

BMSH4302

Introduction to Chronic Disease

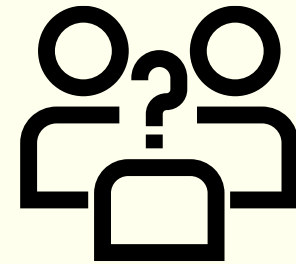
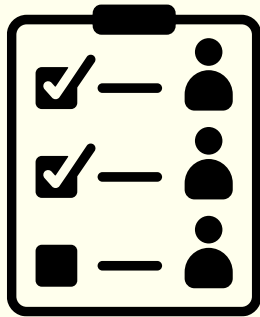
Level 4



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BMSH4302 Introduction to Chronic Disease

Housekeeping:



Pulmonary Disease Recap

- Kahoot!

Metabolic Diseases

Metabolic Diseases: Prevalence

- **Global:** 1.54 billion adults had metabolic syndrome in 2023, more than double the figure from 2000 (Nature Communications, 2025)
- **↑ 15% to 31% in women and 9% to 26% in men**
- **UK:** approximately 1 in 4 adults have metabolic syndrome/17.5m (HEART UK). Components at epidemic levels: 4.6 million with diabetes, 1 in 5 with MASLD, 1 in 3 with hypertension, 64% of adults overweight or obese
- **Wales:** highest diabetes prevalence in the UK (8% of adults). MASLD incidence increased tenfold in 20 years. Prevalence strongly tied to socioeconomic deprivation.

Metabolic Syndrome

Metabolic syndrome describes a cluster of interconnected risk factors:

- central obesity
- insulin resistance
- hypertension
- raised blood glucose (hyperglycaemia)
- abnormal blood lipids (dyslipidaemia)

that occur together

Metabolic Diseases

- These conditions cluster together through shared metabolic mechanisms, particularly insulin resistance
- Metabolic syndrome doubles the risk of cardiovascular disease and increases diabetes risk x5
- Someone living with Type 2 diabetes is far more likely to also have fatty liver disease, to have dyslipidaemia, to have hypertension, to have increased cardiovascular risk
- Thyroid disorders affect approximately 1 in 20 people in the UK, with women disproportionately affected

By the end today's lecture:

We will have covered prevalence, incidence, aetiology, pathology, signs and symptoms, risk factors and effect on quality of life for each of these metabolic conditions:

1. **Type 1 Diabetes** (autoimmune destruction of insulin-producing cells)
2. **Type 2 Diabetes** (insulin resistance and progressive beta cell failure)
3. **MASLD** (metabolic dysfunction-associated steatotic liver disease)
4. **Hypothyroidism/Hashimoto's Thyroiditis** (autoimmune underactivity of the thyroid)
5. **Hyperthyroidism/Graves' Disease** (autoimmune overactivity of the thyroid)

What is Metabolism?

- **METABOLÉ:** Greek 'change'
- + **“ism”** suffix used to create nouns denoting a system of belief, practice, or philosophy

Metabolism consists of a series of reactions that occur within cells of living organisms to sustain life

What is Metabolism?

Metabolism Powers Everything Cellular

- Metabolism is not just about movement or 'burning calories'
- Every cell in the body requires energy for: cell division, DNA repair, immune function, temperature regulation, nerve signalling, digestion, hormone production
- Metabolism = the sum of all chemical reactions that keep cells alive and functioning

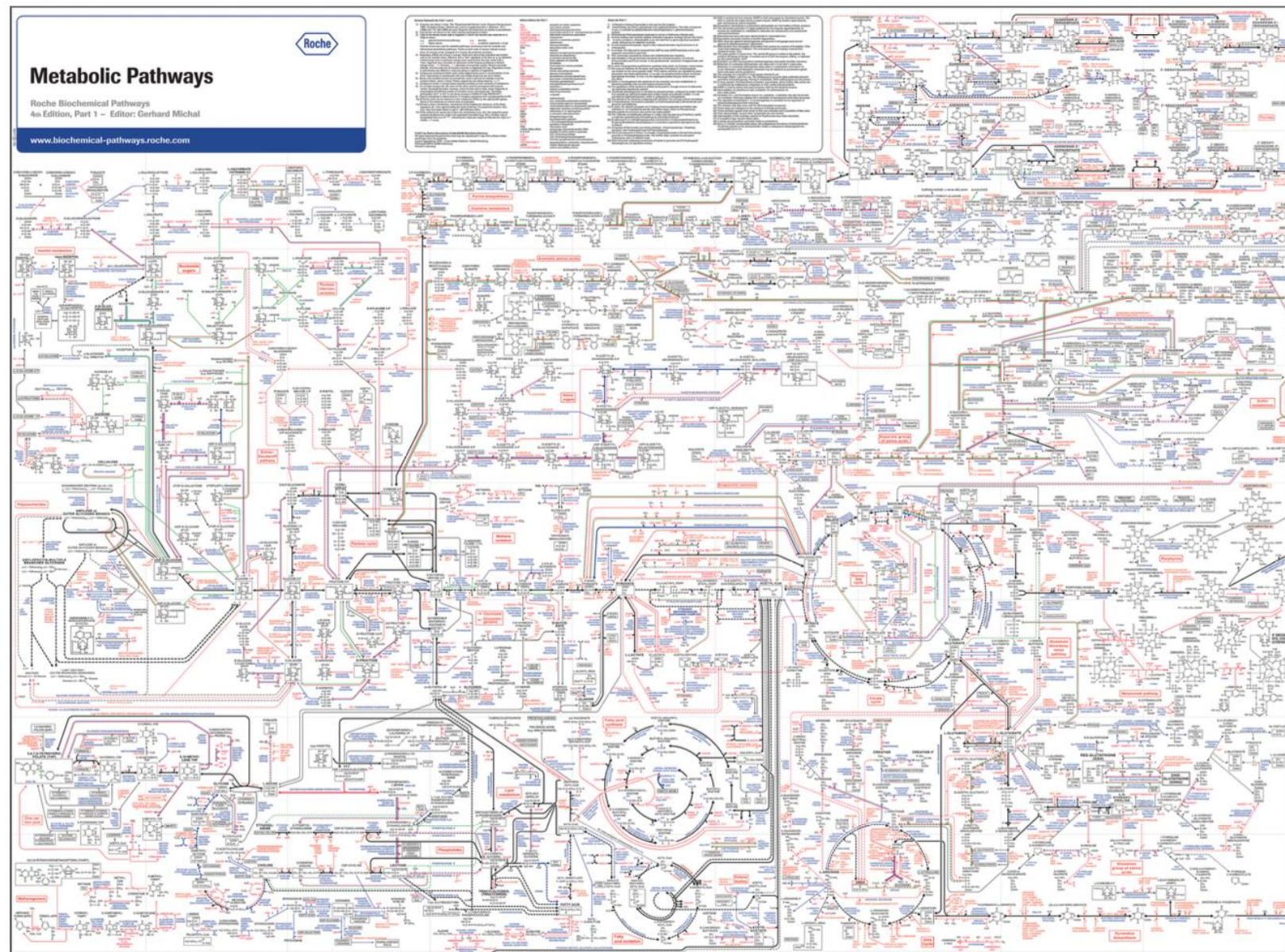


Fig. 4 Schema of metabolic mechanisms. The mechanisms merge into each other as the product of one mechanism serves as the educt of another mechanism (modified after F. Hoffmann-La Roche Ltd, <http://biochemical-pathways.com/#/map/1>; for both a more comprehensive and a more detailed overview of metabolic mechanisms open the original map by F.Hoffmann-La Roche online)

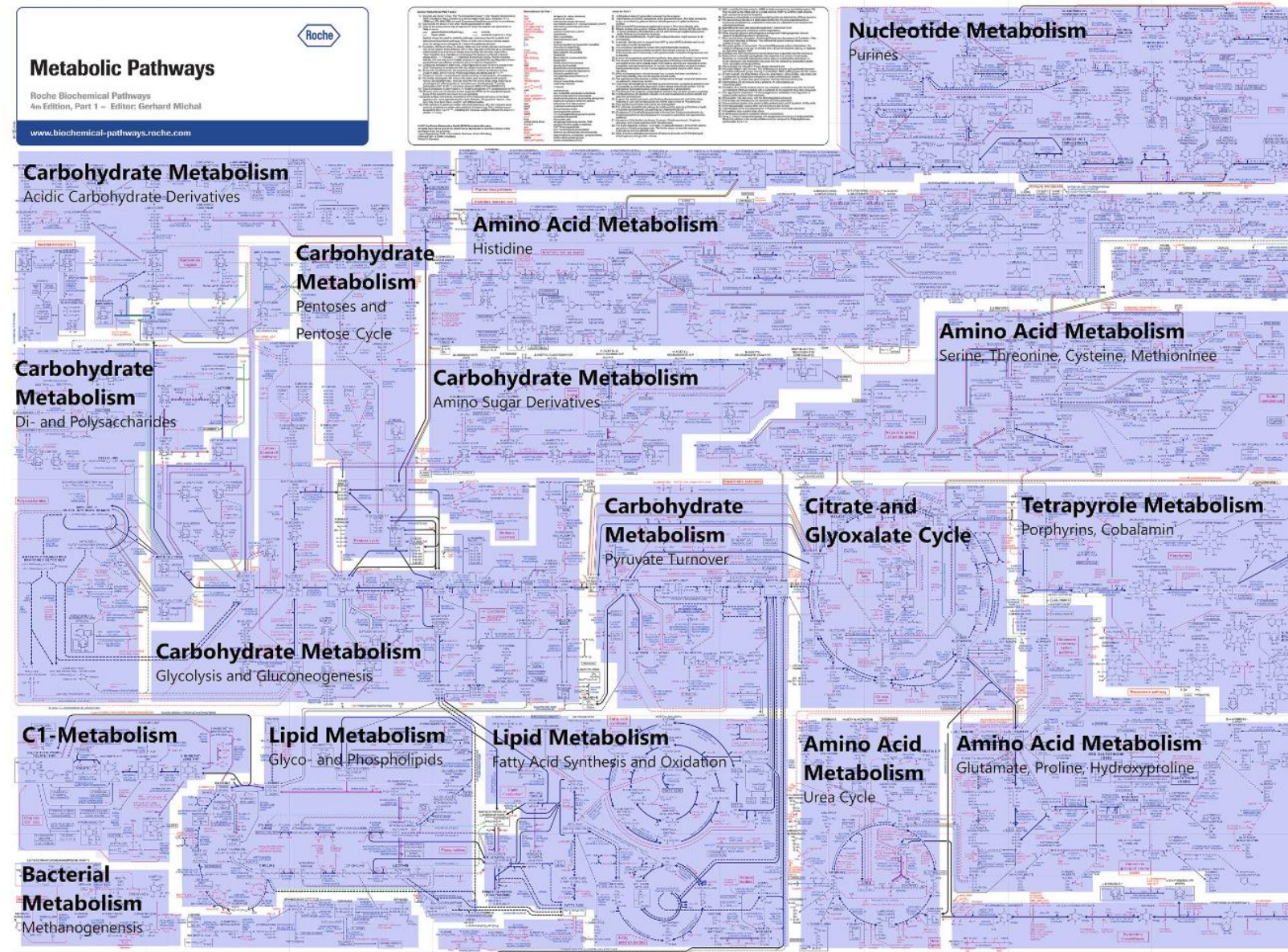


Fig. 5 Schema of metabolic mechanisms, chunked according to their contributions to the organism. Biologists differentiate individual mechanisms epistemologically in terms of their contributions to capacities of the organism that serve survival or reproduction (modified after F. Hoffmann-La Roche Ltd, <http://biochemical-pathways.com/#/map/1>; for both a more comprehensive and a more detailed overview of metabolic mechanisms open the original map by F.Hoffmann-La Roche online)

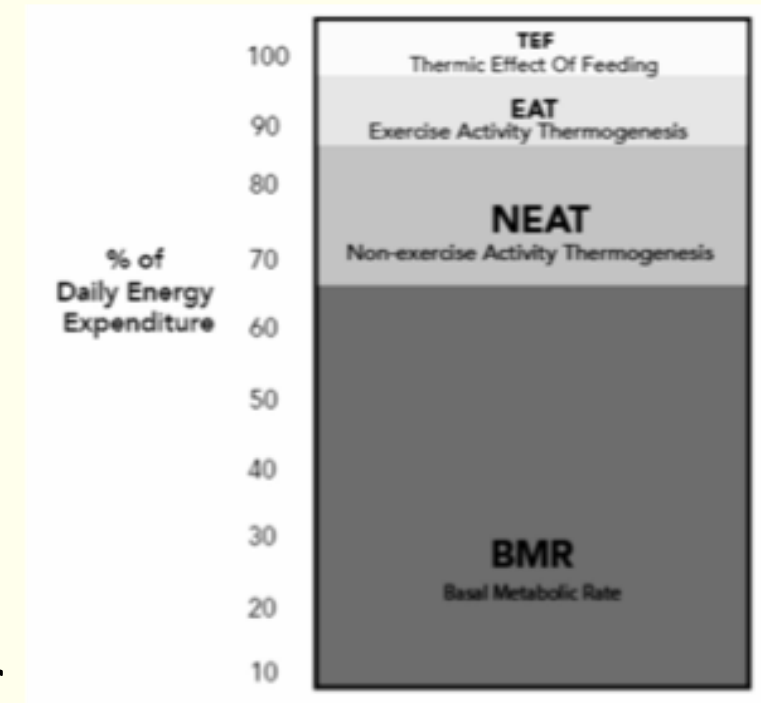
What is a Calorie?

Calories are a measure of energy

- "Small" calories (cal) estimate the amount of energy required to raise the temperature of exactly 1 gram of water by 1 degree Celsius at 1 atmospheric pressure
- "Big" calories, also known as kilocalories (kCal), are more commonly known and refer to a unit of energy equal to the amount of heat energy needed to raise the temperature of one kilogram of water by one degree Celsius

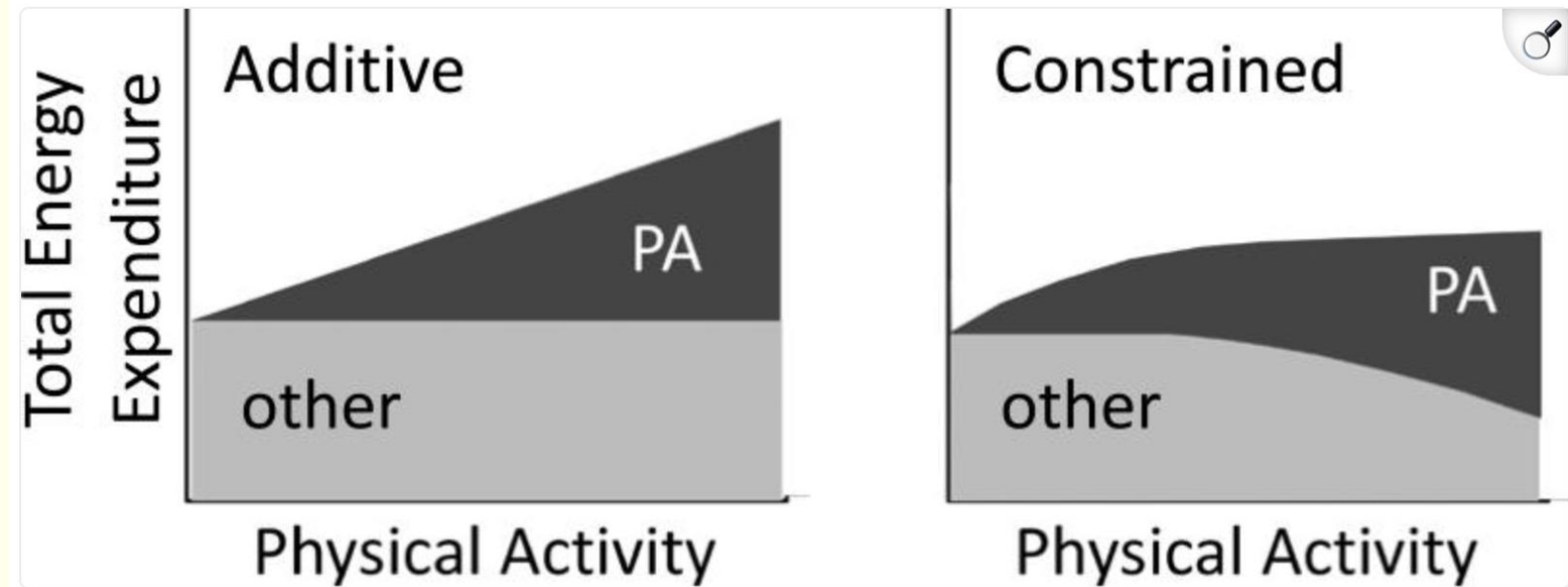
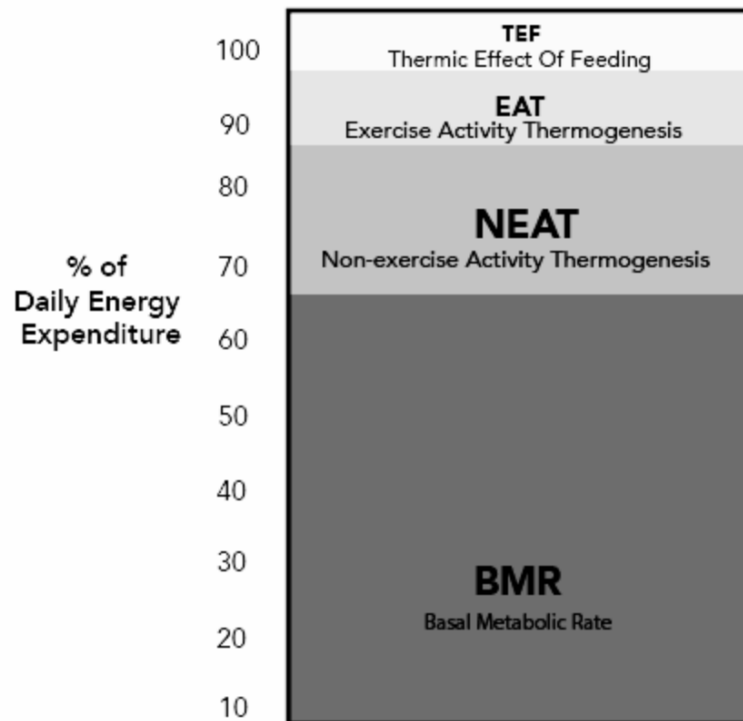
Basal Metabolic Rate (BMR)

- BMR accounts for 60 to 70% of total daily energy expenditure
- This is the energy used just to keep you alive at rest: heart beating, lungs breathing, brain functioning, cells dividing, temperature maintained
- Factors affecting BMR: age, sex, body composition (muscle vs fat), thyroid function, genetics
- Note thyroid function on this list, we return to it later in the session



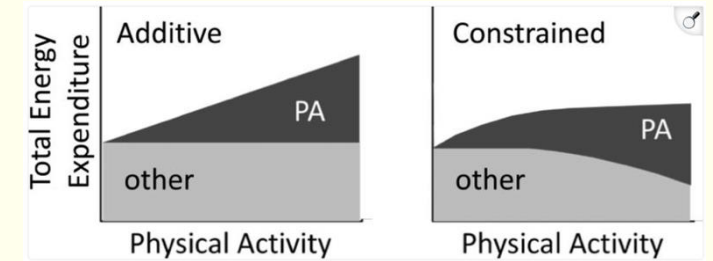


Total Daily Energy Expenditure (TDEE) vs Constrained Energy Model



Source: Pontzer et al, 2015

Basal Metabolic Rate (BMR)

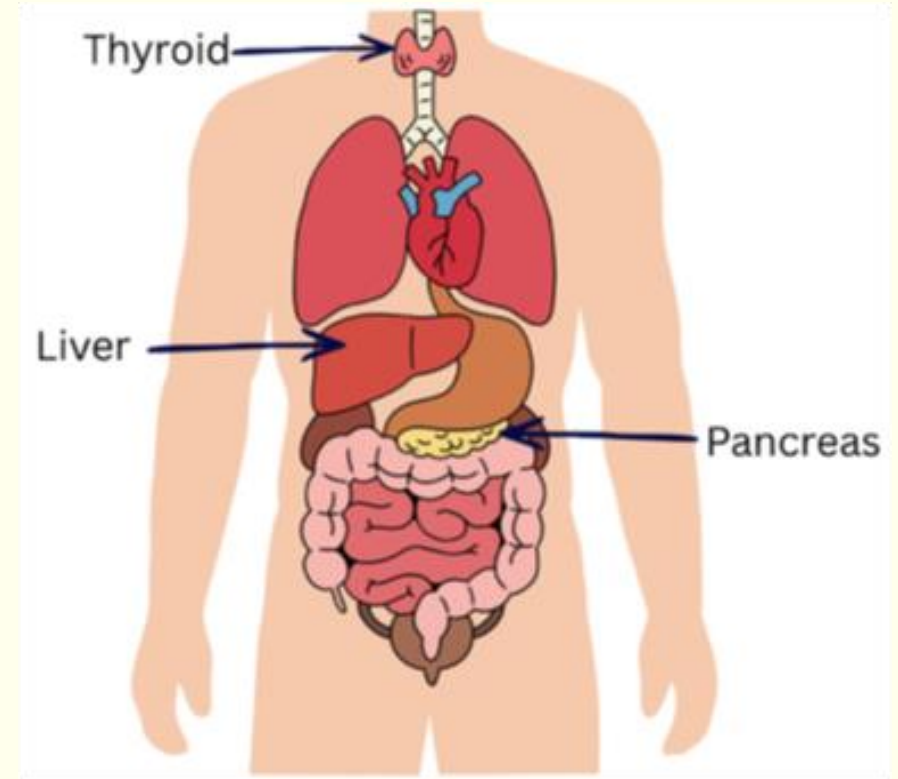


- Traditional 'additive' model: more exercise = more total calories burned (a straight line upwards)
- The Hadza hunter-gatherers of Tanzania: despite walking 15,000+ steps daily, their total daily energy expenditure is similar to sedentary Western populations (Pontzer et al., 2012; 2016)
- The body has a finite energy budget and reallocates between systems rather than simply adding more
- Pontzer's 'constrained' model: total energy expenditure plateaus at higher activity levels

Metabolic Organs

Liver, Pancreas and Thyroid Gland

- Today's session is built around three organs that regulate metabolism.
- Metabolic disease occurs when one of these organs malfunctions
- Because they are interconnected, dysfunction in one often affects the others



Metabolic Organs: what they do

Organ	What it does	Associated Metabolic Disease
Pancreas	Regulates blood glucose via insulin and glucagon	Diabetes
Liver	Metabolic hub: glucose storage, lipid metabolism, detoxification, protein synthesis	MASLD (metabolic dysfunction-associated <u>steatotic liver disease</u>)
Thyroid	Sets the body's metabolic rate via T3 and T4 hormones	Hypothyroidism / Hyperthyroidism



The Immune Spectrum

The immune system can cause chronic disease through three distinct mechanisms. The pattern determines the treatment approach.

1

Autoimmune

MECHANISM

The immune system attacks the body's own healthy tissue. It mistakes "self" for "enemy." There is no external trigger.

CONDITIONS IN THIS MODULE

Type 1 Diabetes (Wk 4)

Hashimoto's (Wk 4)

Graves' Disease (Wk 4)

Rheumatoid Arthritis (Wk 5)

Multiple Sclerosis (Wk 6)

TREATMENT LOGIC

Immunosuppression: dampen the immune system that is attacking healthy tissue

2

Immune Hypersensitivity

MECHANISM

The immune system overreacts to external triggers. The trigger is real, but the inflammatory response is disproportionate to the threat.

CONDITIONS IN THIS MODULE

Asthma (Wk 3)

TREATMENT LOGIC

Anti-inflammatory medication and bronchodilators: control the overreaction

3

Chronic Inflammation

MECHANISM

The immune system responds to genuine ongoing damage, but the sustained inflammatory response causes further destruction. The exposure never stops, so neither does the damage.

CONDITIONS IN THIS MODULE

COPD (Wk 3)

Occupational Lung Disease (Wk 3)

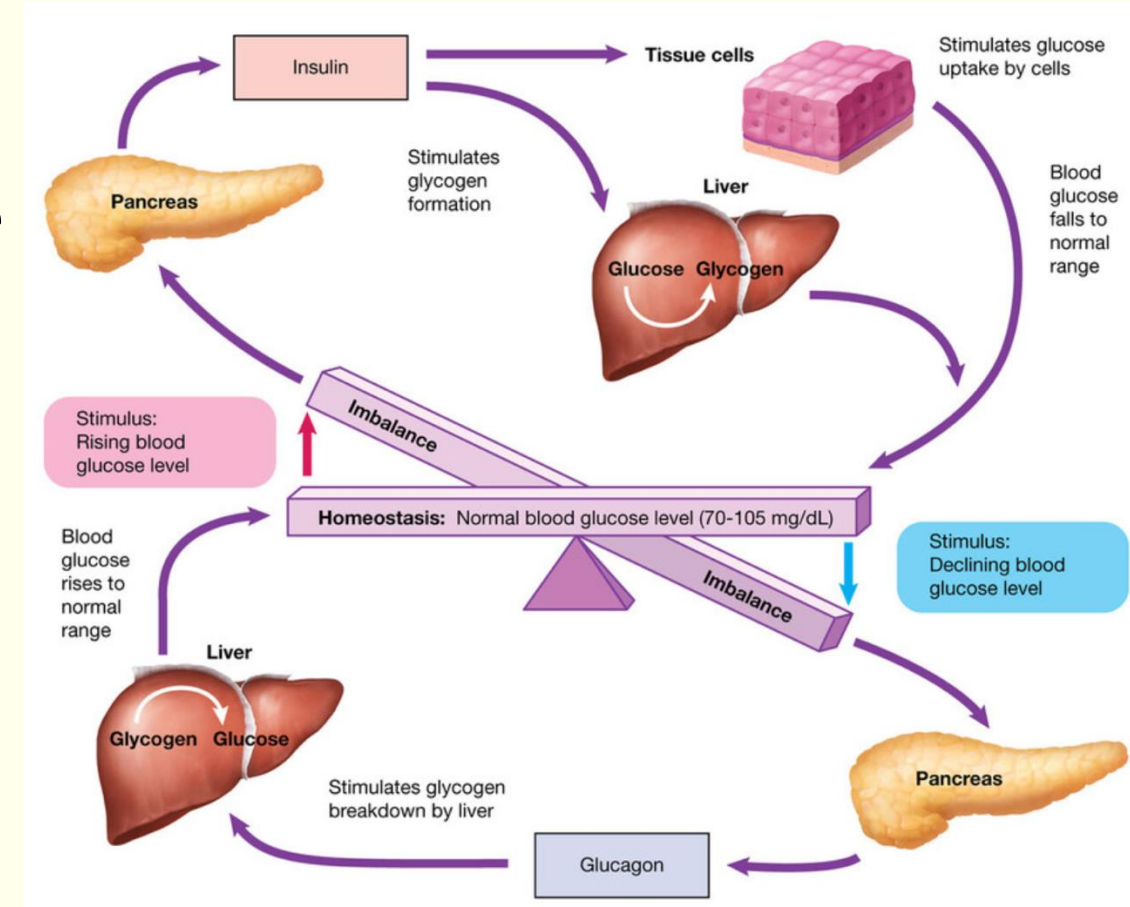
TREATMENT LOGIC

Remove the exposure: stop the harmful substance entering the body

Blood Glucose Regulation

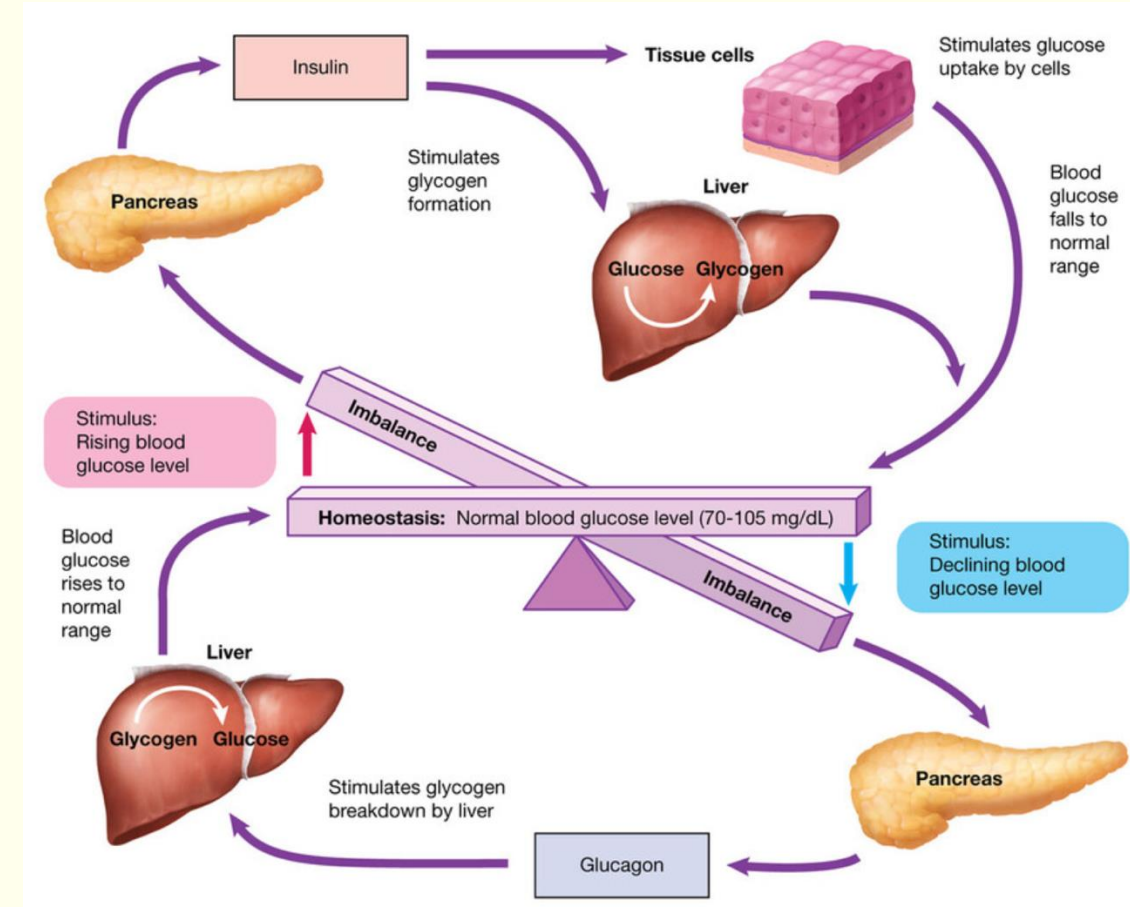
Blood Glucose Regulation

- Stimuli such as eating or stress cause blood glucose levels to rise above the normal range (4 to 7 mmol/L)
- The pancreas detects this imbalance and releases insulin
- Insulin has two effects: it stimulates glucose uptake by tissue cells, and it stimulates the liver to convert glucose into glycogen for storage
- Both actions lower blood glucose back to the normal range



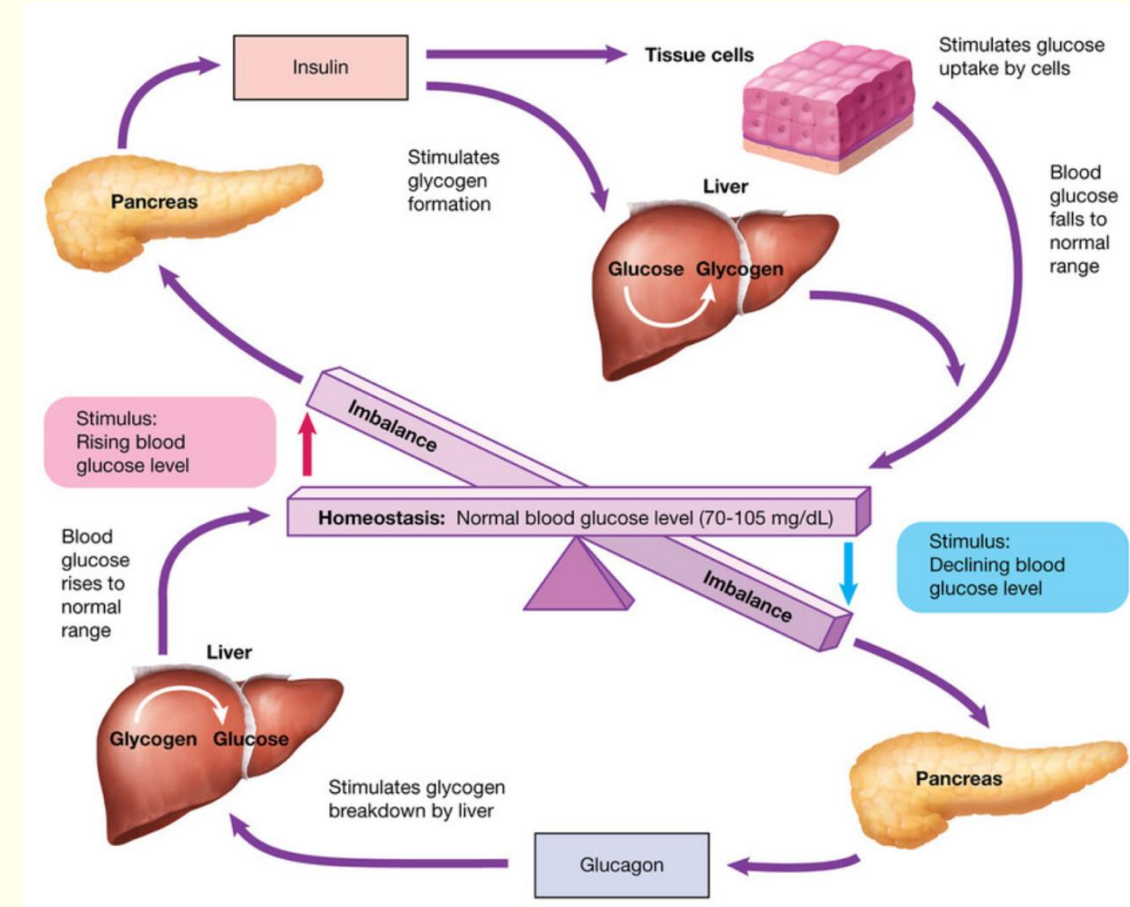
Blood Glucose Regulation

- Stimuli such as fasting or physical activity cause blood glucose to drop below the normal range
- The pancreas detects this imbalance and releases glucagon
- Glucagon stimulates the liver to break down stored glycogen back into glucose, releasing it into the blood
- Blood glucose rises back to the normal range



Blood Glucose Regulation

- The central "seesaw" pivot represents **homeostasis**, the body's drive to maintain blood glucose within a narrow normal range
- Insulin and glucagon work in opposition to keep the system balanced
- The liver is the key storage and release site, appearing in both halves of the cycle
- This is the system that fails in diabetes: in Type 1, insulin is absent; in Type 2, the cells stop responding to it effectively

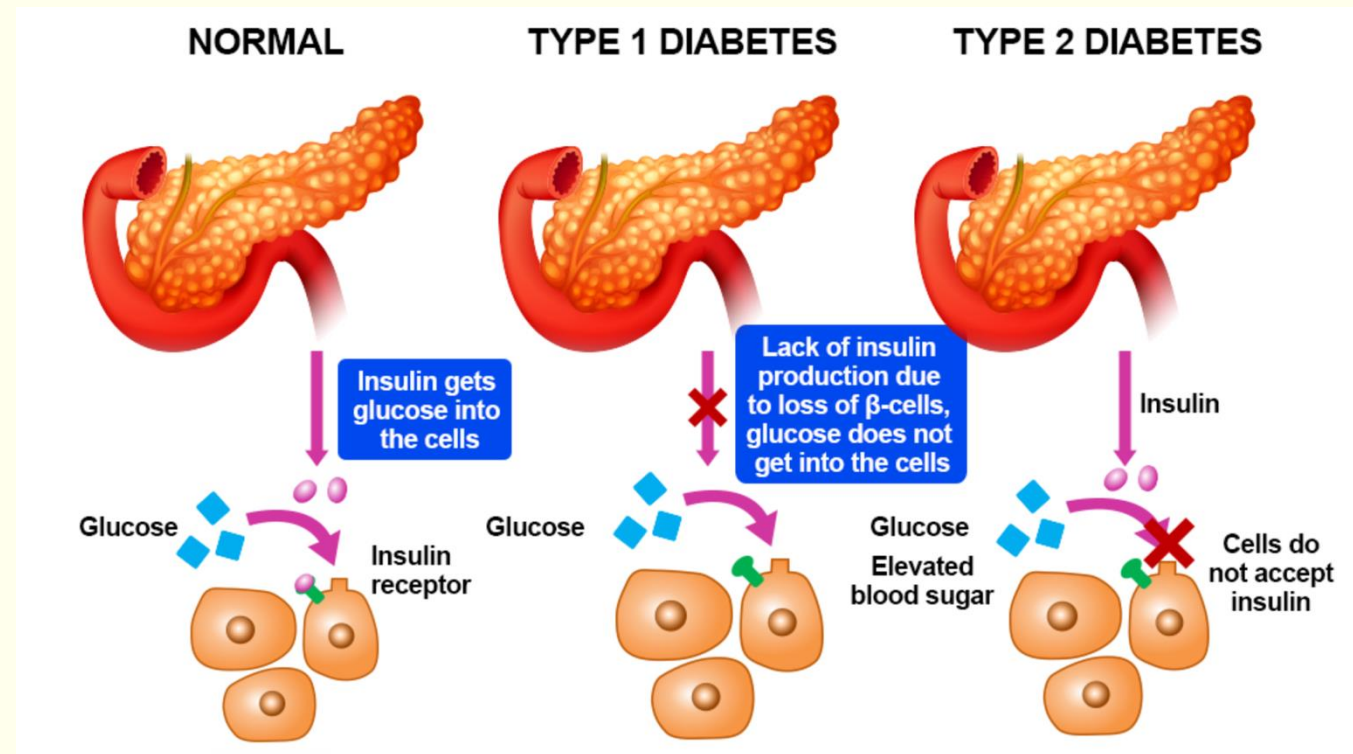


Diabetes

Diabetes

- Type 1
- Type 2
- Latent Autoimmune Diabetes in Adults (LADA)
- Maturity Onset Diabetes of the Young (MODY)
- Type 3c (Pancreatogenic Diabetes)
- Secondary/Drug-Induced Diabetes

Diabetes, Insulin and Insulin Resistance



Type 1 Diabetes

Type 1 Diabetes Prevalence

Globally: an estimated 9.5 million people are living with Type 1 diabetes, including 1.9 million under the age of 20 (IDF Diabetes Atlas, 11th Edition, 2025)

UK: is ranked 5th globally for the highest number of people living with Type 1

- Approximately 400,000 people in the UK have Type 1

Wales: approximately 17,600 people live with Type 1 (8% of the 220,000 total diabetes cases, with prevalence around 0.32%)

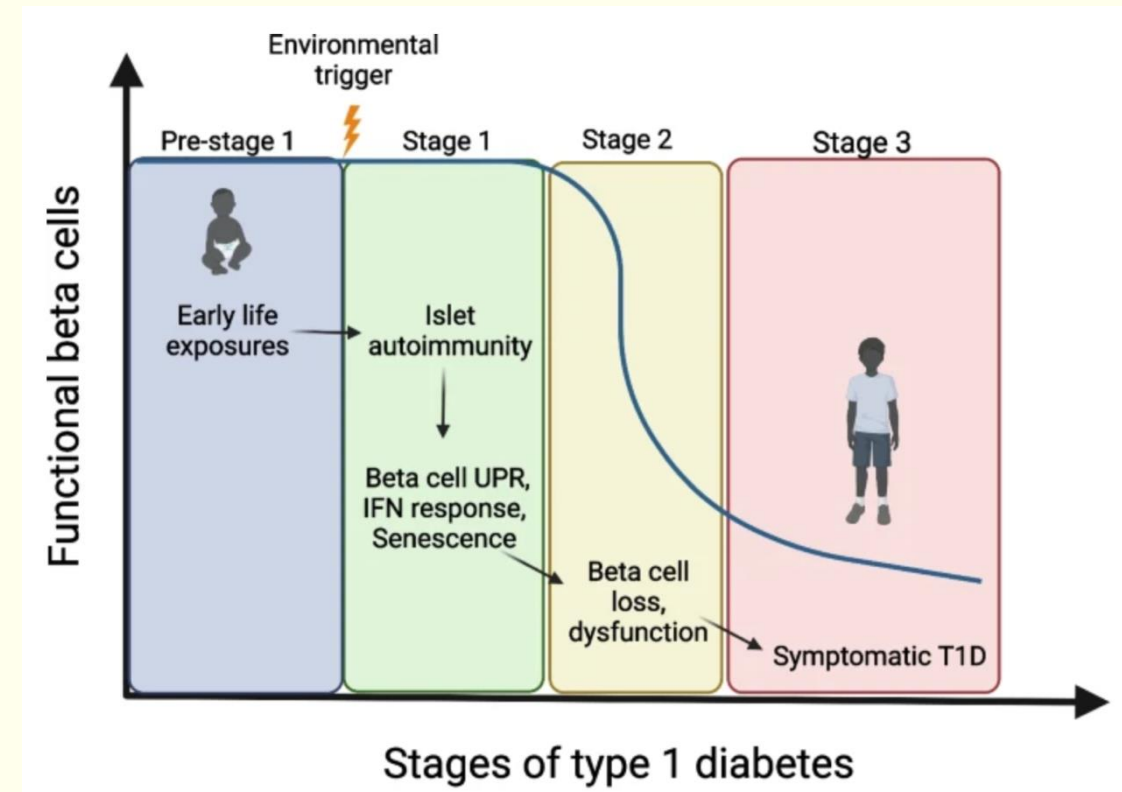
Type 1 Diabetes Incidence

- Type 1 is most commonly diagnosed in children and young adults, though it can occur at any age
- Peak diagnosis age: typically between 10 and 14 years
- Incidence is rising globally at approximately 3 to 4% per year

The reasons for this rise are not fully understood

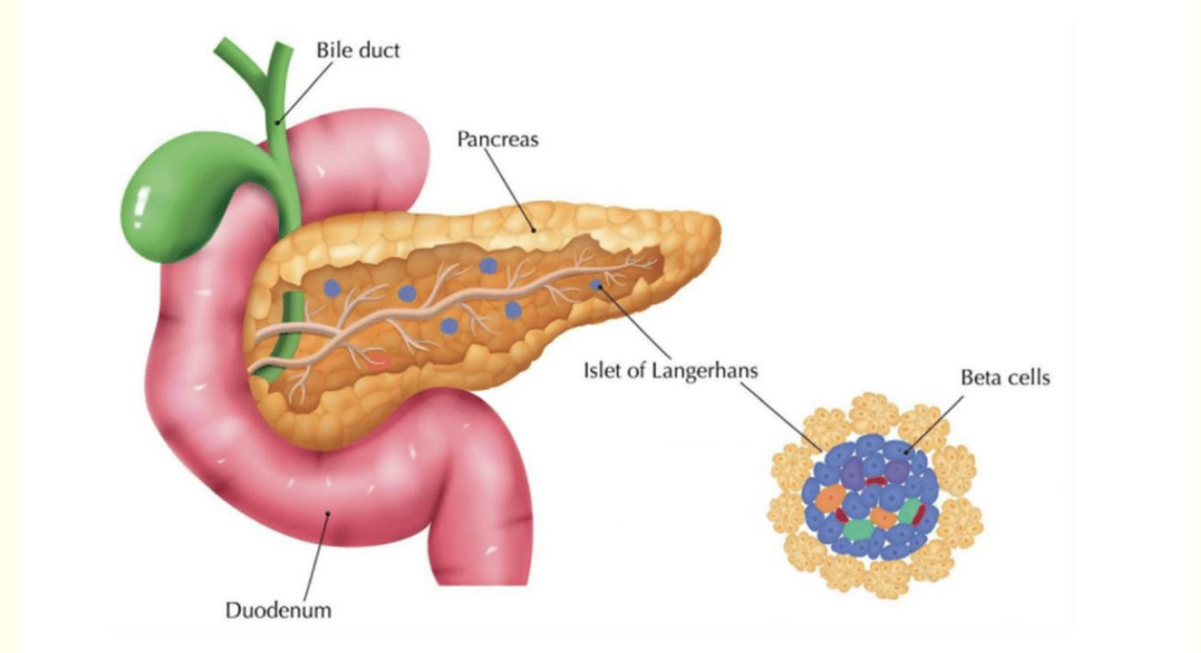
Type 1 Diabetes Aetiology

- **AUTOIMMUNE:** immune system T-cells destroy insulin-producing beta cells of the pancreas
- Immune spectrum pattern 1: the body attacking itself
- Genetic susceptibility: HLA genes (HLA-DR3, HLA-DR4)
- Environmental triggers under investigation: viral infections (enteroviruses), possibly early dietary factors
- **NOT caused by lifestyle: not sugar, not obesity, not inactivity**



Type 1 Diabetes Pathology

- Progressive destruction of beta cells by T-cell mediated autoimmunity
- By the time of diagnosis, 80 to 90% of beta cells are already destroyed
- Absolute insulin deficiency: the body cannot produce insulin at all
- Without exogenous insulin, the condition is fatal



Type 1 Diabetes

Signs and Symptoms

RAPID onset (days to weeks). The key symptoms are known as the '4 Ts':

- **Thirst:** (polydipsia): excessive, unquenchable thirst
- **Toilet:** (polyuria): frequent urination, including at night
- **Tired:** profound fatigue because cells cannot access glucose for energy
- **Thinner:** weight loss despite normal or increased eating, as the body breaks down fat and muscle for fuel

Risk of diabetic ketoacidosis (DKA) at diagnosis or if insulin missed: a medical emergency

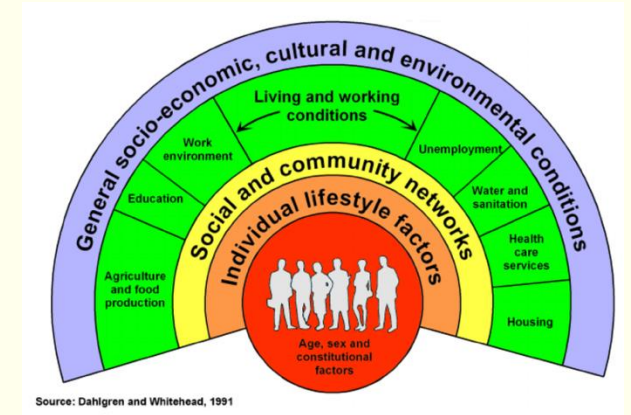
Type 1 Diabetes

Risk Factors

Non-modifiable Risk Factors

All major risk factors are NON-MODIFIABLE

- **Genetic:** susceptibility (HLA-DR3, HLA-DR4)
- **Family history:** of Type 1 diabetes
- Presence of other autoimmune conditions (coeliac disease, autoimmune thyroid disease)
- Autoimmune conditions cluster in families and in individuals
- **Environmental:** triggers (viral infections) are under investigation but not yet confirmed



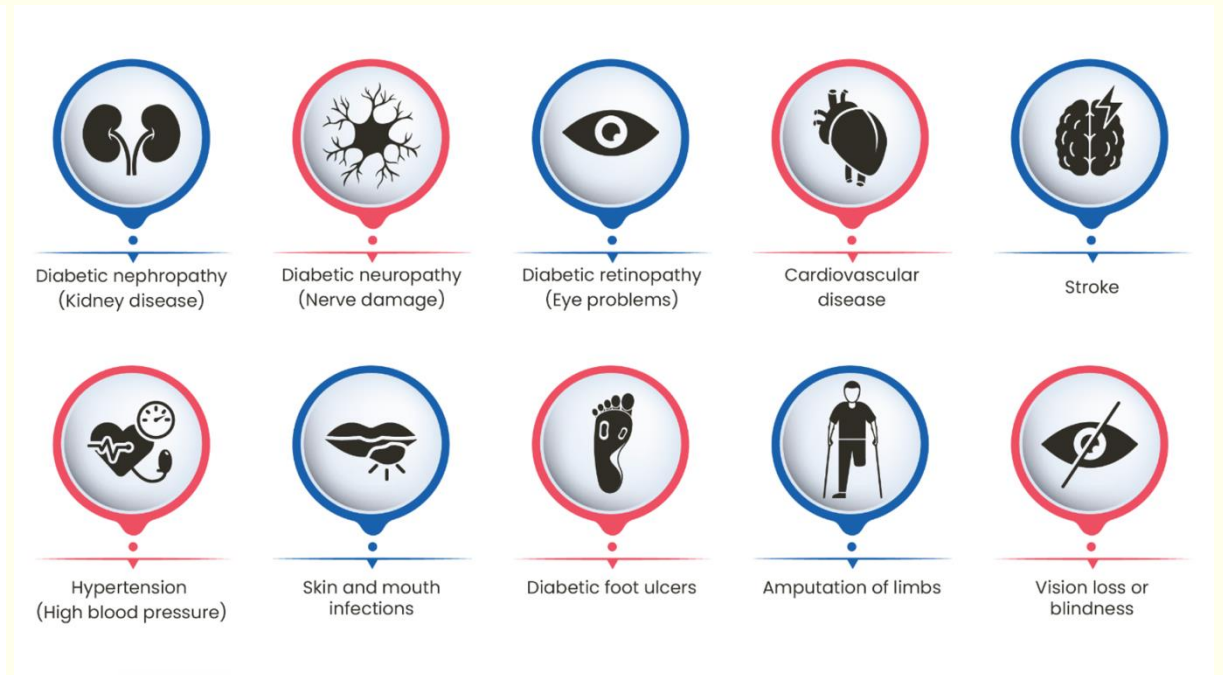
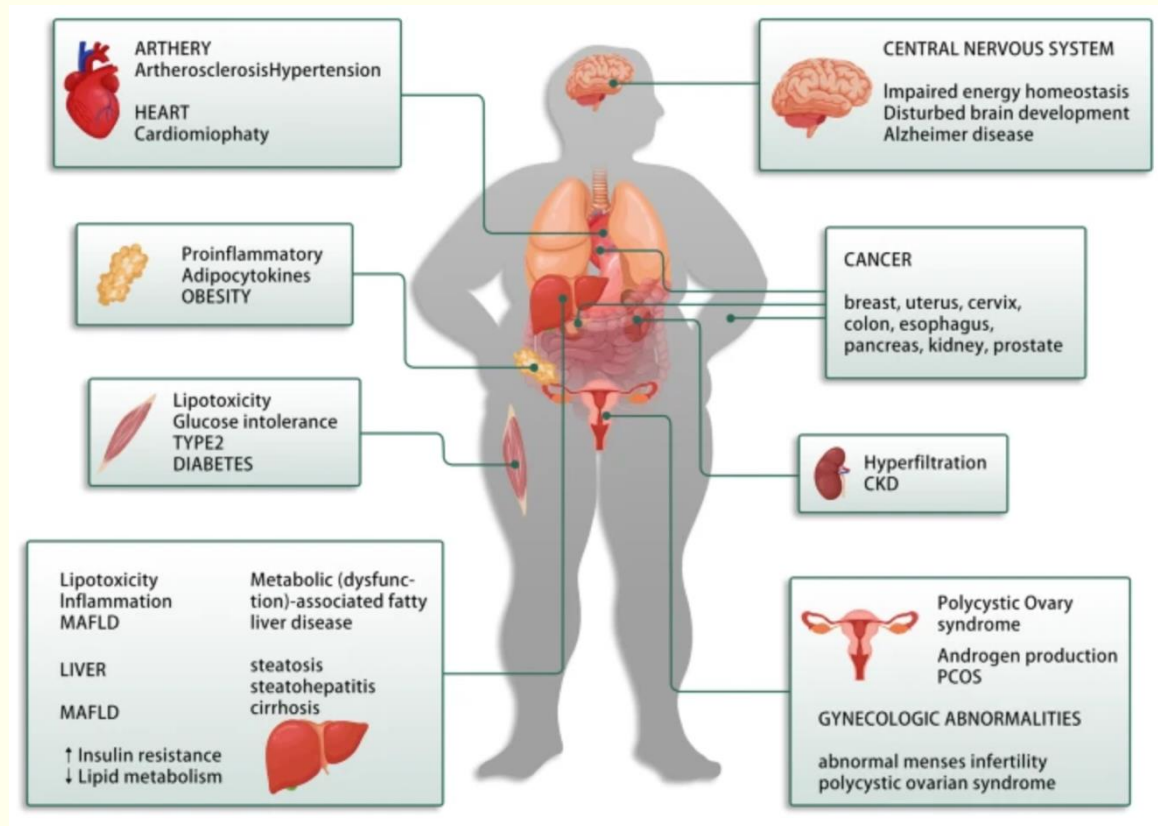
Type 1 Diabetes

Quality of Life

- Lifelong insulin dependency: multiple daily injections or insulin pump
- Constant blood glucose monitoring (increasingly via continuous glucose monitors)
- Ever-present risk of hypoglycaemia: confusion, seizures, loss of consciousness
- Significant psychological burden, particularly in children and young adults
- Impact on education, employment, relationships, and mental health
- Long-term complications: retinopathy (eyes), nephropathy (kidneys), neuropathy (nerves), significantly increased CVD risk

Type 1 Diabetes

Quality of Life



Type 2 Diabetes

Type 2 Diabetes Prevalence

Accounts for approximately 90% of all diabetes globally and in the UK

- **UK:** approximately 4.14 million people diagnosed with Type 2 (Diabetes UK, 2025)
- An estimated 1.3 million more living with undiagnosed Type 2 diabetes
 - A further 6.3 million with prediabetes (blood glucose elevated but below diagnostic threshold)
- **Wales:** approximately 198,000 diagnosed T2 (90% of 220,000 total). Highest prevalence of any UK nation: 7.6% vs 6.9% UK average
 - An estimated 65,000 undiagnosed cases in Wales, with 350,000 at high risk

Type 2 Diabetes Incidence

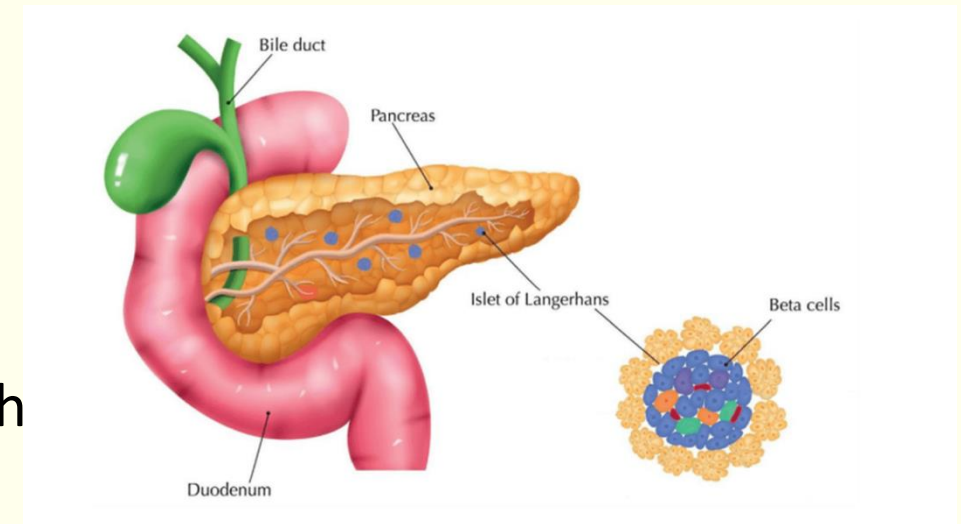
- Type 2 diabetes incidence in the UK is rising, with over 4.6 million people diagnosed as of 2023–2024, nearly 1.3 million people could be living with type 2 diabetes who are yet to be diagnosed (Diabetes UK)
- Critical shift: incidence is moving to younger age groups. The number of under-40s diagnosed increased by 40% between 2016/17 and 2022/23 (168,000 under-40s now affected)
- Mean age at diagnosis has decreased: by 5.5 years in women (to 58.5 years) and 2.5 years in men (to 58.8 years)
- Young-onset T2 is associated with faster beta cell decline, earlier complications, and greater life-years lost

Type 2 Diabetes Aetiology

- Core mechanism: **INSULIN RESISTANCE**. Cells become less responsive to insulin (the locks have changed)
- Pancreas compensates by producing more insulin, but beta cells eventually become exhausted
- Relative insulin deficiency (keys exist but are less effective)
- Multifactorial: genetics, central obesity, physical inactivity, dietary patterns, age, ethnicity
- NOT simply 'eating too much sugar'

Type 2 Diabetes Pathology

- Gradual progression over years, often with a long pre-diabetic phase
- During this phase, the pancreas compensates by overproducing insulin
- Beta cell dysfunction worsens progressively as compensation fails
- Chronic hyperglycaemia damages blood vessels through both microvascular and macrovascular pathways
- Same vascular damage mechanism as discussed in Week 2 (CVD): this is why diabetes is a major cardiovascular risk factor



Type 2 Diabetes

Signs and Symptoms

Insidious onset, often asymptomatic for years (hence the large undiagnosed population)

- When symptoms appear: fatigue, increased thirst, frequent urination, blurred vision
- Slow wound healing, recurrent infections (UTIs, thrush)
- Some patients diagnosed only through routine blood tests or when a complication presents (foot ulcer, retinopathy, cardiovascular event)

Type 2 Diabetes

Risk Factors

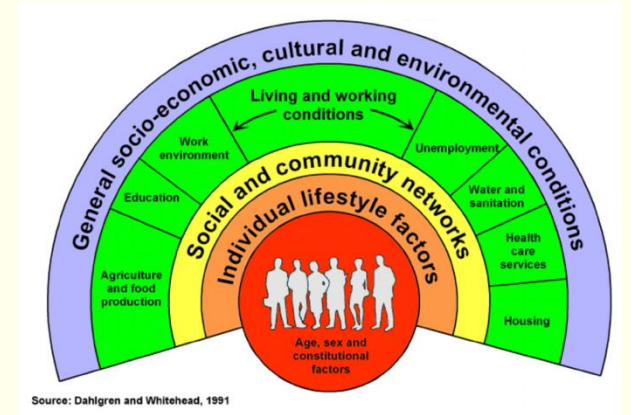
Non-modifiable Risk Factors

Age: (over 40, or over 25 in South Asian/Black populations)

Ethnicity: South Asian, Black Caribbean, Black African populations face 2 to 6 times higher risk than White European populations

Family history: risk increases to 75% if both parents have T2

Clinical History: of gestational diabetes, polycystic ovary syndrome

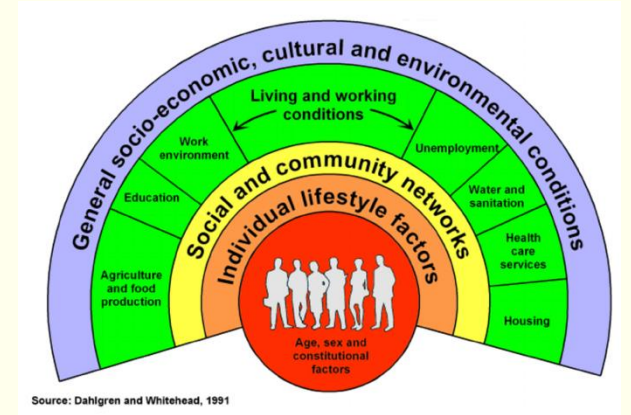


Type 2 Diabetes

Risk Factors

Modifiable Risk Factors

- Central obesity (waist circumference more important than BMI as a predictor)
- Physical inactivity
- Dietary patterns
- Smoking
- Socioeconomic deprivation (access to food, exercise, healthcare)



Type 2 Diabetes

Quality of Life

- Progressive condition: management escalates over time (lifestyle, then oral medication, then possibly insulin)
- Significant self-management burden
- Complications: retinopathy, nephropathy, neuropathy, peripheral arterial disease, foot ulcers/amputations, CVD
- Depression 2 to 3 times more common in people with diabetes
- Diabetes distress: the emotional burden of constant self-management
- Social stigma and blame are persistent problems

Gestational Diabetes

Gestational Diabetes

Gestational diabetes: glucose intolerance first identified during pregnancy

- Affects 4 to 5% of pregnancies in the UK (higher in certain ethnic groups)
- Caused by placental hormones creating insulin resistance
- Usually resolves after delivery
- BUT significantly increases lifetime risk of developing T2 diabetes (up to 50% within 5 to 10 years)

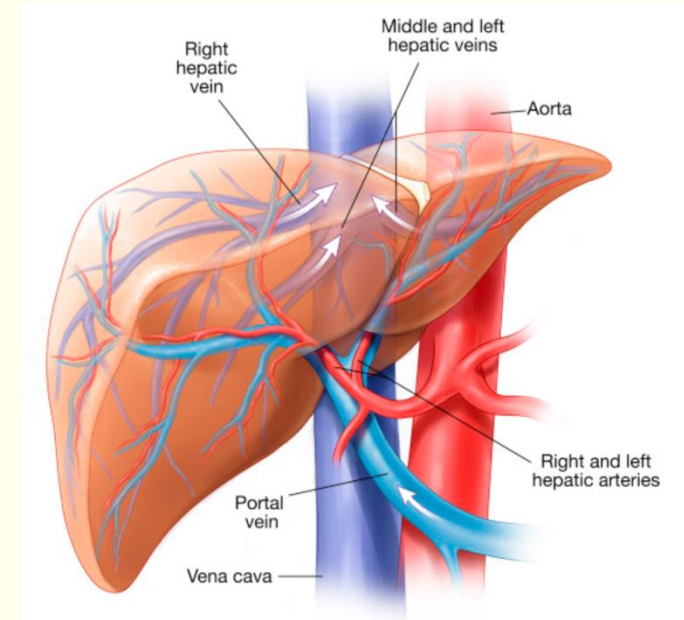
Women with a history of gestational diabetes need long-term metabolic monitoring

The Liver and Metabolic Dysfunction-associated Steatotic Liver Disease (MDSLD)

The Liver

The liver performs over 500 functions

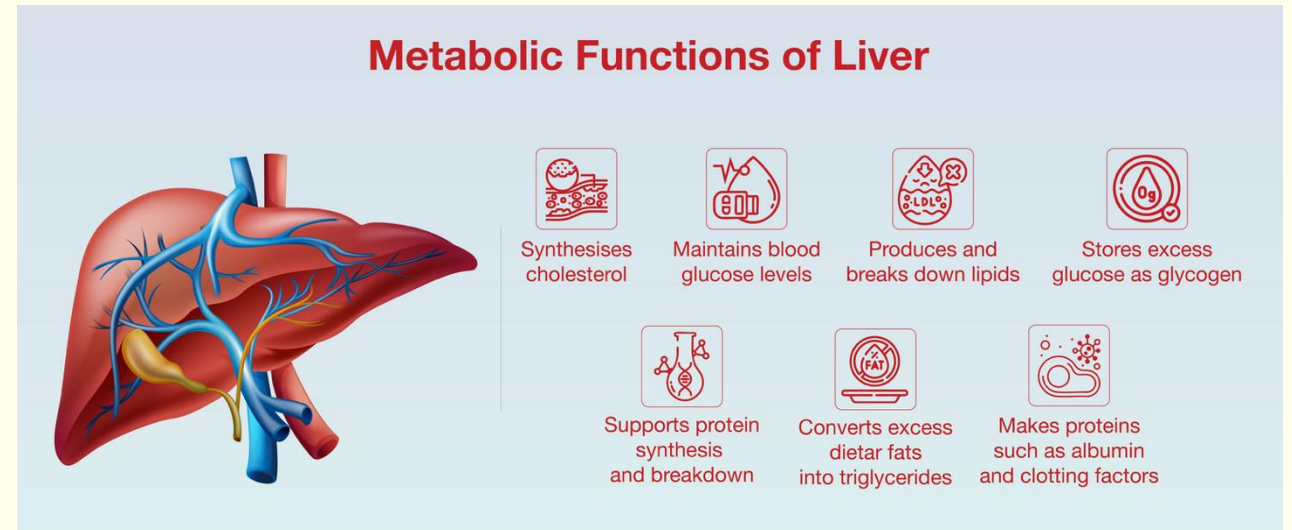
- The liver is the body's metabolic processing plant
- Everything absorbed from the gut passes through the liver first via portal circulation



Metabolic Functions of the Liver

Key metabolic roles:

- Glucose storage and release (as glycogen)
- Lipid metabolism (cholesterol, triglycerides)
- Protein synthesis (albumin, clotting factors)
- Detoxification
- Bile production



Metabolic Dysfunction-associated Steatotic Liver Disease (MDSLD)

- Renamed from NAFLD (non-alcoholic fatty liver disease) in 2023.
- New name: MASLD (metabolic dysfunction-associated steatotic liver disease)
- New name reflects the metabolic aetiology and removes the stigmatising 'non-alcoholic' label
- Diagnosis now requires at least one metabolic risk factor to be present
- Know both terms: NAFLD still appears widely in older literature and clinical practice

MDSLD

Prevalence

Globally: most common chronic liver disease, estimated to affect approximately 30% of the adult population worldwide

- By 2040, global adult prevalence is projected to exceed 55%

UK: estimated 1 in 5 adults affected (British Liver Trust)

- UK forecasts: from 9.9 million prevalent cases in 2024 to 10.4 million by 2032 (GlobalData)

Most cases are undiagnosed because early stages produce no symptoms

MDSLD

Incidence

Globally: new cases of MASLD-related chronic liver disease nearly doubled, from approximately 25 million in 1990 to 48 million in 2021 (Global Burden of Disease, 2021)

- Up to 30% of people with MASLD progress to MASH

UK: rates of new diagnoses are increasing in line with rising obesity and metabolic syndrome

Wales: incidence of MASLD increased tenfold between 1999 and 2019

- MASLD has been the leading cause of new liver disease diagnoses in Wales since 2014, overtaking alcohol-related liver disease
- New cases rising in younger adults and adolescents, mirroring the rise in obesity and metabolic syndrome

MASLD

Aetiology

- Driven by insulin resistance (the same mechanism as Type 2 diabetes, manifesting in a different organ)
- When insulin signalling is impaired, excess free fatty acids accumulate in liver cells (hepatocytes)
- Strongly associated with central obesity, Type 2 diabetes, dyslipidaemia, and metabolic syndrome

MASLD

Pathology

Five stages of progression:

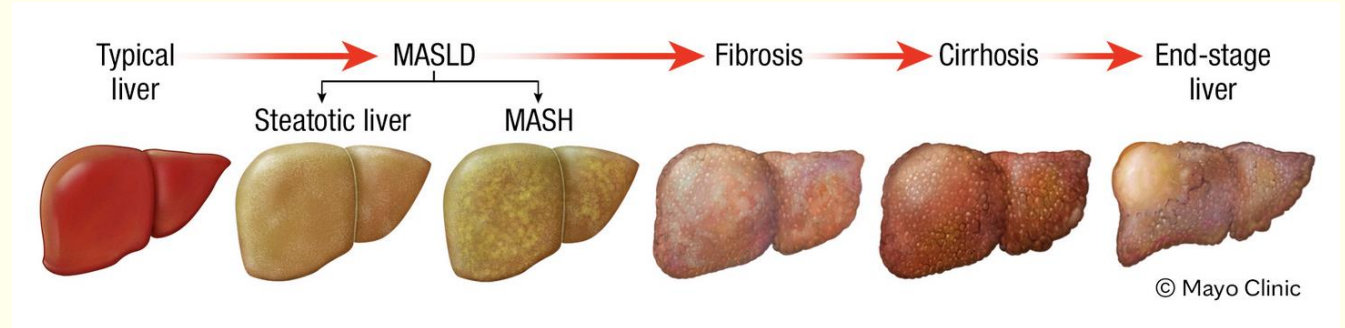
Stage 1: Simple steatosis. Fat accumulates in liver cells. Often benign, may remain stable for years

Stage 2: Steatohepatitis: (MASH, formerly NASH). Fat plus inflammation. The critical transition point

Stage 3: Fibrosis: Chronic inflammation causes scarring of liver tissue. Function begins to decline

Stage 4: Cirrhosis: Irreversible, extensive scarring. Major loss of liver function. Portal hypertension

Stage 5: (in some cases): Hepatocellular carcinoma (liver cancer)



MASLD

Pathology

- Most people remain at the steatosis stage
- Approximately 20 to 30% progress to MASH
- Of those, a smaller proportion develop fibrosis and cirrhosis.



MASLD

Signs and Symptoms

Largely asymptomatic in early stages

- Some patients report fatigue or vague discomfort in the upper right abdomen
- Often found incidentally on blood tests (elevated liver enzymes, particularly ALT) or imaging (ultrasound)
- Advanced disease may present with: jaundice, ascites (fluid accumulation in the abdomen), portal hypertension

MASLD

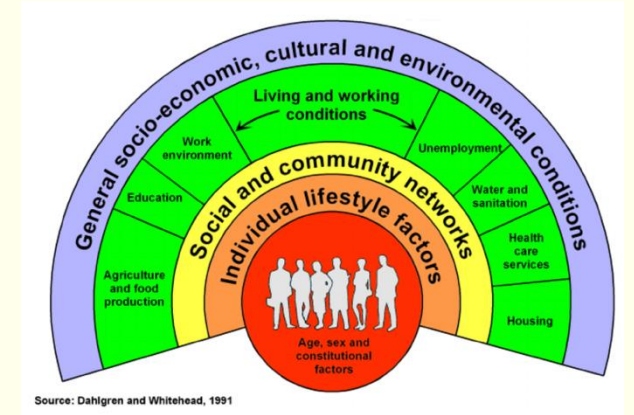
Risk Factors

Non-modifiable Risk Factors

Genetic: The PNPLA3 gene variant affects how the liver processes fat and is associated with increased susceptibility to MASLD and faster progression.

Increasing Age

Ethnicity: higher prevalence in Hispanic populations



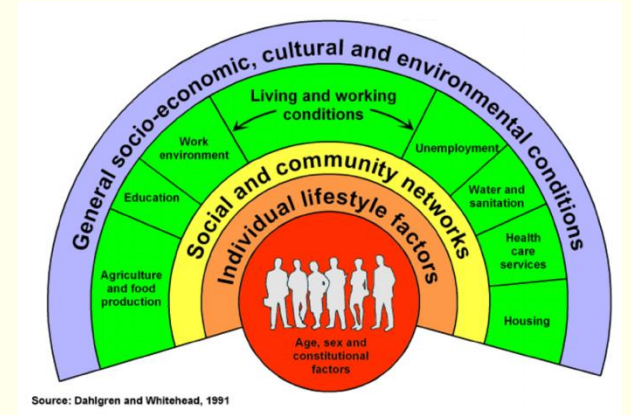
MASLC

Risk Factors

Modifiable Risk Factors

- Central obesity
- Type 2 diabetes
- Dyslipidaemia
- Metabolic syndrome

→ Reducing body weight by 5 to 10% can reverse steatosis at early stages



MASLD

Quality of Life

- Anxiety about disease progression, particularly for those beyond simple steatosis
- Stigma: liver disease is frequently assumed to be alcohol-related
- Limited pharmacological options: lifestyle modification is the primary treatment
- Weight loss is effective but difficult to sustain
- Liver disease mortality in Wales has increased approximately 400% since 1970.
- Premature deaths from chronic liver disease have more than doubled in the last twenty years

Break



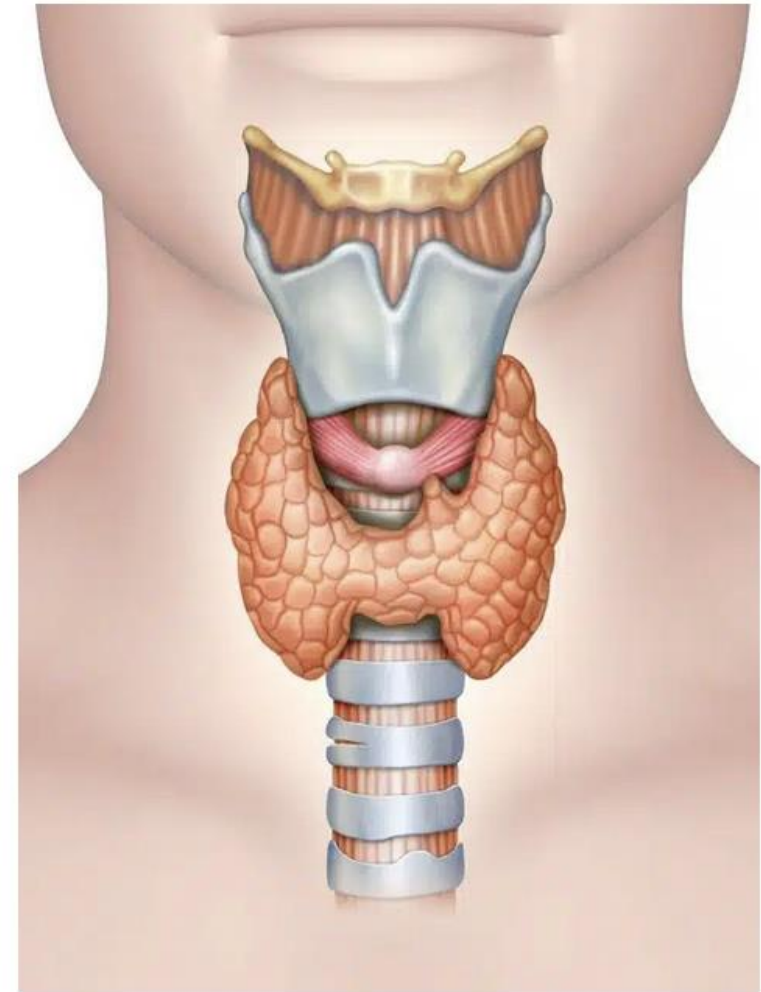
Prifysgol Cymru
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Trawsnewid Addysg, Trawsnewid Bywydau
Transforming Education, Transforming Lives

Thyroid Diseases

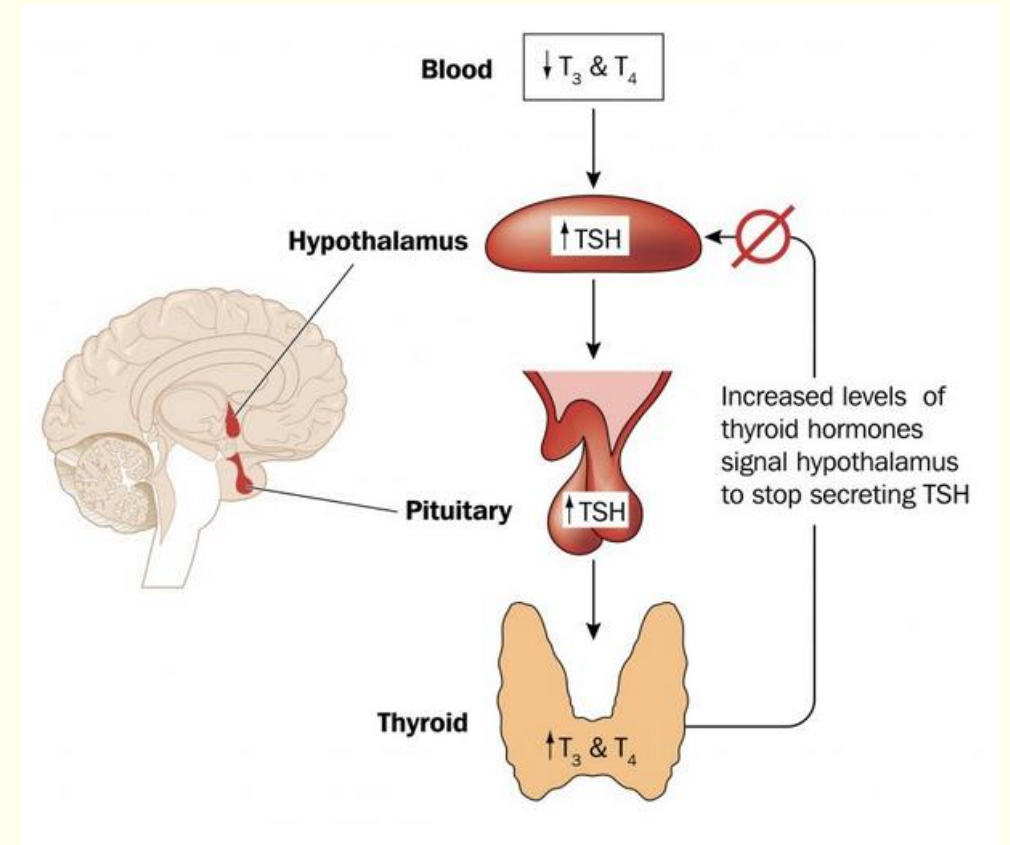
The Thyroid Gland

- The Thyroid gland: a butterfly-shaped gland at the front of the neck
- Produces T3 (triiodothyronine) and T4 (thyroxine)
- These hormones set the body's metabolic rate: how fast or slow every cell works



The Thyroid Gland

- Regulated by TSH (thyroid-stimulating hormone) from the pituitary gland
- Too little thyroid hormone = everything slows down (hypothyroidism)
- Too much thyroid hormone = everything speeds up (hyperthyroidism)
- Both the most common thyroid diseases (Hashimoto's and Graves') are autoimmune



COMPARISON	HYPOTHYROIDISM (Hashimoto's)	HYPERTHYROIDISM (Graves' disease)
Aetiology: Autoimmune	Hashimoto's: antibodies DESTROY thyroid	Graves': antibodies STIMULATE thyroid
Metabolism	Slows down	Speeds up
Weight	Gain	Loss (despite eating more)
Temperature	Cold intolerance	Heat intolerance
Heart rate	Slow (bradycardia)	Fast (tachycardia), palpitations
Energy/mood	Fatigue, depression, brain fog	Anxiety, irritability, insomnia
Bowel	Constipation	Diarrhoea
Skin/hair	Dry skin, brittle hair	Warm moist skin, hair thinning
Unique signs	Puffy face, hoarse voice	Bulging eyes, tremor, goitre
Who?	Women 5 to 10x more; risk rises with age	Women 5 to 10x more; peak 30 to 60 yrs
Treatment	Levothyroxine (lifelong)	Anti-thyroid drugs, radioiodine, or surgery

Pulling it all together

Organ	What it does	Associated Metabolic Disease
Pancreas	Regulates blood glucose via insulin and glucagon	Diabetes
Liver	Metabolic hub: glucose storage, lipid metabolism, detoxification, protein synthesis	MASLD (metabolic dysfunction-associated <u>steatotic</u> liver disease)
Thyroid	Sets the body's metabolic rate via T3 and T4 hormones	Hypothyroidism / Hyperthyroidism

The interconnectivity of chronic diseases

The autoimmune disease thread continues: Week 5 (Rheumatoid Arthritis) and Week 6 (Multiple Sclerosis)

Obesity as a cross-cutting risk factor will be covered properly in Week 10 (Diagnosis, Treatment and Lifestyle Management)

Diabetes complications connect to the CVD content from Week 2 and will reappear in later weeks

The constrained energy model challenges 'calories in, calories out' thinking and has implications for professional practice

Next Week: Musculoskeletal Conditions

Questions?

