Acute Liver Failure
Liver Failure Study Day

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Liver Failure

ACUTE

Jaundice to encephalopathy Time:

< 8weeks

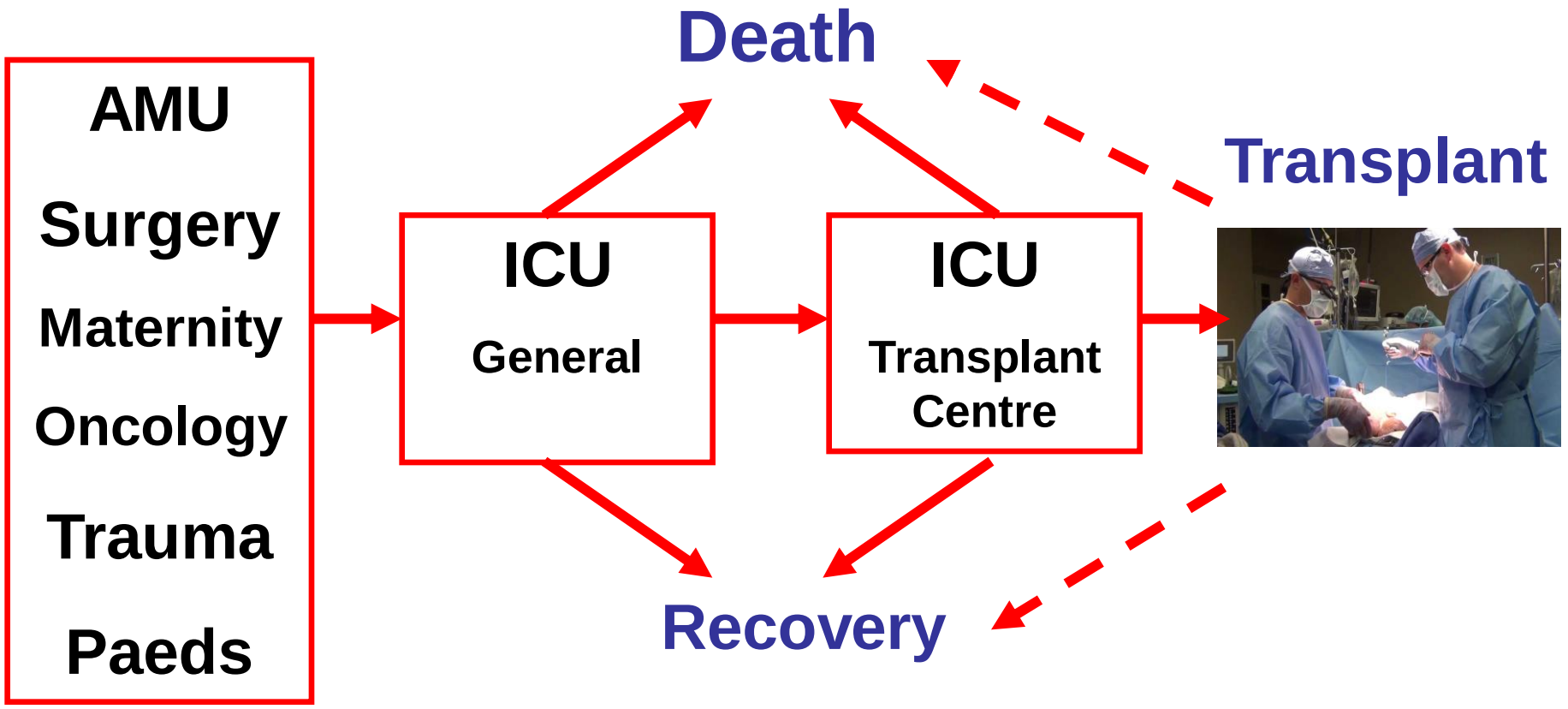
SUB-ACUTE

Encephalopathy within 2 to 6 months of onset of symptoms

CHRONIC

Gradual destruction of liver tissue resulting in impaired liver function

Critical Care & ALF



Introduction - ALF

- **Rare**
- **Unpredictable**
- **No specific therapies except OLTx**
- **Spontaneous recovery - ≤50%**
- **Multidisciplinary approach**

Introduction - ALF

1. **Make the diagnosis**
2. Evaluation
   - Identify aetiology
   - Assess severity and the associated prognosis
3. Management: Prevention or treatment of complications:
   - Support other organs (kidneys etc)
   - Treat sepsis etc
4. Liver transplantation when spontaneous survival is considered unlikely
5. Possible use of liver support devices

Acute Liver Failure

(Jaundice)

+

Coagulopathy (INR>1.5)

+

Encephalopathy

≤26 weeks

NB: Definitions vary

Acute Liver Failure

"Only 3 things you need to know about ALF:"

Prothrombin Time

Prothrombin Time

Prothrombin Time

Acknowledgement: MHD

Clinical grading of HE

Clinical grade	Clinical signs	Flapping tremor
Grade 1 (prodrome)	Alert, euphoric, occasionally depression. Poor concentration, slow mentation and affect, reversed sleep rhythm.	Infrequent at this stage
Grade 2 (impending coma)	Drowsiness, lethargic, inappropriate behavior, disorientation.	Easily elicited
Grade 3 (early coma)	Stuporose but easily rousable, marked confusion, incoherent speech	Usually present
Grade 4 (deep coma)	Coma, unresponsive but may respond to painful stimulus	Usually absent

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EVALUATION

History:

(from family/GP etc)

- **Virus-Travel/Sex/food/IVDU**
- **Drugs:**
  - **Proscribed/Prescribed**
- **Pregnancy: 1st/BP records etc**
- **Wilson's**
- **Magic mushrooms: central EU, USA**
- **Malignancy**
- **Ischaemic hepatitis**
- **Ascites: Budd-Chiari**
- **(Oh and alcohol)**

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- **Ischae**
- **Ascite**
- **(Oh ar**

Examination:

- **Encephalopathy: serial 7's to coma**
- **Absence of signs of CLD**
- **Jaundice – in most**
- **Haemodynamics**
  - Hypotension: bleeding, sepsis, dysrhythmia or reduced SVR
- **Hyperventillation, infection, oedema**
- **Ascites – ?BCS**
- **Liver volume:**
  - Small – sub-acute
  - Large: infiltrated, BCS, CCF
- **Co-morbidity**

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Examinat

- **Encepha**
- **Absence**
- **Jaundic**
- **Haemod**
  - Hypot dysrh
- **Hyperve**
- **Ascites**
- **Liver vo**
  - Small
  - Large
- **Co-morb**

Investigations:

- PT (INR)
- BM, LFT, U+E
- ABG, Lactate
- Group, FBC
- Paracetamol level
- HAV, HBV, HCV, HEV, HSV, EBV, CMV, HIV
- Pregnancy test
- ANA, Autoantibodies
- Caeruloplasmin
- ?Biopsy

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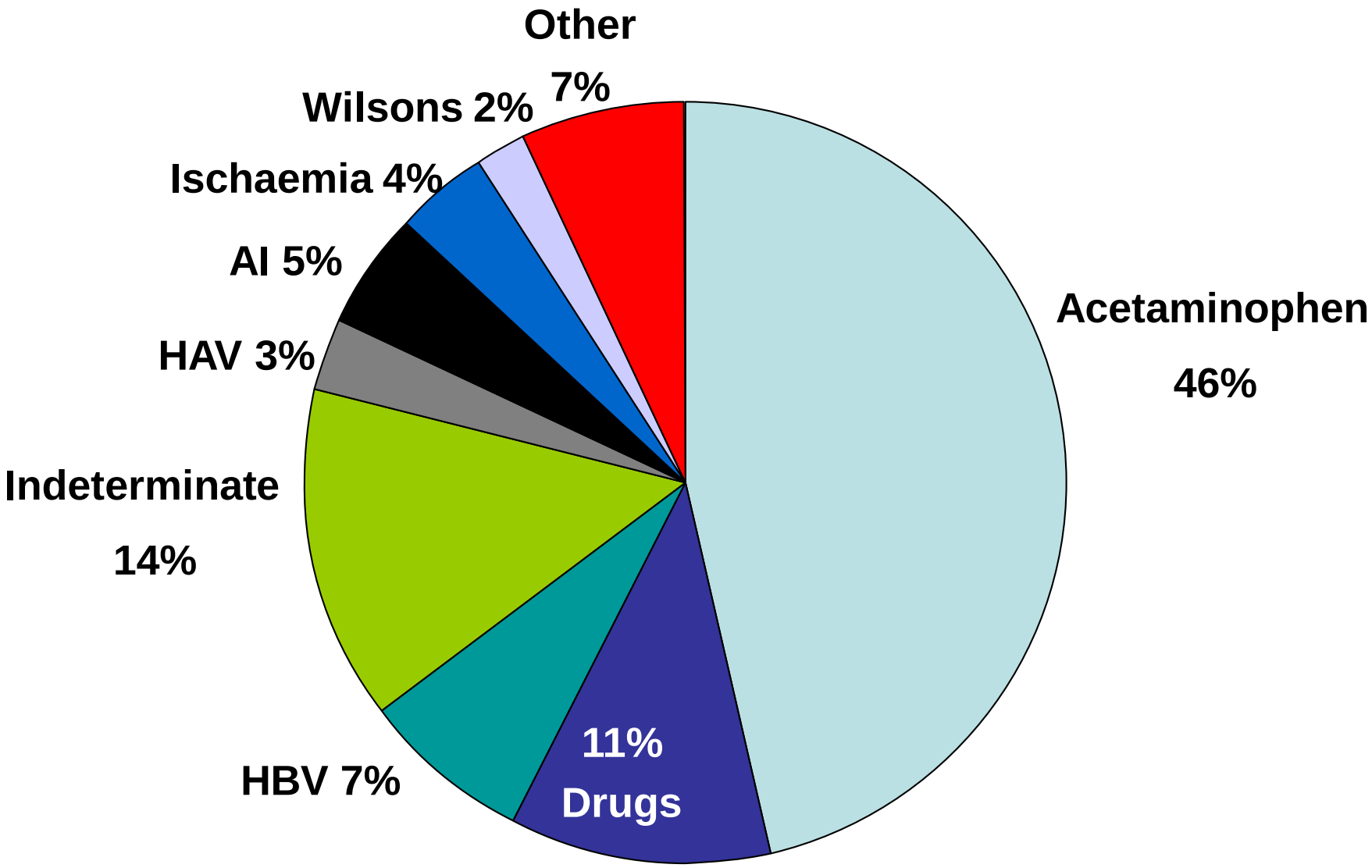
Investiga

- PT (INF
- BM, LF
- ABG, L
- Group,
- Parace
- HAV, H EBV, C
- Pregna
- ANA, A
- Caerul
- ?Biops

Imaging:

- CXR
- USS
  - Normal = helpful
  - Nodular = cirrhosis
- ??CT or MRI
  - Usually unnecessary
  - ?Cancer
  - ?Budd-Chiari

Aetiology of FHF in Adults



Source: US ALF Study Group

Aetiology

	India	UK	USA	France
HBV	31%	9%	7%	45%
HAV	2%	5%	3%	4%
HEV	38%	?	?	?
POD	?	54%	46%	5%
Drugs	5%	7%	11%	15%
Others: NANB	24%	25%%	23%	31%

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Natural History

- Death - cerebral oedema
  - sepsis
  - SIRS
- Respiratory failure
- Acute renal failure
- Bacterial infections
- Fungal infections
- Metabolic disturbance

ALF Diagnosis: Management 1

1. Make diagnosis
2. Establish History, examination and basic lab tests
3. Discuss with Liver Transplant Unit
4. General:
   - ITU/HDU
   - Re-hydrate – volume resuscitation
   - BM's, BP, PR, Urine OP, Oxygen satn
   - Nutrition
   - Encephalopathy grade
5. Raised ICP – bolt, mannitol etc
6. Antimicrobial prophylaxis
7. Few specific therapies:
   - NAC for acetaminophen
   - Prompt delivery in pregnancy related conditions

ALF Diagnosis: Management 2

Mushroom	Charcoal + penicillin
AI	Steroids
Wilsons	Cu chelation, plasmapheresis and antioxidant Rx
Acute HBV	Tenofovir
HSV	Acyclovir
Budd-Chiari	TIPS etc
Veno-occlusive disease	Defibrotide
Adenovirus	Cedofovir
Dengue	Paracetomol
Malignancy (lymphoma, leukaemia)	Chemotherapy

ALF Diagnosis: Management 3

- Renal failure: CVVHD
- Intubate for encephalopathy>Grade 2.
- Coagulopathy: gastric protection
- Nutrition
- Mechanical ventillation
- Haemodynamic support: vasopressors etc
- Do *NOT* correct coagulopathy unless necessary
- Discuss with specialist centre – ***safe transfer***

POD

- History:
  - ?staggered/timing/total amount
  - Intentional or accidental
  - Weight is critical
- Sub-conjunctival haemorrhage
- ALT in 1000's (Bili may be low/normal)
- Increasing susceptibility to paracetamol toxicity
  - regular alcohol consumption
  - antiepileptic therapy (via enzyme induction)
  - malnutrition.
- Treatment:
  - N-acetyl cysteine - <4hours
  - IV fluids – rehydrate
  - Consider antibiotics + antifungals

POD

- Discuss early with Transplant centre if PT rising
- PT monitoring 6-hrly
- Beware of secondary rise

Drugs causing ALF

Commoner causes

- Paracetamol,
- Halothane,
- Isoniazid/rifampicin
- NSAIDs
- Sulphonamides
- Sodium valproate
- Carbamazepine,
- Ecstasy

Rarer causes

- Benoxyprofen
- Phenytoin
- Isoflurane & enflurane
- Tetracycline & ketoconazole
- Allopurinol
- MAOIs
- Disulphiram
- Amiodarone
- Methyldopa, TCA's, PTU, Au, 2,3,-dideoxyinosine (ddI)

Drug-induced ALF

- Usually within 6 months after initiation
- Herbal preparations, weight loss agents & other ‘supplements’
- NAC

Pregnancy-related

Last trimester
Triad: Jaundice+coagulopathy+Low platelets
+/- Hypoglycaemia

- Acute fatty liver of pregnancy
  - preferentially affects primagravids carrying a male
  - Pain
  - LCHAD
- HELLP syndrome
  - Haemolysis
  - Elevated liver enzymes
  - Low platelets
- Pre-eclampsia or eclampsia
  - is characterised by high transaminase activities

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Last trimester
Triad: Jaundice+coagulo
+/- Hypoglycaemia

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  - J
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1.Recognition
2.Early Delivery
3. Watch carefully post delivery

Amanita phalloides

- History:
  - severe gastrointestinal symptoms (nausea, vomiting, diarrhea, abdominal cramping), which occur within hours to a day of ingestion
- Gastric lavage and activated charcoal via nasogastric tube
- Fluid resuscitation
- NAC
- Penicillin G and silibinin (silymarin or milk thistle) (no trials)
- Consider OLTx

WILSON'S DISEASE

- Younger patients
- Low ALP and Urate
- Coombs-negative haemolysis (Unconjugated bilirubin is High)
- K-F rings in ½ patients
- Low caeruloplasmin (High Copper)……
- Renal dysfunction
- For Transplant Centre

Others

- **Ischaemic Hepatitis**
  - Hypotension/hypovolaemia
  - Kidney function
  - PT↑>>bili ↑
  - Cardiovascular monitoring + support
- **Budd-Chiari**
  - Enlarged tender liver
  - Ascites
  - Early discussion +/- transfer (TiPs, OLTX etcx)
- **Malignancy**

- **Sero-negative etc**

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POLICY POL195/5

Liver Transplantation: Selection Criteria and Recipient Registration

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1. Conditions that are considered for transplantation

1.1 Adult patients

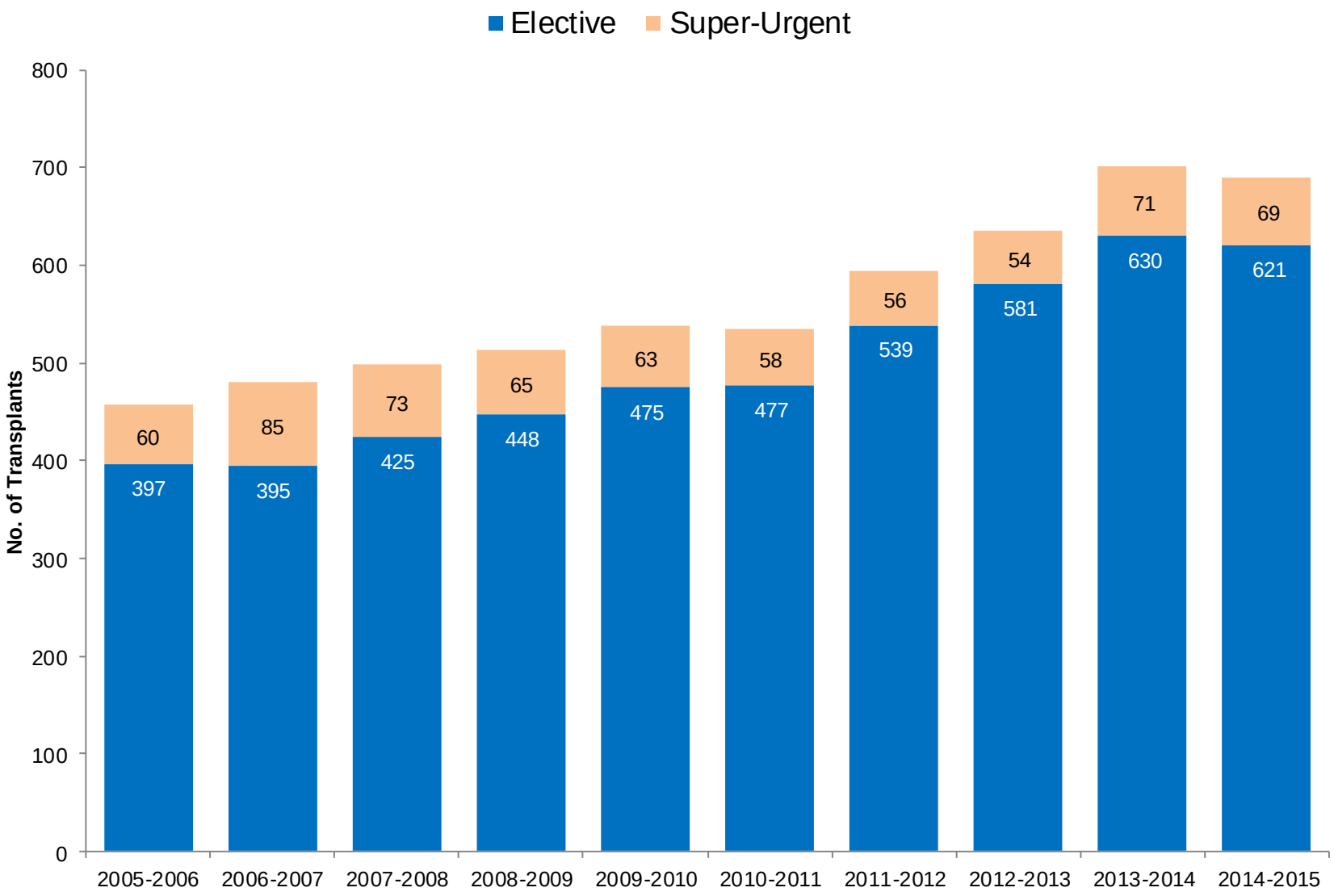
Most adult patients with liver disease are not managed in transplant centres. Patients referred for assessment for liver transplant will include those with the following broad categories of conditions:

- Acute liver failure
  - Multi-system disorder in which severe acute impairment of liver function with encephalopathy occurs within 8 weeks of the onset of symptoms and no recognised underlying chronic liver disease
- Chronic liver disease; any cirrhosis which may be due to:
  - Alcoholic liver disease
  - Non-alcoholic fatty liver disease
  - Chronic viral hepatitis B, C, D
  - Autoimmune liver diseases: primary biliary cirrhosis, primary sclerosing cholangitis, chronic active liver disease and overlap syndromes
  - Genetic haemochromatosis
  - Wilson's disease

POLICY POL195/5
Liver Transplantation: Selection Criteria and Recipient Registration

- Categories 1-4: Paracetamol (POD)
- Category 5: Favourable non-POD
- Category 6: unfavourable non-POD
- Category 7: Wilson's or Budd-Chiari
- Category 8-9: Post Transplant re-list criteria
- Category 10: "Total absence of liver function"
- Category 11: Post live donor ALF
- Category 20: Children <2yrs with multi-system disease etc

Deceased donor liver only transplants for adults



Catches for the unwary

- Inform Transplant centre early
- Oedematous gallbladder
- “nodular” liver (acute necrosis) is not cirrhosis
- Ensure family informed of prognosis

Conclusions

- Coagulopathy + Encephalopathy + Jaundice
- Evaluate: History/Examine/Investigation
- ?Evidence of chronic liver disease
- Discuss early with transplant centre
- Specific ‘antidotes’
- Multidisciplinary approach in ICU