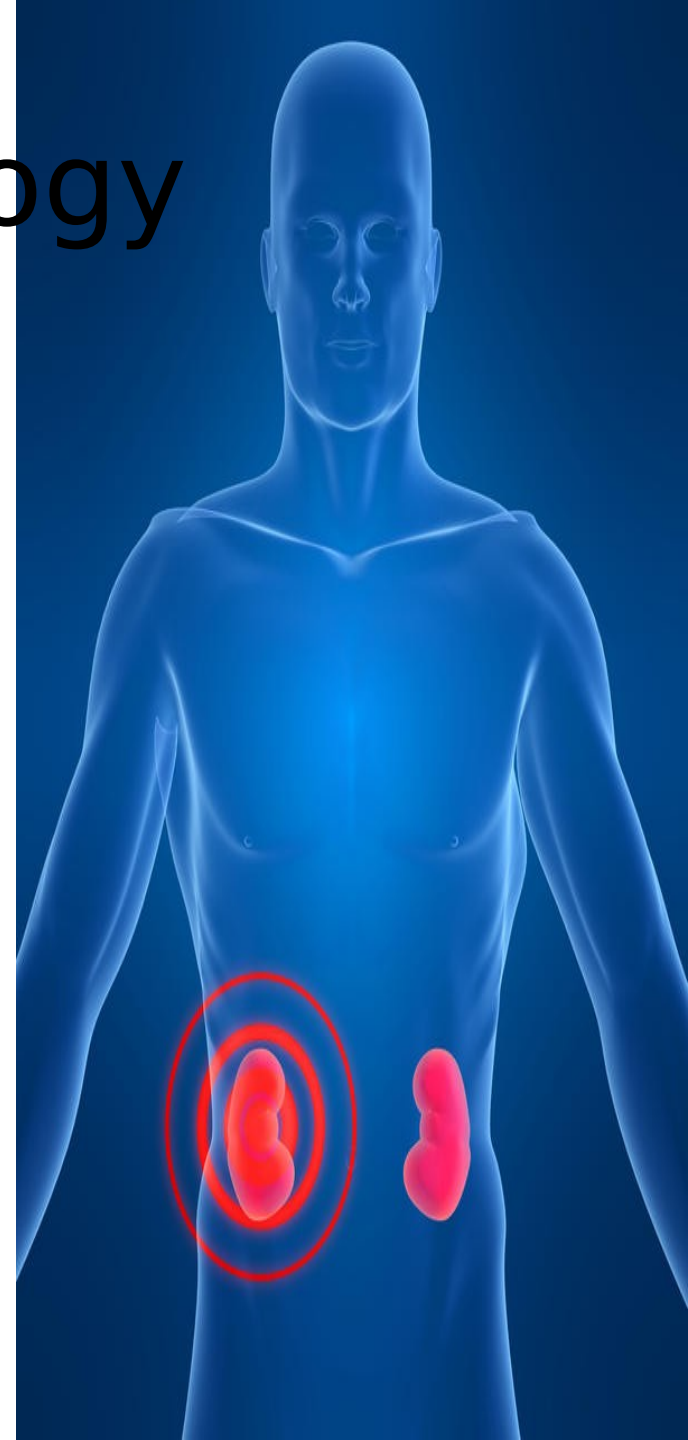
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Renal pathophysiology

- Obstructive jaundice patients are at high risk for ARF
- Occurs in 8-10% of pts requiring surgery for relief of obs jaundice
- Eventual mortality – **70-80%**



Renal Pathophysiology...

Causes

- **Cardiovascular instability** □ reduced RBF
 - **Systemic hypotension**
 - Depressed contractility of heart
 - Presence of large anatomical a-v shunts
 - Bradykinin, sub P, VIP, glucagon, prostacycline & ANF
 - Defective vascular reactivity – **bile acids**
- **Endotoxemia** □ renal vasoconstriction

Renal Pathophysiology...

Causes

- **Hypovolemia / Blood loss**

- Impaired vasoconstrictor response to hypovolemia / haemorrhage
 - Limits normal redistribution of splanchnic blood to the central circulation
 - Even moderate hemorrhage can lead to severe hypotension and ATN

- Direct toxic effects of bile constituents:

- **Do not** exert a direct nephrotoxic effect

Renal Pathophysiology... Management

- Preoperative IV fluid therapy to maintain adequate IV volume
 - Most effective precaution to reduce post-op renal dysfunction
- **Correction of volume deficits**
 - Increase renal blood flow
 - Urinary excretion of hepatic metabolites
 - Decrease circulating conc of toxic substances



Renal Pathophysiology...

Management

- **Urine Output Monitoring**

- Maintain urine output $> 1\text{ml/kg}$

- **Mannitol**

- To flush bilirubin from renal tubules
- S. bil $< 8\text{ mg\%}$ - i.v. fluids + antibiotics
- S. bil $> 8\text{mg\%}$ - i.v. fluids+ antibiotics
+ mannitol($0.25\text{-}1\text{ gm/kg}$)



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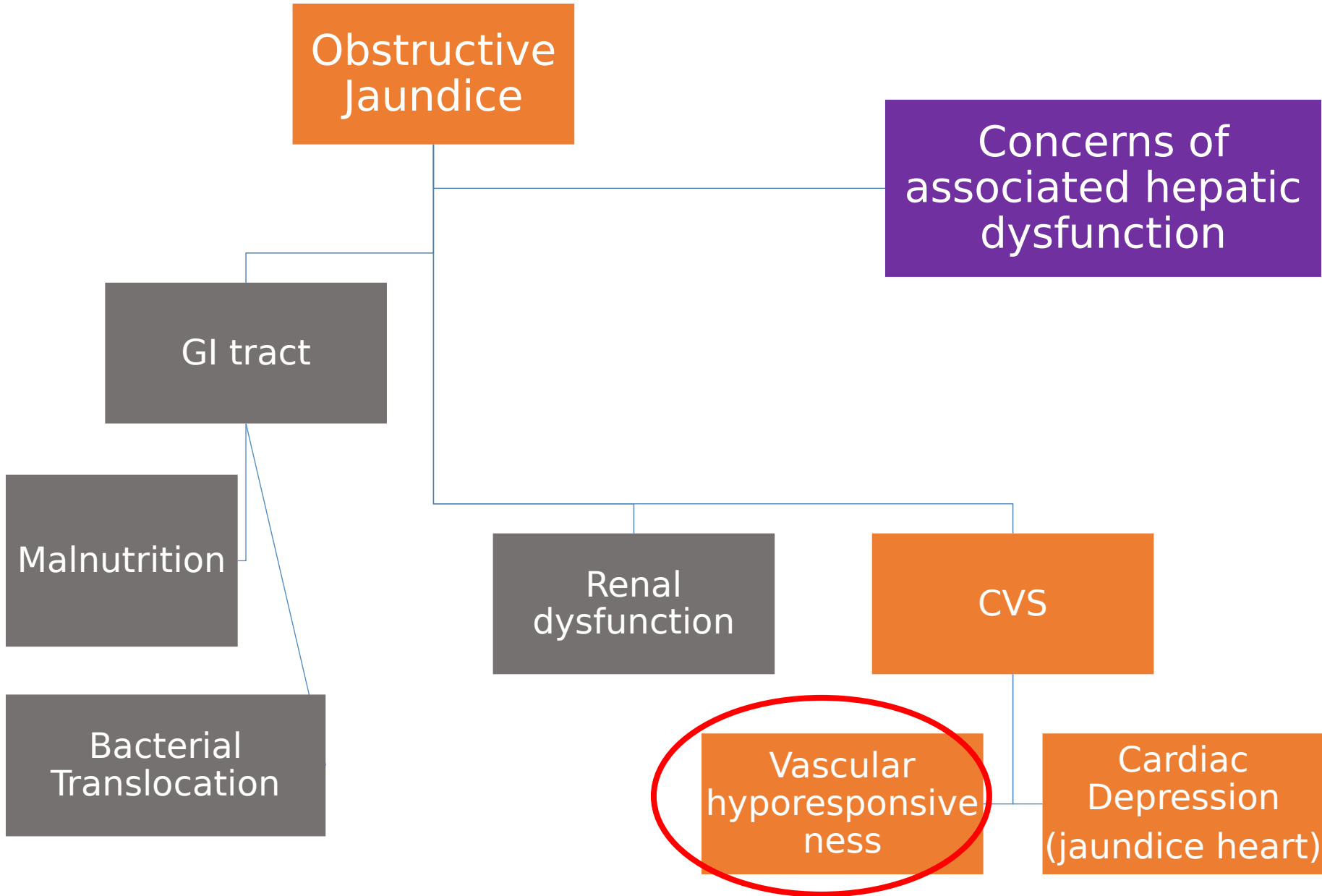
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Pathophysiology ...CVS.. **Vascular hypo-responsiveness**

Vascular hypo-responsiveness causes:

- Decreased vascular resistance
- Exaggerated risk of perioperative hypotension

Pathophysiology ...CVS.. Vascular hypo-responsiveness

Mechanisms

- **Underlying volume depletion**
 - Renal Na/H antiporter involvement
- **Role of NO**
 - Bile salts increase eNOS mRNA expression □ NO production
- **Impaired baroreflex sensitivity**
 - Due to increased level of plasma ANF

Pathophysiology ...

CVS.. Vascular hyporesponsiveness

Mechanisms...

- Involvement of various receptors
 - Activation of BK Ca channels by bile acids
 - Mediation by M3 receptors
 - Defects in vascular alpha 1 receptors
 - Role of Farnesoid X receptor (FXR) in NO dependant vasodilatation

Pathophysiology ...CVS.. Vascular hypo-responsiveness

- Vascular hyporesponsiveness and hypotension- exaggerated by **underlying hypovolemia**
- Diuretic and natriuretic effects of bile salts
 - IV & EC dehydration
 - Impaired tubular reabsorption of Na^+

Obstructive
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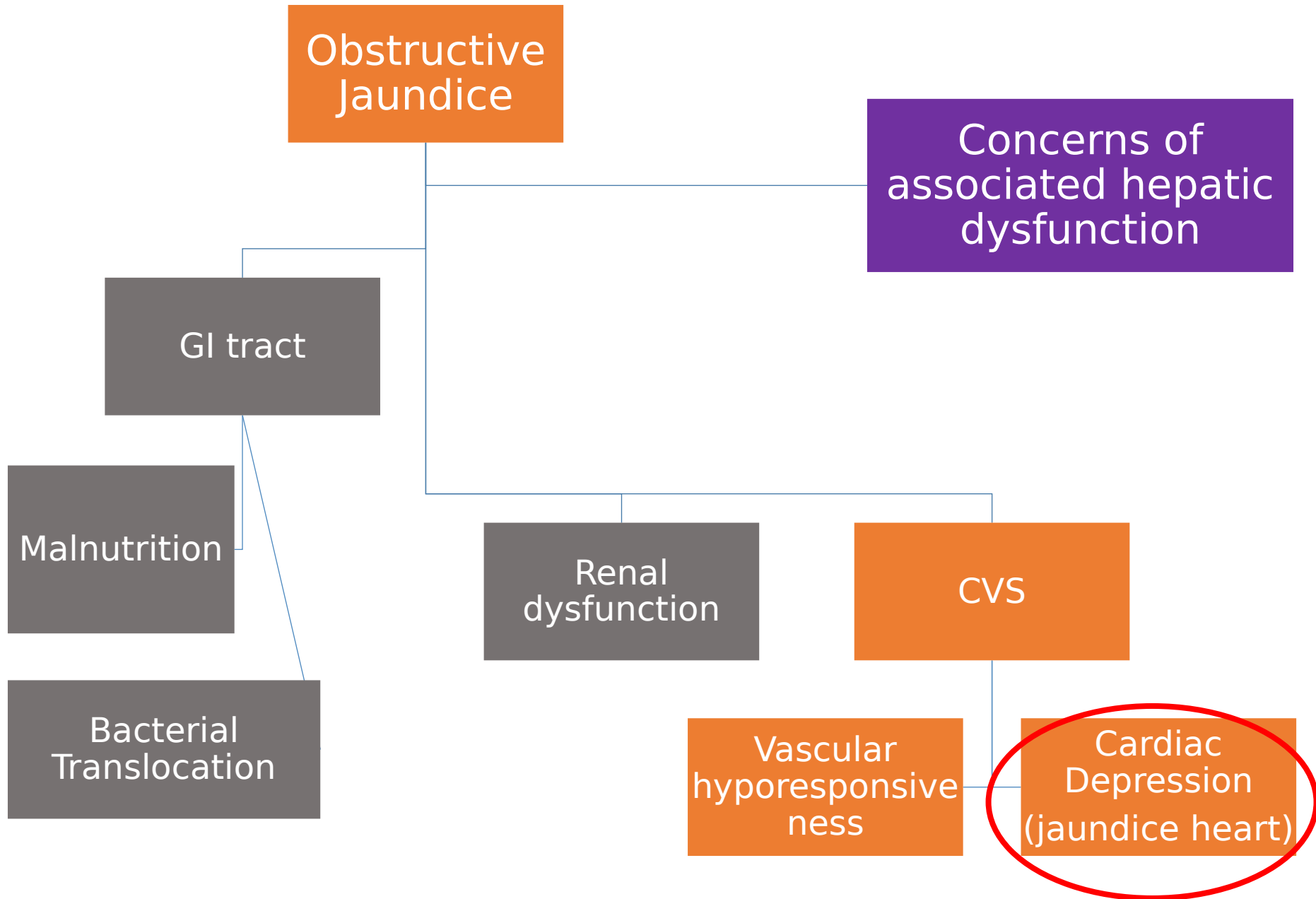
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Pathophysiology ...

CVS.. Jaundice heart... Causes

- **Bile salts**

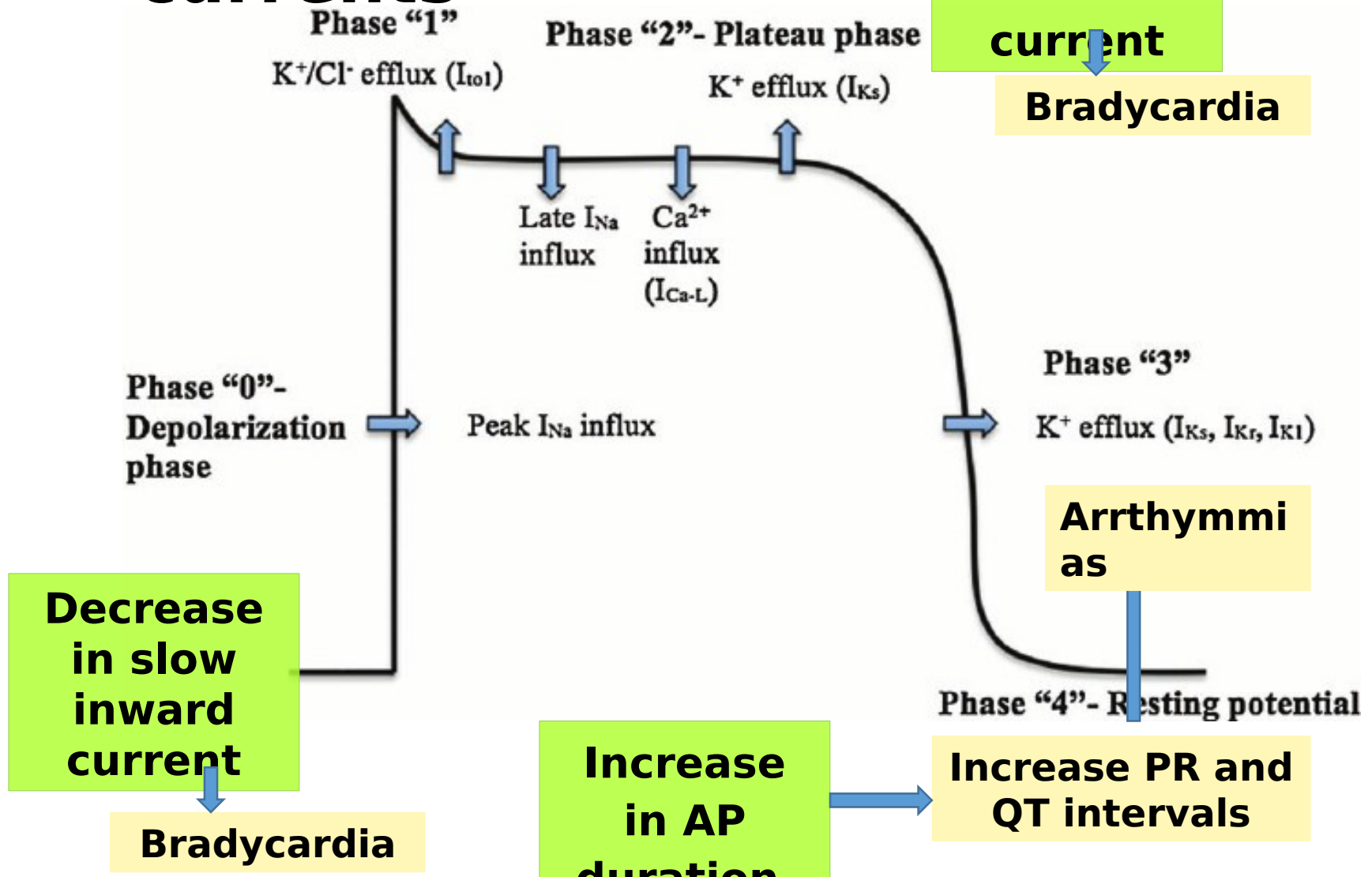
- functional antagonist of Isoprenaline
- Form a monolayer on surface of the cell membrane → mechanical interference with membrane function
- Alteration in “pacemaker” function of cardiac myocytes by bile acids
- -ve inotropic effect

Pathophysiology ...
CVS.. Jaundice heart... Causes...

- **Role of multiple receptors**

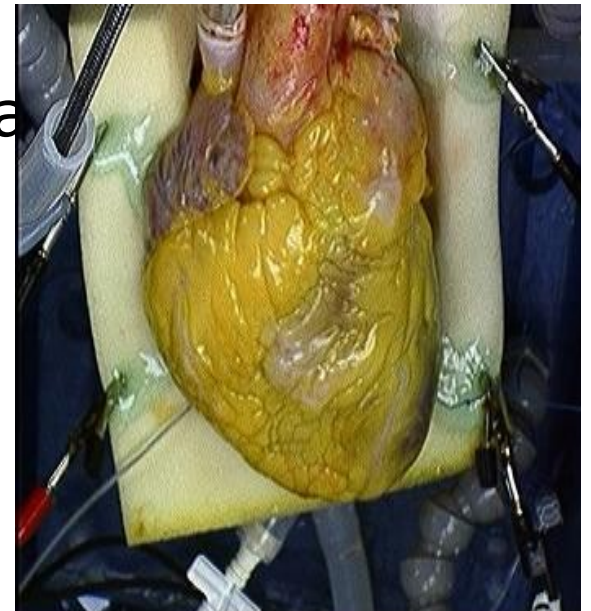
- Guanosine-binding protein couple receptor
- Muscarinic receptor (M2)
- Glycogen synthase kinase-3b
- TGR5 (a novel G-protein-coupled receptor)

Alternations of membrane currents



Pathophysiology ...CVS.. Jaundice heart

- **Bradycardia / hypotension**
 - Mediated by cholinergic mechanism
 - Atropine sensitive
- **Blunted contractile response**
 - Vasoconstrictor drugs
 - β -adrenoreceptor stimulation
 - Angiotensin II stimulation



Pathophysiology ...

CVS.. Jaundice heart...

- Depressed cardiovascular function can give rise to
 - Low systemic pressure/ hypotension
 - Pre renal failure

Pathophysiology ...

Others

- **Serum bile acids**

- Pruritis
- Haemolysis of RBCs



- **Hypercholesterolemia**

- Atheromatosis
- Xanthomas



Obstructive
Jaundice

```
graph TD; A[Obstructive Jaundice] --- B[Concerns of associated hepatic dysfunction]; A --- C[GI tract]; A --- D[Renal dysfunction]; A --- E[CVS]; C --- F[Malnutrition]; C --- G[Bacterial Translocation]; E --- H[Vascular hyporesponsiveness]; E --- I[Cardiac Depression (jaundice heart)];
```

This flowchart illustrates the complications associated with obstructive jaundice. The central node is 'Obstructive Jaundice', which branches into four main categories: 'Concerns of associated hepatic dysfunction', 'GI tract', 'Renal dysfunction', and 'CVS'. The 'GI tract' category further branches into 'Malnutrition' and 'Bacterial Translocation'. The 'CVS' category branches into 'Vascular hyporesponsiveness' and 'Cardiac Depression (jaundice heart)'.

Concerns of
associated hepatic
dysfunction

GI tract

Malnutrition

Bacterial
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Renal
dysfunction

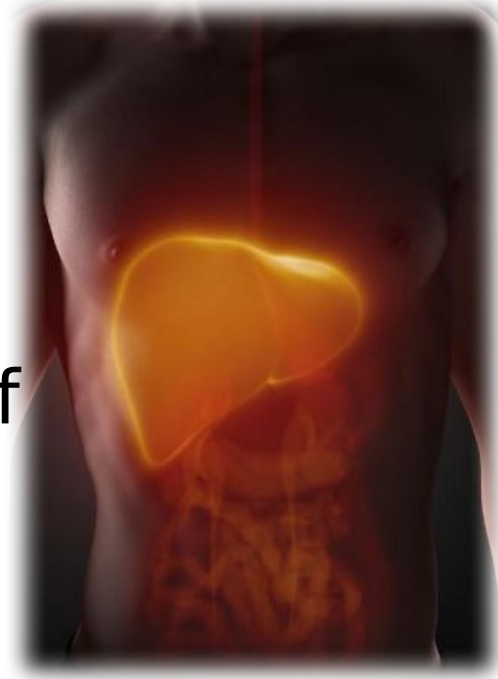
CVS

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Concerns of hepatic dysfunction

- Reduced hepatic blood flow
- Metabolism & biliary excretion of
- Impaired hepatic elimination



Effects on Drugs...**Pre-hepatic effects**

- **Increased Vd**

- Ascites
- Increased total-body water compartments
- Higher loading dose may be required

- **Decreased serum albumin**

- Acidic & neutral drugs primarily bind to **albumin**
- Increased free drug concentration
- Reduced infusion requirements



Effects on Drugs....**Hepatic Drugs effects**

- **Hepatic blood flow**

- ***Large extraction ratios*** (e.g., lidocaine, meperidine): Clearance depends upon:

- Hepatic blood flow
- Portosystemic shunting that exclude certain drugs from elimination

- ***Low-extraction drugs*** (e.g., benzodiazepines)

- Protein binding - unbound drug available for elimination
- Intrinsic hepatic clearance & metabolism as per severity of hepatocellular dysfunction

Effects on Drugs....**Hepatic Drugs effects**

- Cholestasis-induced alterations in the entero-hepatic circulation
- Metabolism of enteral drugs

Obstructive jaundice and Anaesthesia... Drugs...

- **Unconjugated bilirubin**

- Leads to oxidative injury, loss of membrane asymmetry, calcium intrusion
- Contributes to encephalopathy by hyperbilirubinemia
- Excitotoxic damage
- Central **glutamatergic** synapses
 - Induces pre-synaptic neuro-degeneration
 - Disorderly release & uptake of glutamate
- Defective **serotonergic** neuro-transmission

- **Effects of anaesthesia drugs accentuates**

Obstructive jaundice and anesthesia...Drugs...

- **Inhalational agents in presence of low albumin**
 - Attenuation of local side-chain dynamics
 - Stabilization of folded protein conformations
 - May represent fundamental modes of action of volatile agents
 - Distorted IV drug binding

Bound volatile general anesthetics alter both local protein dynamics and global protein stability.
Anesthesiology 1999 Jan;90(1):235-45.

Summary..

Obstructive Jaundice...

Perioperative Concerns

- Coagulopathies
- Infection
- Renal dysfunction
- Cardiovascular depression
- Alterations in drug pharmacodynamics
- Assessed and reversed preoperatively



Patient Evaluation

Preoperative Evaluation ... History

- Risk factors
- CLD symptoms
- Prior episodes of jaundice
- Relation to surgical procedures, anesthesia
- Others
 - Alcohol
 - Drugs, raw seafood
 - Medications
 - Tattoos

Preoperative Evaluation...

Symptoms

- Fatigue, anorexia
- Fever
 - Fever with rigors – Cholangitis
 - low grade fever – Neoplasms
 - Fever with joint pains - PSC
- Weight loss
- Nausea, vomiting
- Easy bruising, GI bleeding
- Pruritus
- Dark-colored urine
- Biliary colic, abdominal distention

Look for symptoms! (Pain upper abdomen)

- **Absence of pain:**

- ***Malignant obstruction of the bile duct:***

- Gradual onset
 - Associated with anorexia, weight loss, & acholic, soft or loose stools

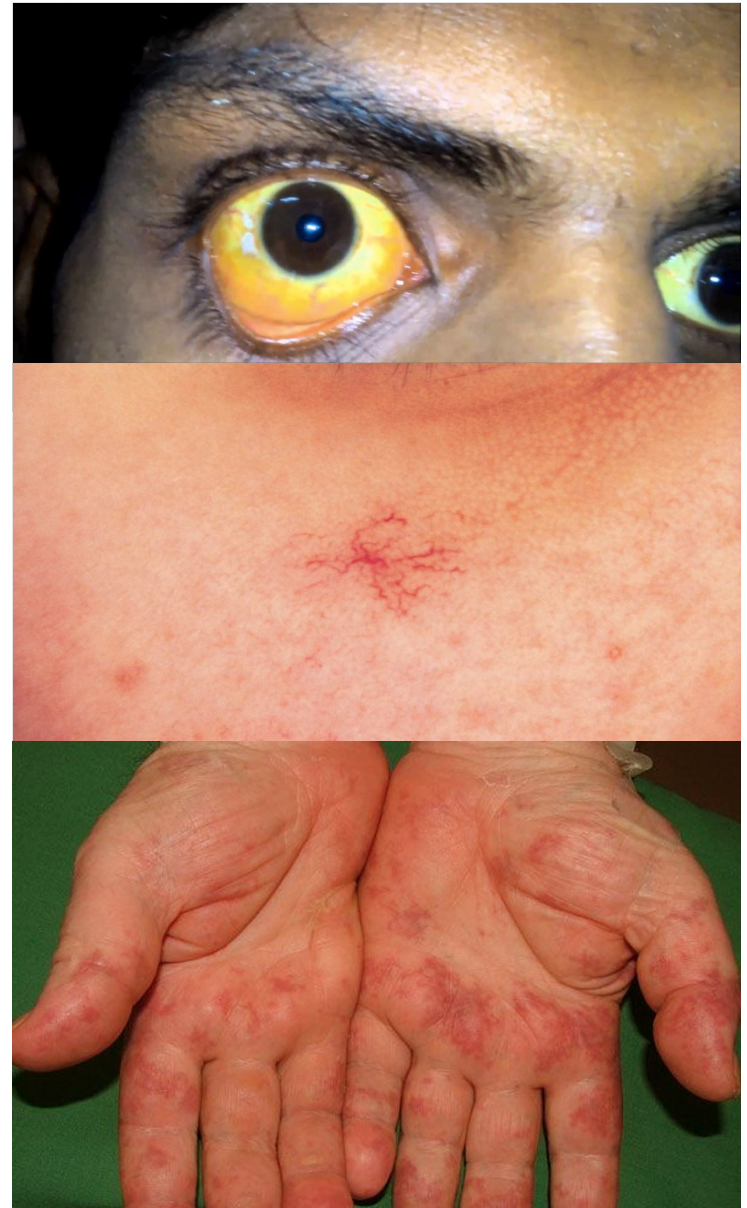
- ***Nonbiliary causes:***

- Increased bilirubin production
 - Hemolysis, blood transfusions, or ineffective erythropoieses
 - Decreased bilirubin clearance due to hereditary defects:
 - Dubin-Johnson syndrome & Rotor syndrome

Preoperative Evaluation... Examination

Active liver disease

- Icterus
- Palmar erythema
- Spider angiomas
- Gynecomastia
- Hepatosplenomegaly
- Ascites
- Testicular atrophy
- Petechiae
- Ecchymoses
- Asterixis





Preoperative Evaluation... Investigations



- Routine lab tests for LFT in the absence of clinical findings
 - **Not warranted**
 - False positive results high
 - True positive results infrequent in asymptomatic patients

Preoperative Evaluation Investigations...

Recommendations

- **Asymptomatic patients**
 - Tests not recommended
 - Abnormal results- repeat tests
- **Minor elevations of liver enzyme**
 - Less than twice the normal value
 - No clinical importance
 - Proceed with surgery



Preoperative Evaluation Investigations...

- **To know the pattern & extend of the disease**
 - Liver Function Tests
- **To assess the synthetic ability of the liver**
 - Albumin- < 2.5 gm% - severe damage
 - Albumin/globulin ratio - reversed.
 - Prothrombin time $\rightarrow 1.5$ sec over control
 - INR - > 1.3
- **To assess the general condition of the patient**
 - Haematological panel, metabolic panel, renal panel

Liver Function Tests

- **S. Bilirubin** : Conjugated/unconjugated
- **Hepatocellular damage**
 - **AST(SGOT)** 0 – 35 IU/L
 - Extrahepatic sources- heart /skeletal muscle/ kidney/ brain, less specific
 - **ALT(SGPT)**
 - Alcoholic hepatitis - SGOT/SGPT > 2 (deficiency of pyridoxine-5-PO₄)
 - In advanced liver cell injury, levels may be normal or low due to massive loss of parenchymal tissue

Liver Function Tests

- **Hepatocellular damage**
 - **Glutathione S transferase**
 - = **Ligandins**
 - Phase II metabolic isoenzymes
 - Acidic, basic, neutral & microsomal GST
 - Acidic: **almost exclusively within the biliary epithelium**
 - Colonic mucosa
 - Villi and crypts: acidic and neutral
 - GB epithelium: acidic and basic GST
 - Villi & microsomal only in the crypts: basic

Liver Function Tests...

- **Hepatobiliary obstruction**

- **ALP**(35-100 IU/L)

- Derived from plasma membrane of bile duct cells
 - Extrahepatic sources- bone, intestine, liver, placenta

- **5-Nucleotidase**

- Specific

- **Gamma Glutamyl Transferase**

- Alcohol / drug induced
 - Most sensitive indicator of biliary tract disease
 - Limited usefulness due to poor specificity

Assess general condition of patient

(i) **Haematological**
Hb, TLC, DLC,
Platelet Count
Clotting factors
(**PT**, PTTK)

(ii) **Cardiorespiratory**
Chest X-ray
ECG
Blood gases

(iii) **Metabolic panel-**

- Serum proteins
- Serum glucose
- Electrolytes

(iv) **Renal panel**

- Urea / Creatinine

Urinary-Urea/ Creatinine
Electrolyte

(iv) **Hepatic imaging**

(v) Microbiological –

- Culture
- **Hep. B marker**
- **Viral antibodies**

Surgical risk in liver disease

- **Surgery contraindicated**

- Acute/ fulminant hepatitis, Alcoholic hepatitis, Severe chronic hepatitis

- **Variable risk**

- Child Pugh classification, MELD score

- **Obstructive jaundice**

- Cardiac surgery, Hepatic resection
- Trauma, Abdominal surgery

- **Minimal increased risk**

- Mild chronic hepatitis
- Non Alcoholic Steato Hepatitis
- Autoimmune hepatitis
- Hemochromatosis, Wilsons disease

Risk factors for Operative mortality in Obstructive Jaundice

1. Hematocrit <30%
2. Serum bilirubin >11mg%
3. Malignant biliary obstruction

Factors 1, 2,3-
All 3 factors-
mortality 60%
No factor-
mortality 5%

4. Azotemia
5. Hypoalbuminemia
6. Cholangitis

Factors 4,5,6-
Predictors of
poor outcome

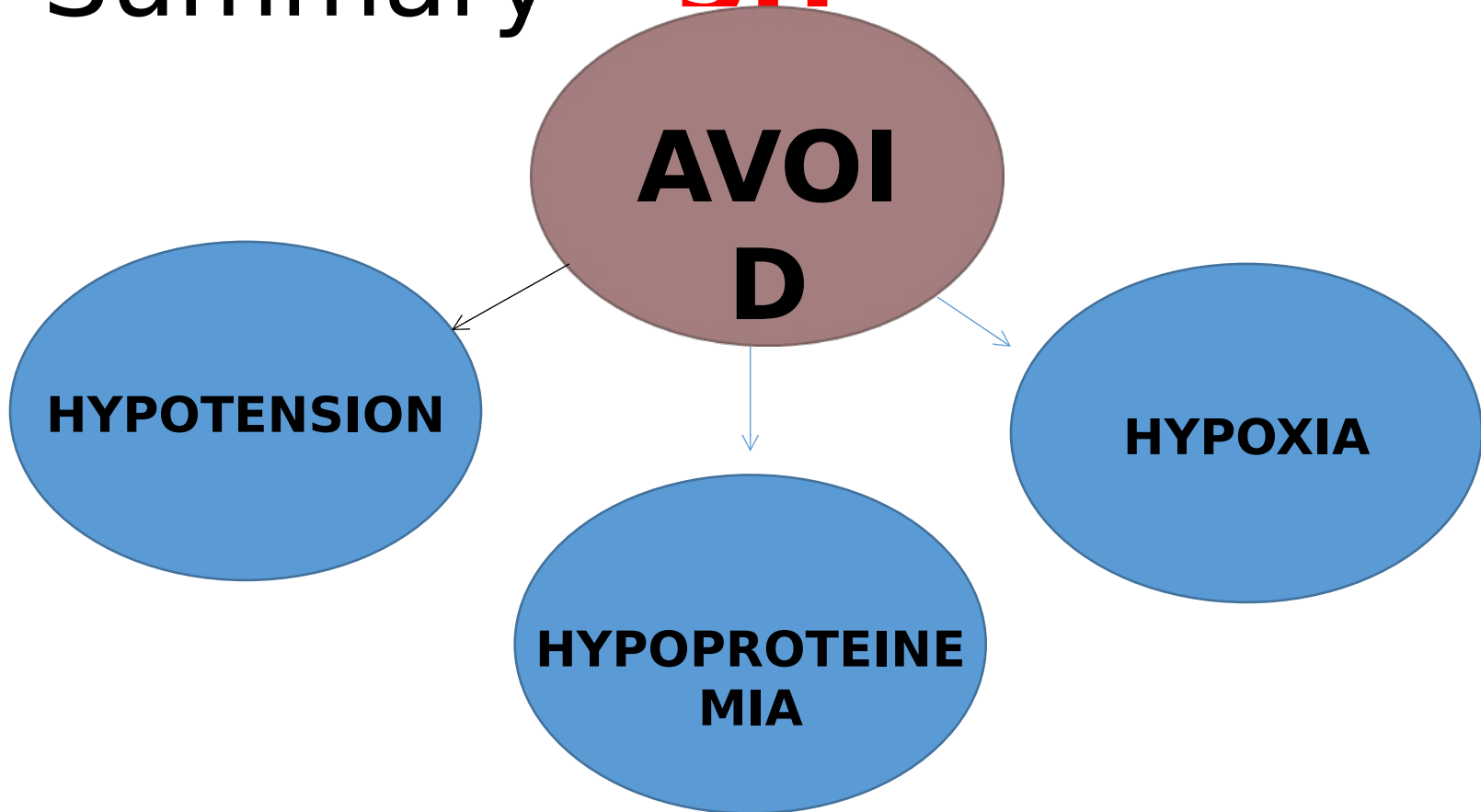
Perioperative management- Recommendations

- Coagulation reversal
- Anti infection
- Nutrition support
- Cardiovascular evaluation
- Perioperative fluid therapy
- Hemodynamic optimization.
- Preoperative biliary drainage



Goals of Anaesthesia...

Summary - **3H**



- Maintain O₂ supply – demand relationship in liver

AVOID

- Sympathetic stimulation
- Hypotension
 - Blood loss
 - Regional Anaesthesia
- Hypoxia
- Hepatic venous congestion
 - Extreme head down
 - Positive pressure ventilation

Goals of Anaesthesia...

Summary

- ▢ **Minimize physiological insult to kidney**

- ▢ Avoid / correct pre renal failure
- ▢ I/V saline & mannitol pre & postop
- ▢ Meticulous fluid balance
- ▢ Use Aminoglycosides carefully
- ▢ Avoid all NSAIDS

- ▢ **Treat infection** –cholangitis

- ▢ **Choose appropriate anaesthetic agent**

- ▢ Metabolism of drugs + Effect on HBF
- ▢ Adequate depth
 - ▢ Avoid sympathetic stimulation

No conclusive evidence for

- ? Preop percutaneous biliary drainage
- Gut sterilization
- Polymyxin B
- Oral bile salts

Pre-operative instructions

- **Avoid pre-medication** as increased responsiveness to sedative action
- **Anxiolytic** – oral short acting benzodiazines
- Oral H2 antagonist
- Vit. K– 10 mg X 3 day
- If Bilirubin > 8 mg% –
 - I/V fluid – 1-2 ml/kg/hr.
 - Mannitol – 100 ml of 20% 2 hrs preop.
- Order morning PT / S. Electrolyte
- Preop urinary catheter & CVP

Monitoring

- ECG
- Non invasive Blood Pressure monitoring
- Capnography
- Pulse oximetry
- Urine output
- Neuromuscular monitoring
- Temperature

Biochemical

B.Sugar,ABG

S.Electrolytes

- CVP
- Invasive BP

Hematological

Hb,PT,PTTK,TEG

Obstructive jaundice and anesthesia...Anaesthetic Technique

- **General Anaesthesia**

- Regional anaesthesia (Epidural anaesthesia) as supplement to G.A.
- Supplemental for intraoperative analgesia and for postoperative analgesia
- Concerns – coagulopathy & hypotension

- **Pre-oxygenation**

Obstructive jaundice and anesthesia....Anaesthetic Technique

- **Induction**

- **Thiopentone**

- slow titrated dose → avoid hypotension

- **Propofol**

- No effect on single intravenous bolus
 - No effect on propofol infusions*
 - safe in obstructive jaundice with normal cardiac function at low and intermediate doses

- **Etomidate**

- Reduced requirement

* Song JC et al. *Acta Anaesthesiol Scand.* 2009; 53(10):1329-35.

Obstructive jaundice and anesthesia... Drugs...

- Difference in effect on Propofol and Etomidate
- Attributed to different targets of the two drugs
 - Etomidate – acts only on GABA receptors
 - Propofol – acts on GABA receptors + glycine, M1 muscarinic, nicotinic receptors

Obstructive jaundice and anesthesia...

Drugs...

Muscle relaxant

- Suxamethonium – Rapid sequence Induction
- Non-depolarizers
 - Titrated doses
- **Atracurium** (drug of choice) - Hoffman's elimination
- Vecuronium 0.15mg/ kg body wt
- Rocuronium 0.6mg/kg body wt
 - Impaired biliary elimination
 - Prolonged neuromuscular effect

Obstructive jaundice and anesthesia...Drugs...

drug	Hepatic degradation %	Biliary excretion (unchanged)%	Renal Excretion (unchanged)%	Plasma hydrolysis	Elimination half life(min) - N	Elimination half life(min) - hepatic failure
Rocuronium	10 - 20	50 - 70	10 - 25	no	87	97
Vecuronium	20-30	40-75	15-25	no	50-110	49-198
Atracurium	-	NS	10	YES	21	20-25
Cis atracurium	-	NS	NS	NO	22-30	21
Sch	-	-	-	YES	16.6 secs	same

Ensure neuromuscular monitoring

Obstructive jaundice and anesthesia...Drugs...

Volatile Anesthetics

- Useful & well tolerated
- Can be entirely eliminated
- Increased sensitivity
- Disadv-
 - CVS instability → vasodilation → ↓ perfusion pressure → ↓ blood velocity → ↑ oxygen extraction → ↓ HBF & oxygen supply

Obstructive jaundice and anesthesia... Drugs...

- **Isoflurane**—best maint. of HBF & oxygen
- **Desflurane**
 - Serum total bilirubin inversely related to MAC_{awake} of desflurane
 - Low blood solubility, undergo minimal metabolism in vivo
 - Minimal alteration in pharmacokinetic characteristics

Obstructive jaundice and anesthesia...Drugs...

Opioids

- Well tolerated in smaller doses
- **Fentanyl**- Preferred
 - Maintain hepatic oxygen demand supply
- **Morphine** – Phase II metabolism
- **Spasm of Sphincter Of Oddi** – uncommon
 - Interpretation of operative cholangiography & biliary pressures
 - Low incidence - All patients do not show this response
 - Intraop manipulation of BD system → spasm
 - **Fentanyl > Morphine > Pethidine > Butorphenol**
- **Treatment**
 - nalaxone, glucagon, atropine, NTG

Obstructive jaundice and anesthesia...

Drugs...

In associated hepatic dysfunction:

- Avoid / reduce dose
- Benzodiazepines
 - $t_{1/2}$ ↑ by 100%
- Lidocaine
 - $t_{1/2}$ ↑ by 300%

Obstructive jaundice and anesthesia...

Anaesthetic Techniques

IPPV -

- Maintain eucapnia
- Liver low pressure tissue bed
- Avoid large V_T & high airway pressures

Postoperative Period

- All well □ Extubate
- Unstable
 - Continue IPPV in Post op. period
 - Fluid & Electrolyte imbalance corrected
 - CVS stability achieved.
 - Hypothermia corrected.
 - Urine Output 1 ml/kg/hr.

Adequate analgesia (Small doses)

Postoperative Monitoring

- Look for signs of hepatic decompensation
 - Sr Bilirubin and Prothrombin time- best indicators
- Transient rise in serum bilirubin
 - Multiple blood transfusion
 - Excess bleeding
 - Infection
- Renal function
- Serum Glucose
 - Hypoglycemia



THANK YOU