The North West London Hospitals NHS
NHS Trust

Metabolic complications

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Overview

- Gallstones
- Renal stones
- PN associated metabolic bone disease
- D-lactic acidosis
- Diabetes

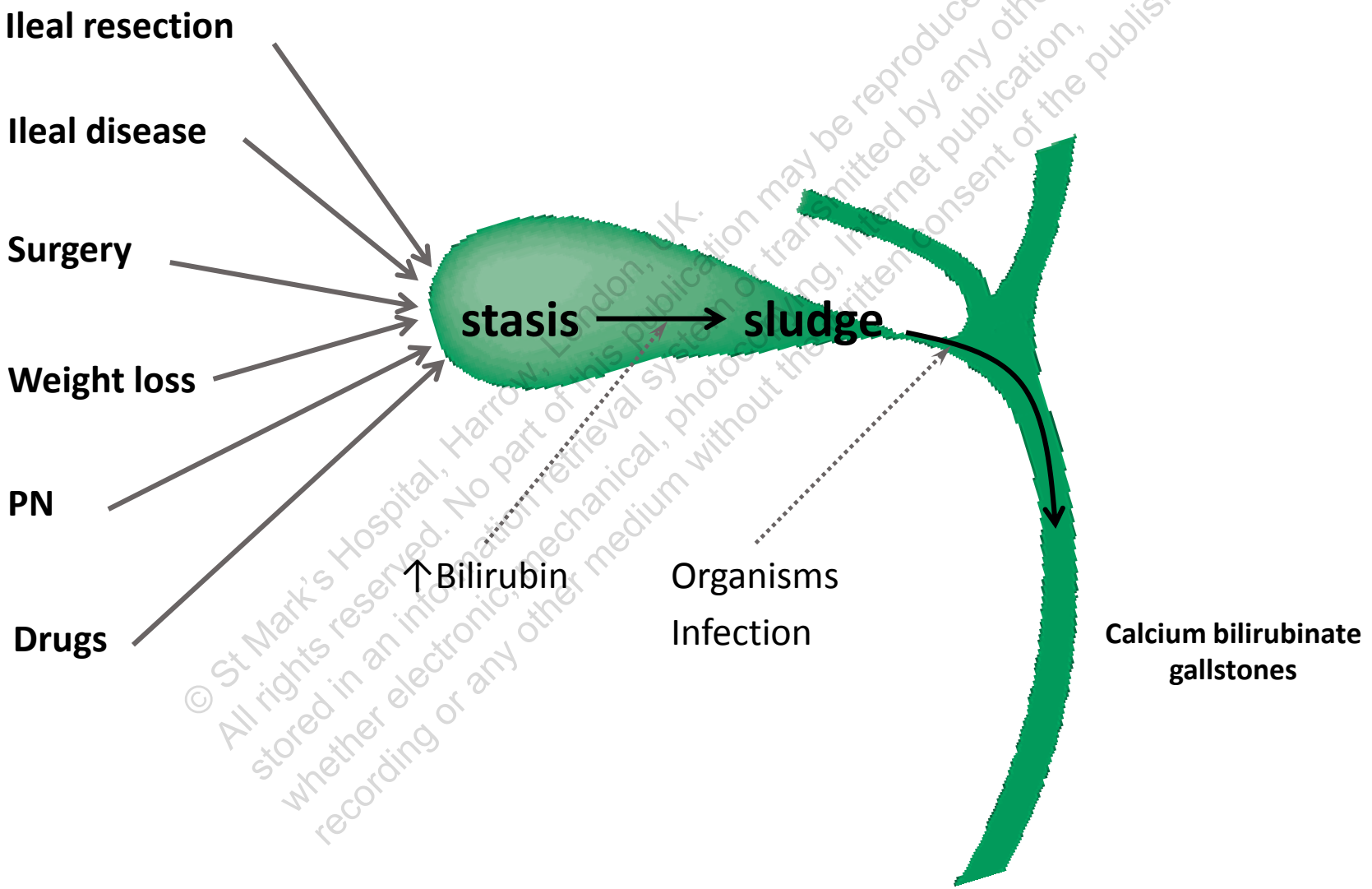
Gallstones - prevalence

Cholesterol **Intermediate** **Pigment**

- 44% patients with jejunocolonic anastomosis
- 43% patients with jejunostomy
- 63% men vs 32% women (p<0.05)
- Presence of the colon is not protective

Nightingale *et al* Gut 1992;33:1493-97

Gallstones - causes



Prevention & management

Prevention

Remove gallbladder

- Prophylactic cholecystectomy

Promote gallbladder emptying

- Oral/enteral nutrition
- Cholecystokinin (stimulates emptying)
- Avoid octreotide

Change bile composition

- Ursodeoxycholic acid
- Antibiotics (bacteria required for pigment stones)

Management

Cholecystectomy

- Symptomatic gallstones
- Stones in the CBD
- Cholecystitis

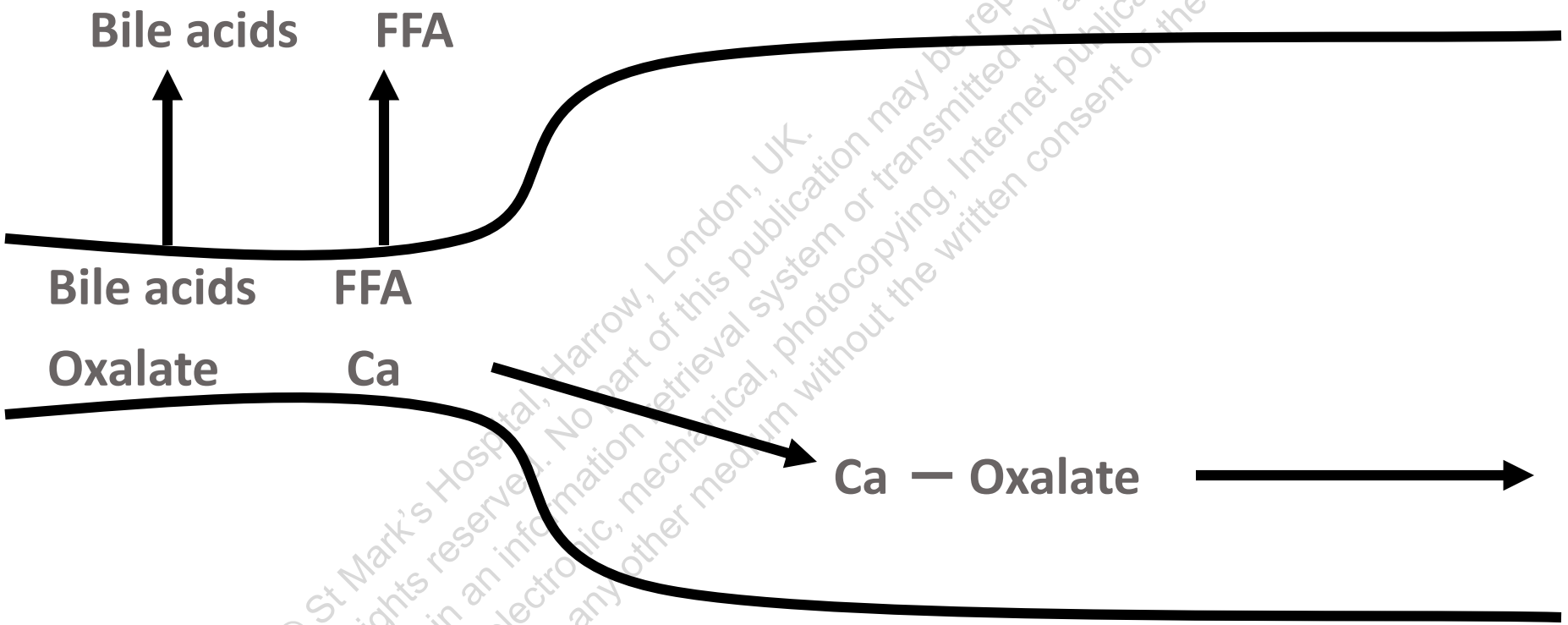
Buchman (2001) *Dig Dis Sci*,46:1

Renal stones

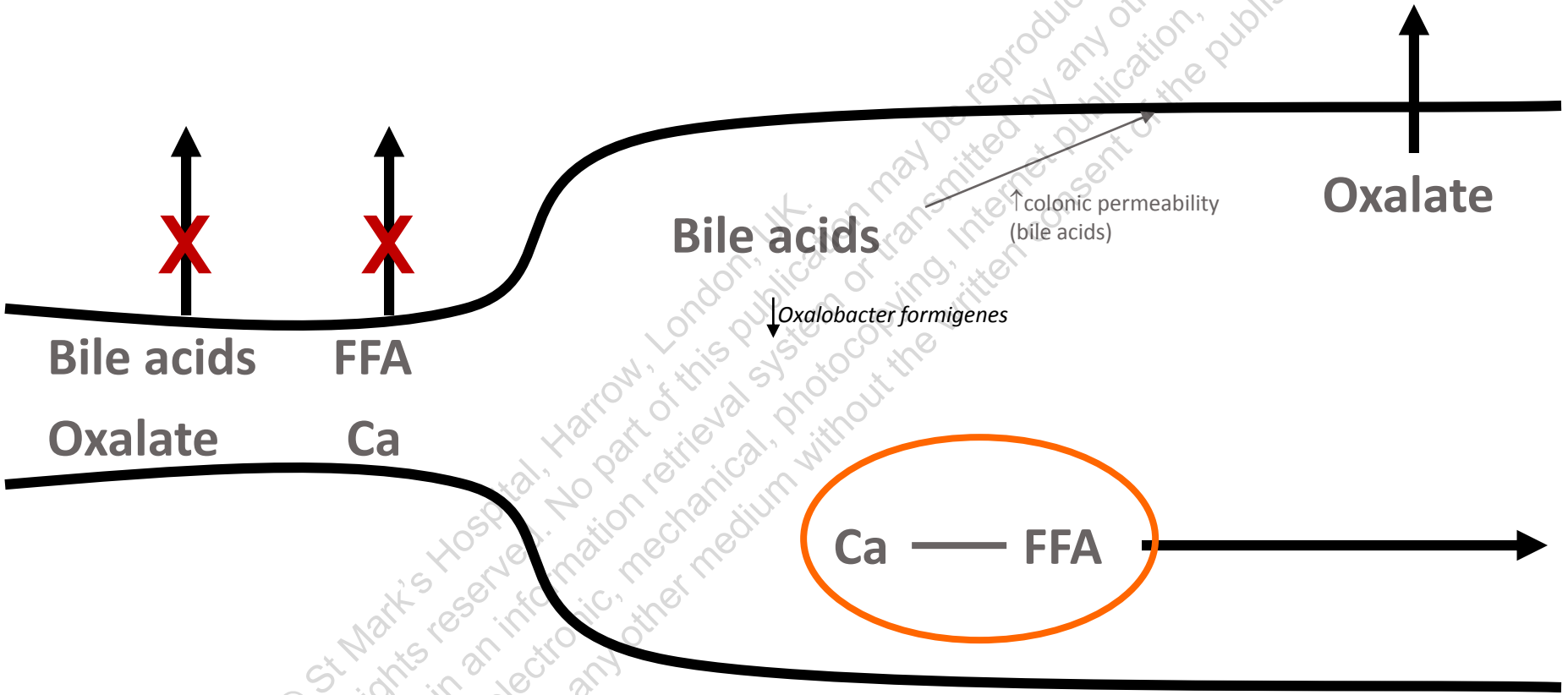
25% jejunocolonic patients develop symptomatic renal stones

Nightingale *et al* (1992)*Gut*;33:1493

Normal absorption



Jejuno-colic anastomosis



Renal Stones: Prevention

- Avoid high oxalate
  - Spinach, beetroot, rhubarb, peanuts, branflakes, nuts, soya, chocolate, parsley & tea
- Fat in moderation
- Encourage calcium intake
- Avoid chronic dehydration

Kasidas (1980) *J Hum Nutr*, 34:255

PN associated metabolic bone disease

Incidence

- Incidence unknown but estimated between 67-75%
  Many patients are asymptomatic
- Common symptoms are:
  - Bone pain - mainly in the lower joints
  - Back pain
  - Fractures particularly vertebral
  - Loss of height

Pironi, L. (2006) Metabolic bone disease in long-term HPN patients. In: Bozzetti, F., Staun, M., van Gossum, A. (eds) Home parenteral nutrition. Oxon, CABI. pp. 159.

Causes

- Likely multi-factorial
- General and lifestyle factors - age, sex, menopause, alcohol and smoking, reduced sunlight, immobility
- Other drugs - corticosteroids & heparin
- Underlying disease
  - Malabsorption of Ca, Mg & Vitamins D & K
  - Metabolic acidosis due to bacterial overgrowth
  - Chronic malnutrition
  - Chronic inflammation

HPN related factors

- Aluminium toxicity
  - High concentrations in 1980s.
- Deficiency or toxicity of micronutrients
- Increased calcium excretion induced by various causes
  - High concentrations of amino acids, glucose, sodium, calcium
  - Reversed by high concentrations of phosphate

ESPEN-HAN working group

No. centres / patients	9 / 165
Age (years)	52 ± 16 (19-85)
M:F	76:89
BMI (kg/m^2)	21.8 ± 3.4 (13-36)
Duration of HPN (m)	61 ± 53 (6-295)
Osteopaenia	**84%**
Osteoporosis	**41%**

Pironi *et al* (2002) *Clin Nutr* 21:289

ESPEN-HAN follow-up study

65 patients

Repeat DEXA after 18 ± 6 months

Mean Z score

- ↑ lumbar spine
- unchanged at femoral neck

Multiple regression

- Female sex
- Age starting HPN

HPN not associated with reduced bone density Low bone density relates to general risk factors

Pironi *et al* (2004) *Clin Nutr*, 23:1288

Metabolic bone disease & HPN

Prevention & treatment

- NICE, 2006
  - Recommends baseline DEXA scan & every 2 years
- Lifestyle
  - Regular exercise, stop smoking
  - Sunlight exposure, limit alcohol
  - Healthy BMI
- Amending the HPN formula
  - Review nitrogen, Vit D, PO4, Ca & Mg
- Monitor vitamin D, phosphate, Ca, Mg & PTH
- Wean steroids
- Bisphosphates (pamidronate & zolendronate)

Haderslev *et al* (2002) *Am J Clin Nutr* 76, 482

D-lactic acidosis

- Fermentation of carbohydrate in the colon
- Jejuno-colon patients
- Ataxia, slurred speech, altered affect
- Suspect if → Acidosis
Large anion gap
Normal blood L-lactate

Treatment to reduce colonic lactate

Diet: ↓ mono & oligo-saccharides
↑ polysaccharides

Oral neomycin or vancomycin

Essential fatty acid deficiency

- Patients at risk if on PN with limited oral intake
- Can develop signs and symptoms within 3 weeks
- Dermatitis, steatosis, haematological disturbances, reduced immune function
- Observational studies
  - 56 HPN patients, assessed EFA status
  - At risk if <200cm and no IV lipid
  - 500ml 20% Intralipid x1/week was adequate

Jeppesen et al (1998) Am J Clin Nutr,68:128

  - Oral & cutaneous sunflower & safflower oil
  - Can treat EFAD if on lipid free PN

Richardson & Sgoutas (1975) *Am J Clin Nutr*, 28:258
Millller *et al* (1987) *Am J Clin Nutr, 46:419*

Metabolic complications

Nutrient	Effect of deficiency
Glucose	Hypoglycaemia, weight loss
Essential fatty acids	Hair loss, dermatitis, delayed wound healing
Nitrogen/protein	Poor wound healing and lack of muscle mass/growth
Electrolytes	Reduced serum concentrations, refeeding
Zinc	Dermatitis, diarrhoea, rash, ↓ immunity
Selenium	Skeletal & cardiomyopathy
Copper	Anaemia, neutropenia, bleeding, arrhythmia
Chromium	Glucose intolerance, neuropathy
Water soluble vitamins	Cardiomyopathy, neuropathy, mouth lesions, anaemia, pellagra, Wernicke-Korsakov encephalopathy
Vitamin A	Night blindness
Vitamin D	Osteomalacia

Metabolic complications

Nutrient	Effect of excess
Glucose	Hyperglycaemia, hyperosmolar dehydration, ↑ CO2 production, refeeding syndrome, steatosis
Fat	Hyperlipidaemia, cholestasis
Nitrogen	Ureamia
Electrolytes	Elevated serum concentrations
Zinc	Nausea/vomiting, Cu & Fe deficiency
Selenium	Nail dystrophy and GI disturbances
Copper	Associated with cholestasis
Manganese	Associated with cholestasis, neurological impairment
Vitamin A	Liver disease, skin rash
Vitamin D	Hypercalcaemia

(T1) Diabetes management in PN

- Difficult – get DM team in early
- Night feed and oral intake during day
  - Easier to dose if same thing done each day
  - Know the g CHO in PN (1:10-20)
- No national guidelines exist
  - JBDS guidelines for enteral feeding in stroke principles apply
- 4 hourly blood sugar monitoring with ketone testing above 15mmol/L
- Review doses after 48 hours, or after hypo

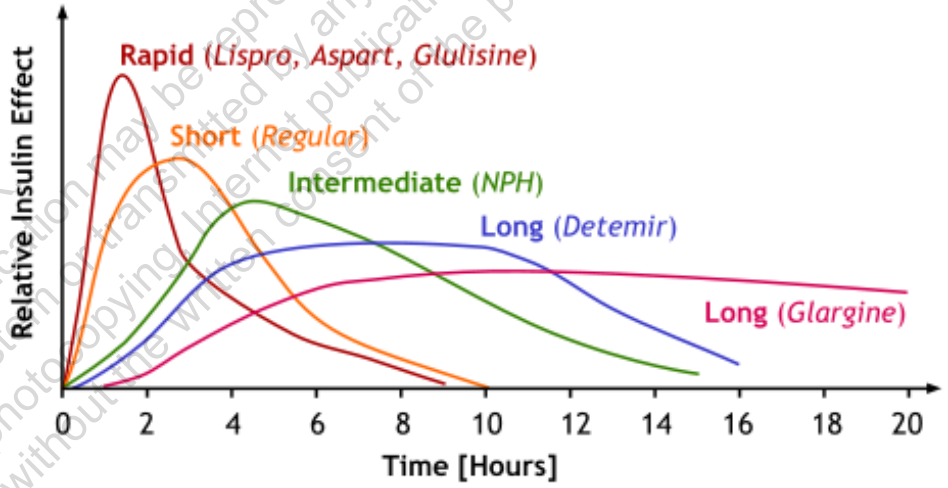
http://www.diabetologists-abcd.org.uk/JBDS/JBDS_IP_Enteral_Feeding_Stroke.pdf

Diabetes insulin regimes

- **ALWAYS KEEP USUAL BACKGROUND INSULIN**
- VRII until at target feed volume (and rate)
  - Gives idea of insulin requirement
- Get off iv insulin ASAP
- Always give insulin to cover PN at the start of feed

Diabetes insulin regimes starting point

- Calculate the total insulin dose required from VRII
- If feed around 24 hours
  - isophane insulin (Insulatard, Humulin I) 12 hour apart
  - watch longer acting analogue insulins (Lantus, Levemir) flat profile, half life too long
- If feed 16-20 hours
  - use 30% mix insulin (Mixtard 30, Humulin M3) with isophane mid way (Insulatard, Humulin I)
- If feed under 10 hours
  - use 30% mixed insulin at the start of feed



Type of action	Chemical name	Brand name
Rapid	Insulin lispro	Humalog
	Insulin aspart	NovoRapid
	Insulin Glulisine	Apidra
Short	Soluble insulin	Actrapid
		Humulin S
		Insuman Rapid
Intermediate	Isophane insulin suspension/NPH	Humulin I and Insulatard
	Insulin zinc suspension	Hypurine Bovine
Long	Insulin glargine	Lantus
	Insulin detemir	Levemir
	Insulin degludec	Tresiba

Hypoglycaemia and PN in non DM

Hypoglycaemia

- Can happen at the start or end of feed
- More common in chronically low BMI
- Tremulous after feed stops, improves with food
- Slower rate at first/ last 2 hours feed

Nesidioblastosis

- RARE
- Hypos at random times during the day/night on and off PN/feed
- Hyperinsulinaemia causing hypo- not insulinoma
- Treat with pancreatic reduction surgery (drastic) or diazoxide

Tse-Ling F et al 1989 Diabetes Care 12:108-114

Summary

Gallstones	Pigment stones
	44% patients with jejunocolonic anastomosis 43% patients with jejunostomy
Renal stones	Calcium oxalate stones
	25% jejunum-colon patients
Bone disease	High prevalence but PN not causative Review HPN formula & lifestyle
D-lactic acidosis	Jejunocolic patients
	More frequent when coexisting renal failure
EFA deficiency	Patients at risk if on lipid-free PN with limited oral intake
Diabetes	Involve DM team early