Non-alcoholic fatty liver disease (NAFLD)

WHAT IS NAFLD? 
- Non-alcoholic fatty liver disease.
- Presence of hepatic fat in people who do not consume excessive alcohol.
- Most common reason for mildly abnormal liver test results.

SUBCLASSIFICATIONS:
- NAFL (non-alcoholic fatty liver)
- NASH (non-alcoholic steatohepatitis)

CAUSES
Although the exact cause of NAFLD remains unknown, growing evidence suggests excessive consumption of sugars (sucrose and fructose) may act as a major contributor in the development and severity of NAFLD.

Risk factors include:
- Obesity
- High cholesterol
- High triglycerides
- Type 2 diabetes
- Insulin resistance
- Leptin resistance
- Hepatic iron

WHAT HAPPENS INSIDE THE LIVER?
- Lipotoxicity
- Endoplasmic reticulum stress

PROGRESSION OF NAFLD
1. NORMAL
2. NAFL
   - Obesity
   - Insulin resistance
   - Free fatty acids
   - High cholesterol
3. NASH
   - 10-25% NAFL develops into NASH
   - Oxidative stress
   - Mitochondrial dysfunction
   - Gut-derived endotoxins
   - Inflammatory cytokines
   - =20% NASH progresses to cirrhosis over 20-30 years
   - Unsuccessful or no treatment
4. CIRRHOSIS
   - Most severe

EVIDENCE-BASED SOLUTIONS
- Milk thistle
  * Silybum marianum
  - Hepatoprotective, stabilises cell and lysosomal membranes, antioxidant, chelates iron, accelerates regeneration of hepatocytes, anti-inflammatory, antifibrotic
- Coffee
  * Coffea arabica
  - Hepatoprotective, antioxidant, anti-inflammatory, antifibrotic, improves insulin sensitivity
- Zinc
  - Antioxidant, anti-inflammatory, antifibrotic, deficiency linked to insulin resistance, involved in cell proliferation, maintains cell membrane integrity
- Vitamin E
  * Alpha-tocopherol
  - Antioxidant, anti-inflammatory, antifibrotic
  * Gamma-tocotrienol
  - Regulates fatty acid metabolism, reduces endoplasmic reticulum stress, antioxidant, anti-inflammatory

SYMPTOMS
- Fatigue
- Weight gain
- Pain in upper right abdomen
- Usually ASYMPTOMATIC.

DIAGNOSTIC CRITERIA
A definitive diagnosis of NAFLD depends on three factors:
1. Evidence of fatty infiltration (imaging or biopsy).
2. Exclusion of significant alcohol consumption.
3. Exclusion of other causes of hepatic steatosis (e.g., medications, surgery, metabolic disorders).