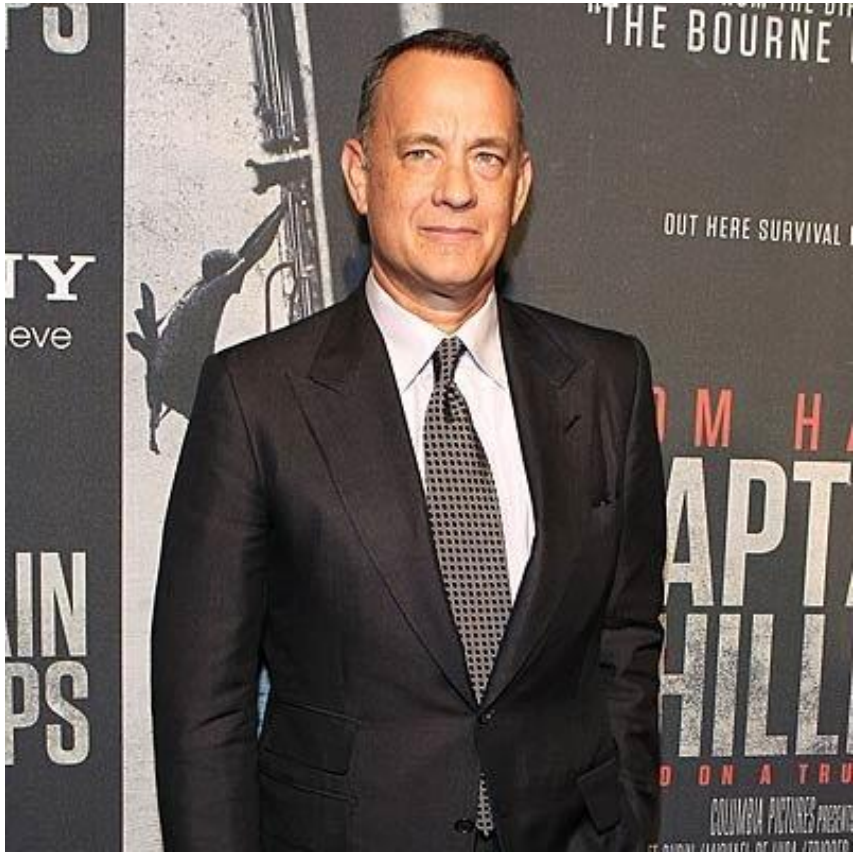
Cathy Lynch

UP 2019

Acknowledgement to Mrs. Karen Bettanay

Wasim Akram (T1)

Tom Hanks (T2)



Objectives

- **Overview of Diabetes**

- **Use cases to**
  - Discuss clinical use of medications
  - Consider factors influencing drug selection
  - Identify ADRs and areas of concern for drugs used in diabetes
  - Identify monitoring required for patients taking these medication
  - Discuss complications and risk factors

Diabetes – the stats

In 2015

- 1 in 11 adults has diabetes (415 million)
- 12% of global health expenditure is spent on diabetes
- One in two (46.5%) adults with diabetes is undiagnosed
- 75% of people with diabetes live in low- and middle-income countries
- ↓ life expectancy by 15 years(65% of deaths-heart disease, CVA)
- leading cause of new cases of blindness among adults(20-74)
- leading cause of ESRF, accounting for 44% of new cases
- 73% BP> 130/80 mmHg or use prescription medications for HTN
- 60-70% mild-severe forms of neurological disease

In Sri Lanka

- **Prevalence**
  - 10.3% with diabetes
  - 11.5% with pre-diabetes

- **Risk factors identified**
  - family history
  - urban residence
  - age
  - higher BMI and larger waist circumference
  - sedentary lifestyle
  - hypertension

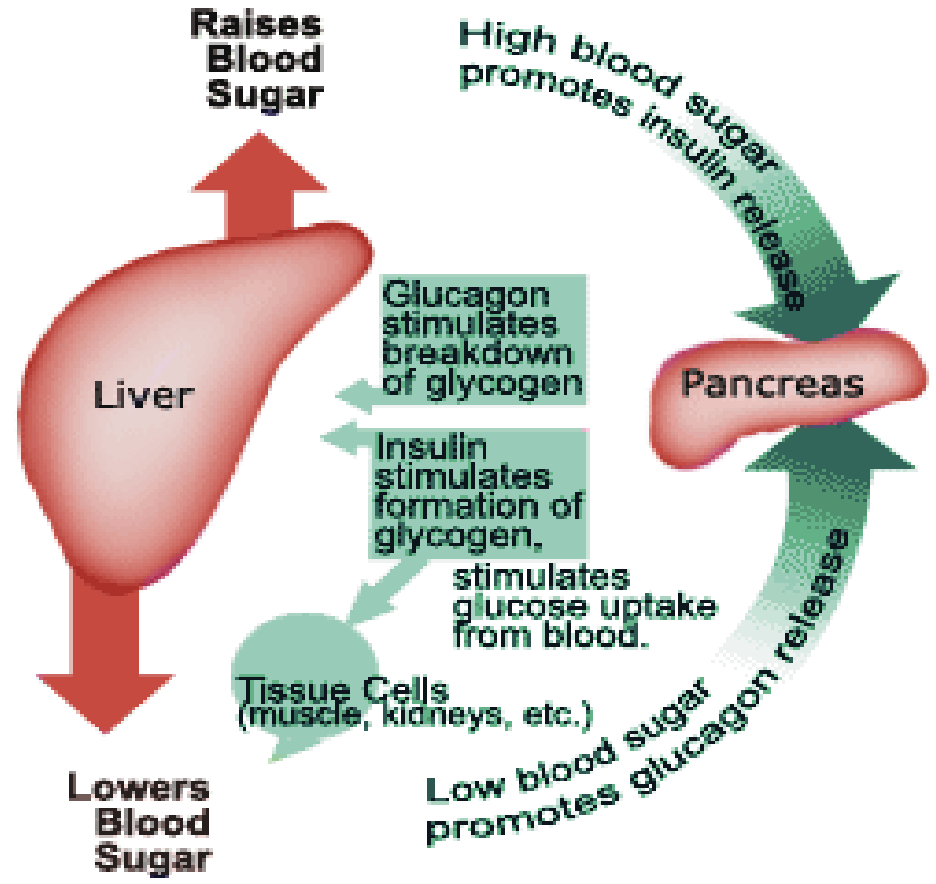
BMC Public Health 2012 Ranil JayawardenaEmail author, Priyanga Ranasinghe, Nuala M Byrne, Mario J Soares, Prasad Katulanda and Andrew P Hillsa

Activity

In groups, discuss

1. What happens in diabetes (think pancreas, liver, blood stream and cells)?
2. What are the actions of insulin?
3. What are the different types of diabetes?
4. What is the difference between Type 1 and Type 2?
5. What drugs can induce diabetes?
6. What are the symptoms of diabetes?
7. What are some of the tests used in diabetes?
8. What are some of the risk factors for diabetes?
9. What are some of the complications of diabetes?
10. Why do we need medication?

What happens



Chemistry involved in normal regulation of blood sugar

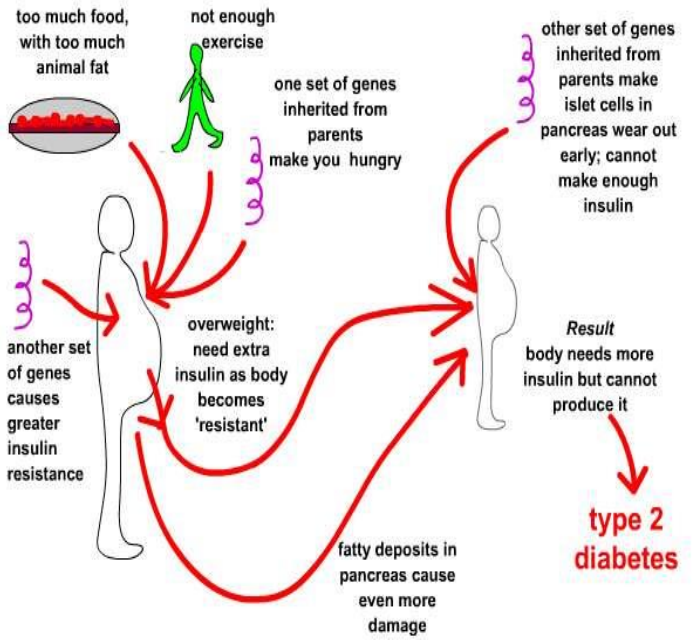
Insulin Actions

- Lowers blood glucose by facilitating glucose uptake in skeletal muscle and adipose tissue
- Prevents fat and glycogen breakdown
- Reduces hepatic glucose output
- Decreases lipolysis and stimulates lipid synthesis
- Increases protein synthesis

ie. an anabolic hormone

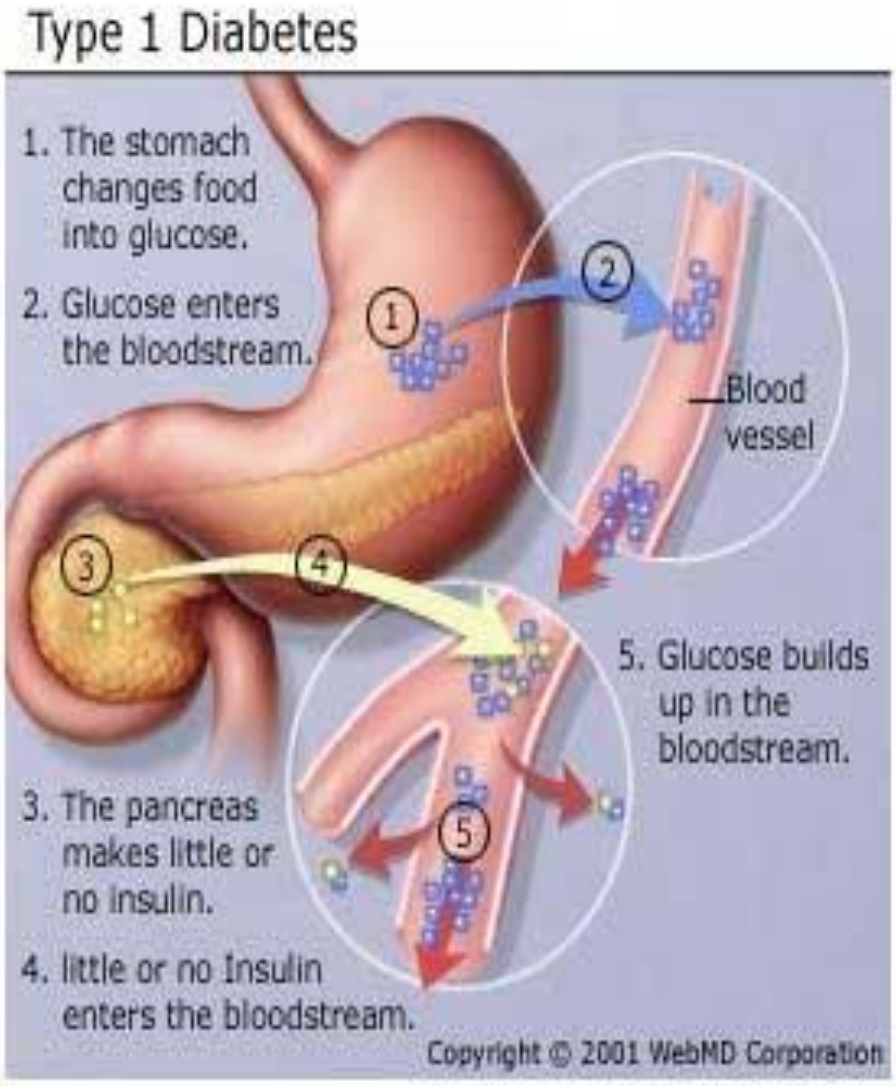
Types of diabetes

- Type 1 diabetes
- Type 2 diabetes
- Gestational diabetes
- Drug induced diabetes



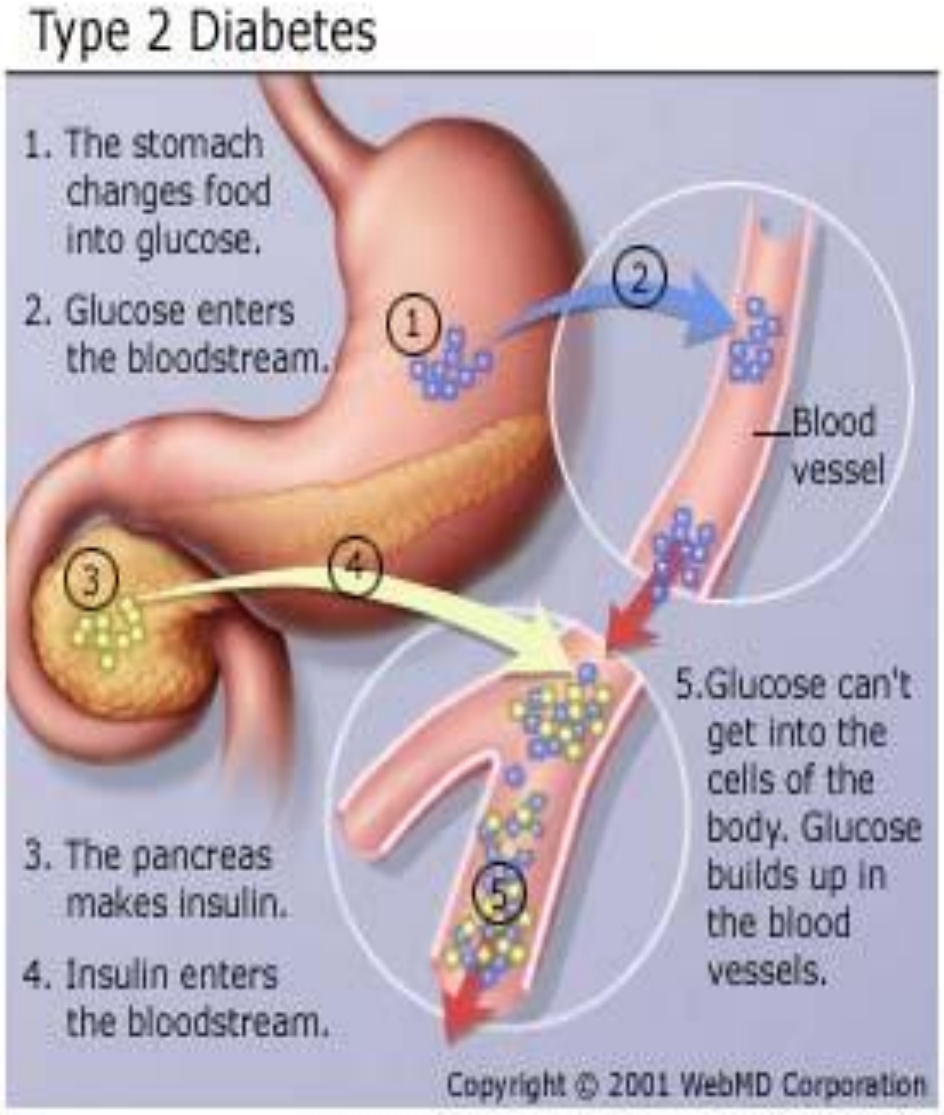
Type 1 Diabetes Mellitus (T1DM)

- Immune-mediated destruction of insulin producing beta cells
- Young (generally)-can occur at any age
- Genetic susceptibility
- Rapid onset
- Ketosis
- Insulin deficient
- Recent weight loss
-



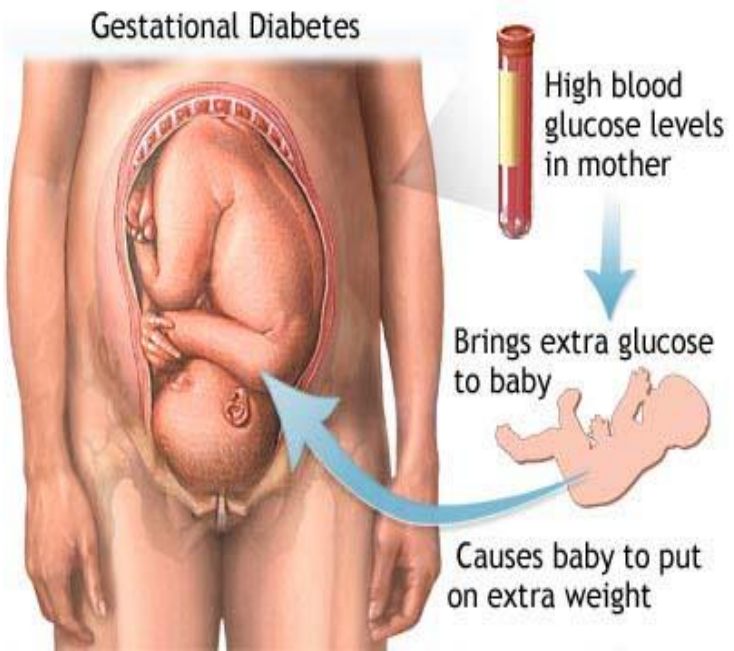
Type 2 Diabetes Mellitus (T2DM)

- Onset in Middle Age (generally)
- Slow onset
- Often asymptomatic
- Insufficient insulin is produced and body is resistant to insulin
- Not prone to ketosis
- Life style factors eg overweight
- High risk groups –indigenous, and southern Asian
- Most common form



Gestational Diabetes

- Occurs during pregnancy
- Usually goes away after delivery (10-50% Type 2 within 5 yrs)
- Up to 9% develop gestational diabetes around 24th-28thweek
- Risk factors
  - age > 30yrs
  - family history of type 2 diabetes
  - overweight
  - certain ethnic groups



Drug Induced Diabetes ?
Any ideas

- Prednisone
- Atypical antipsychotics such as olanzapine, clozapine
- Thiazide diuretics
- Beta blockers
- Thyroid hormone
- Interferon
- Cyclosporin , tacrolimus
- Proteases (eg ritonivir, indinavir)

Insulin Resistance

Risk factors:

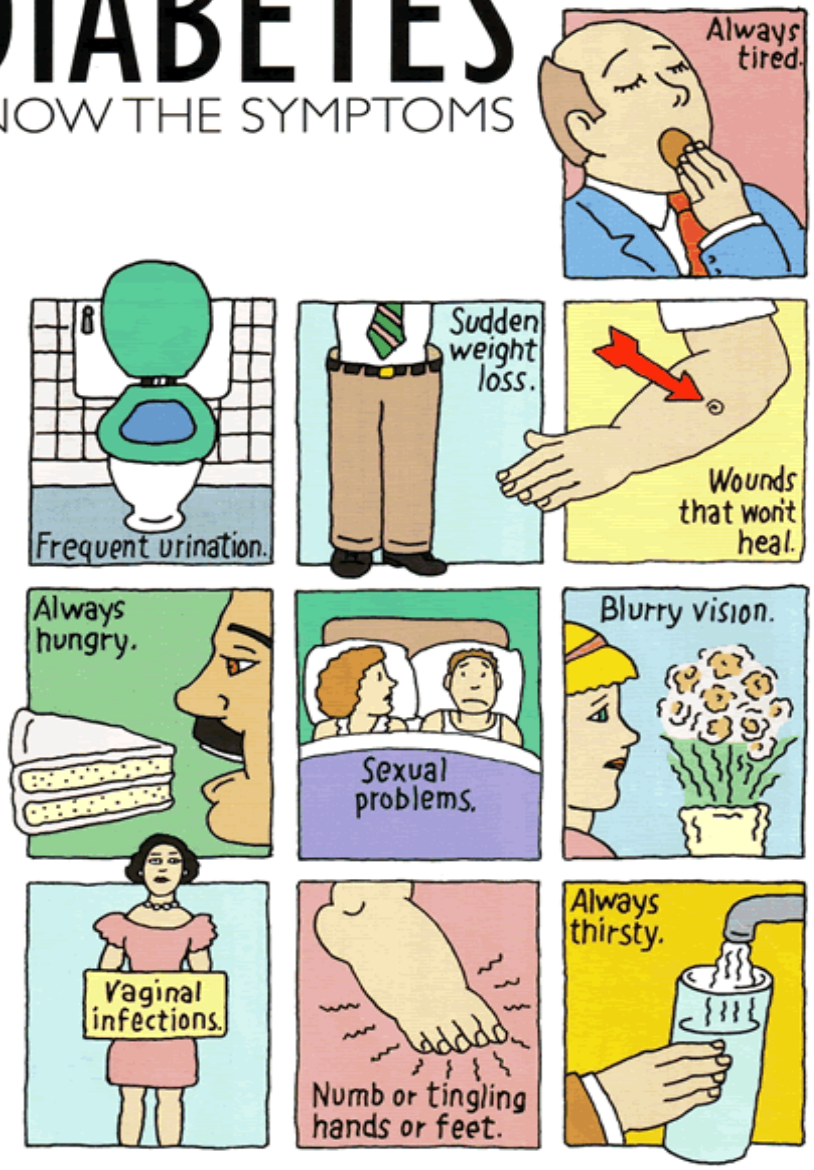
- Obesity, especially if "central"
- Pregnancy
- Polycystic ovarian syndrome
- Insulin resistant parent(s)
- Inactivity
- Systemic illness/drugs
- Rarities e.g. some genetic defects

Symptoms of Diabetes

- Excessive thirst
- Passing more urine
- Skin infections
- Blurred vision
- Unexplained weight loss
- Mood swings
- Headaches
- Feeling tired and lethargic
- Always feeling hungry
- Slow healing cuts
- Itching
- Feeling dizzy
- Leg cramps

DIABETES

KNOW THE SYMPTOMS



If you have any of these symptoms, see your doctor. For more information about diabetes call Eli Lilly and Company at 1-800-545-5979 or Boehringer Mannheim Corporation at 1-800-858-8072.

Provided as an educational service by Eli Lilly and Company and Boehringer Mannheim Corporation

Measurements

- **Fasting blood glucose test** -check blood glucose levels after fasting for between 12 and 14 hours. You can drink water
- **Random blood glucose test** -check blood glucose levels at various times during the day.
- **Oral glucose tolerance test (OGGT)** -high glucose drink consumed and blood samples taken at regular intervals for two hours after the drink.
- **Glucose Challenge Test** -(often used in screening for gestational diabetes) 50g or 75g glucose drink over 10 mins. Venous blood test in 1 hr. At risk of diabetes if 7.8 mmol/L(50g) or 8mmol/L (75g) then do OGTT

Diagnostic thresholds for diabetes (Table 18.2) [NB1] [NB2]

Test	Prediabetes thresholds	Diabetes thresholds
glycated haemoglobin (HbA1c) [NB3]	no Australian HbA1c values for prediabetes defined at the time of writing; see Interpreting HbA1c diagnostic tests]	48 mmol/mol (6.5%) or more [NB4]
venous blood glucose concentration [NB5]		
fasting	6.1 to 6.9 mmol/L	7 mmol/L or more
nonfasting	between 7.8 and 11 mmol/L, consider further diagnostic testing	11.1 mmol/L or more
oral glucose tolerance test		
venous blood glucose concentration 2 hours after a 75 g oral glucose tolerance test [NB5]	7.8 to 11 mmol/L	11.1 mmol/L or more

Treatment targets

- Adjust treatment targets individually
- Intensive treatment may be inappropriate, eg when risk of (and from) hypoglycaemia is unacceptable, such as in severe concomitant disease, the very elderly
- Generally, treatment targets are:
  - fasting blood glucose, <6 mmol/L (106mg/dL)
    - Pre-diabetes 100-126mg/dL (Diabetes Sri Lanka)
  - random blood glucose, < 7.8mmol/L (140mg/dL)

Monitoring Glycated Haemoglobin (HbA1c)

- Good guide of average blood glucose level over last 3 months
- Hb is present in everyone's red blood cells. Glucose sticks to red blood cells. The more glucose in your blood the more that will stick to your red blood cells
- A red blood cell lives for 120 days.
- Test measures how many blood cells have glucose stuck to them and thus an idea of the average blood glucose over the last 3 months.
- Non diabetic HbA1c 4 - 6% (20 – 42mmol/mol) i.e. On the average 6 red blood cells out of a 100 have glucose attached to them
- HbA1c of 6.5% (48mmol/mol) is diagnostic of diabetes

Monitoring BSL

Blood sugar level (BSL)

Serum glucose level

Capillary blood sugar(CBS)

- drop of blood placed on a strip
- millimoles per litre (mmol/L)
- mg/dL

Ketones

- use urine test strips or blood monitoring
- can use same glucometer as BSL but different strips specific for ketones

At Risk Patient Groups for T2DM

- People from
  - the Indian subcontinent
  - people of Chinese origin ≥ 35 yrs
  - indigenous Australians
- Impaired OGTT, impaired fasting glucose
- Age > 45 with 1 or more of the following:
  - Obesity BMI ≥ 30
  - HTN
  - Poly Cystic Ovary Syndrome who are obese
  - Cardiovascular disease

The Australian Type 2 Diabetes Risk Assessment Tool (AUSDRISK)

1. Your age group

Under 35 years	☐	0 points
35 – 44 years	☐	2 points
45 – 54 years	☐	4 points
55 – 64 years	☐	6 points
65 years or over	☐	8 points

2. Your gender

Female	☐	0 points
Male	☐	3 points

3. Your ethnicity/country of birth:

3a. Are you of Aboriginal, Torres Strait Islander, Pacific Islander or Maori descent?

No	☐	0 points
Yes	☐	2 points

3b. Where were you born?

Australia	☐	0 points
Asia (including the Indian sub-continent), Middle East, North Africa, Southern Europe	☐	2 points
Other	☐	0 points

4. Have either of your parents, or any of your brothers or sisters been diagnosed with diabetes (type 1 or type 2)?

No	☐	0 points
Yes	☐	3 points

5. Have you ever been found to have high blood glucose (sugar) (for example, in a health examination, during an illness, during pregnancy)?

No	☐	0 points
Yes	☐	6 points

6. Are you currently taking medication for high blood pressure?

No	☐	0 points
Yes	☐	2 points

7. Do you currently smoke cigarettes or any other tobacco products on a daily basis?

No	☐	0 points
Yes	☐	2 points

8. How often do you eat vegetables or fruit?

Every day	☐	0 points
Not every day	☐	1 point

9. On average, would you say you do at least 2.5 hours of physical activity per week (for example, 30 minutes a day on 5 or more days a week)?

Yes	☐	0 points
No	☐	2 points

10. Your waist measurement taken below the ribs (usually at the level of the navel, and while standing)

Waist measurement (cm) ☐

For those of Asian or Aboriginal or Torres Strait Islander descent:

Men	Women		
Less than 90 cm	Less than 80 cm	☐	0 points
90 – 100 cm	80 – 90 cm	☐	4 points
More than 100 cm	More than 90 cm	☐	7 points

For all others:

Men	Women		
Less than 102 cm	Less than 88 cm	☐	0 points
102 – 110 cm	88 – 100 cm	☐	4 points
More than 110 cm	More than 100 cm	☐	7 points

Add up your points ☐

Your risk of developing type 2 diabetes within 5 years*:

☐ *5 or less: Low risk*
Approximately one person in every 100 will develop diabetes.

☐ *6-11: Intermediate risk*
For scores of 6-8, approximately one person in every 50 will develop diabetes. For scores of 9-11, approximately one person in every 30 will develop diabetes.

☐ *12 or more: High risk*
For scores of 12-15, approximately one person in every 14 will develop diabetes. For scores of 16-19, approximately one person in every 7 will develop diabetes. For scores of 20 and above, approximately one person in every 3 will develop diabetes.

*The overall score may overestimate the risk of diabetes in those aged less than 25 years.

If you scored 6-11 points in the AUSDRISK you may be at increased risk of type 2 diabetes. Discuss your score and your individual risk with your doctor. Improving your lifestyle may help reduce your risk of developing type 2 diabetes.

If you scored 12 points or more in the AUSDRISK you may have undiagnosed type 2 diabetes or be at high risk of developing the disease. See your doctor about having a fasting blood glucose test. Act now to prevent type 2 diabetes.

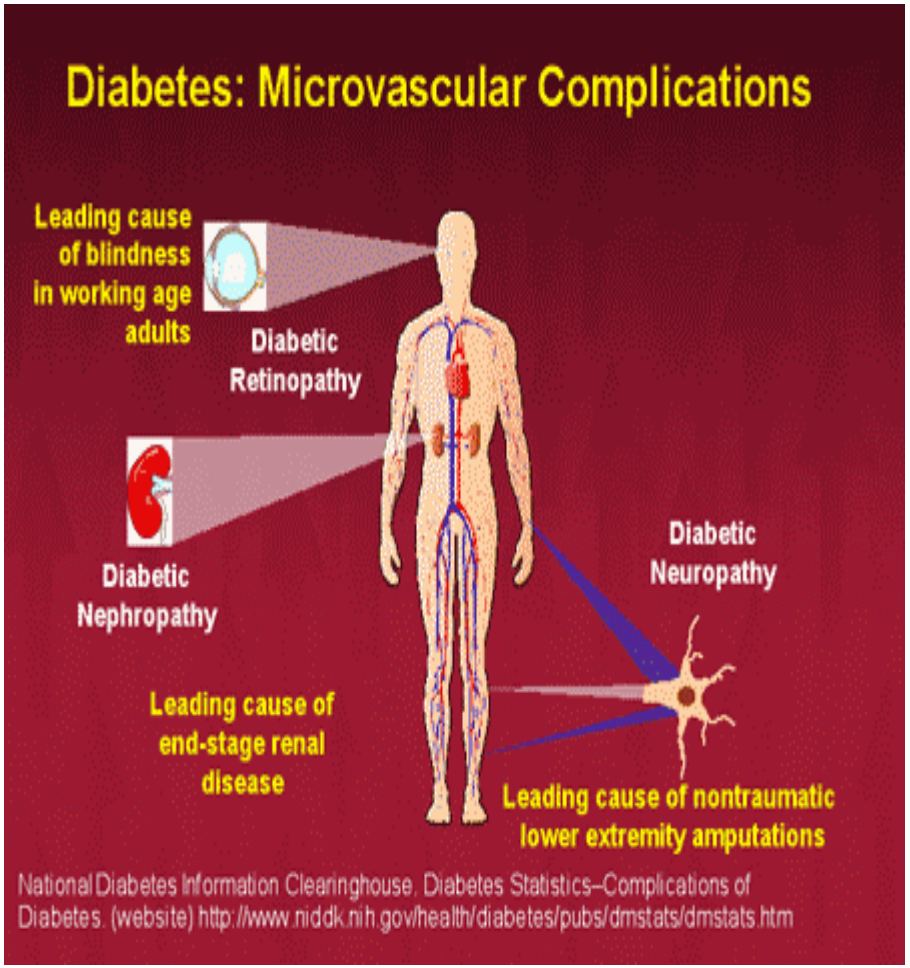
Microvascular complications of DM

Disease of the smallest blood vessels:

- eyes (retinopathy)
- nerves (neuropathy) mainly affecting feet
- kidneys (nephropathy)

The walls of the vessels become:

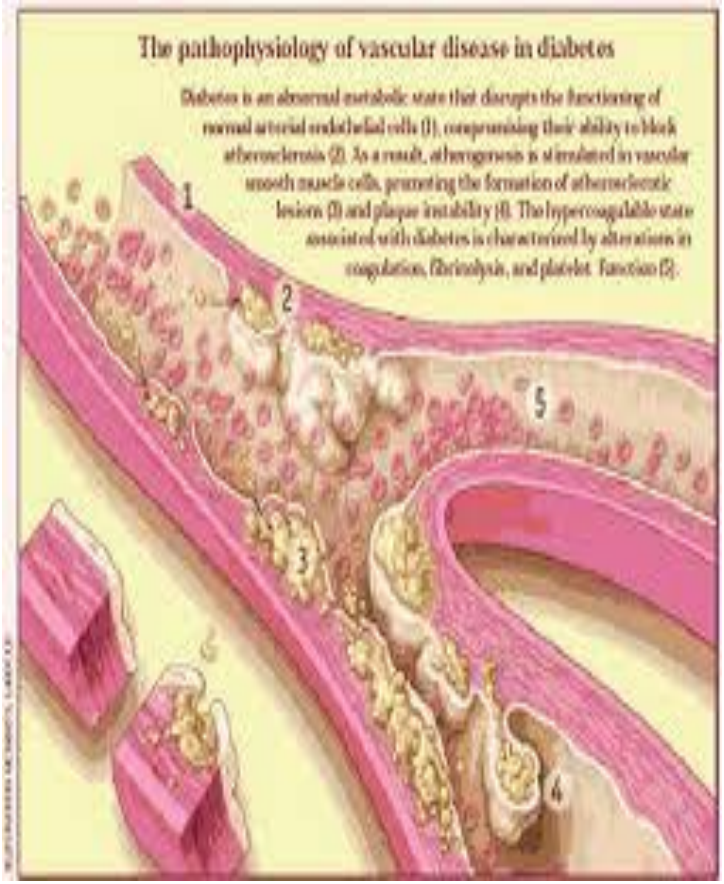
- thick but weak
- then bleed
- leak protein
- slow the flow of blood to the cells



Macrovascular complications of DM

Disease of large blood vessels:

- Lipids and blood clots build up in vessels
  - Heart- atherosclerosis, coronary heart disease and hypertension
  - Brain- stroke(CVA)
  - Legs-peripheral vascular disease



Primary Prevention of T2DM

- Maintaining healthy weight by diet and exercise
- Maintain healthy blood pressure
- Stop smoking

Why do we need medication?

- to optimise quality of life
- to relieve Sx of hyperglycemia
- to avoid acute complications of hyperglycemia
- to avoid hypoglycemia
- to decrease diabetes-related morbidity and mortality
- to control of other cardiovascular risk factors, such as hypertension, dyslipidaemia(must also address smoking and excess weight) NB control of above factors is at least as important as tight glycaemic control

Consider:

Diabetes Management Plan, Self Management and Integrated Care

Management plans

- Set goals
- Plans for
  - dietary intake
  - exercise
  - medication management
  - sick day management
  - reduction of cardiovascular risks eg smoking cessation
  - Self management
- Schedule for screening for complications

Evidence for Treatment in T1DM

Diabetes Control & Complications Trial (DCCT)

- 1400 patients with Type 1 diabetes
- Control-usual treatment
- Intensive insulin regime-multiple daily doses or continuous s/c infusion
- Followed up for periods of up to 9 years
- Control - HbA_{1c} 9, Intervention HbA_{1c}-7

Results

Outcome	% risk reduction intervention v control
Sustained deterioration in retinopathy	63
Development of severe retinopathy	47
Development of microalbuminuria	39
Development of clinical neuropathy	60

Evidence for Treatment

Epidemiology of Diabetes Interventions and Complications (EDIC)

Used same cohort of patients as Diabetes Control & Complications Trial (DCCT)

Results

Outcome	% risk reduction intervention v control
Any cardiovascular disease event	42
Any nonfatal myocardial infarction, stroke, or death from cardiovascular disease	57

Evidence for Treating in T2DM

UKPDS

- The largest clinical research study of diabetes ever conduced for Type 2 diabetes
- Dietary control with minimal drug treatment or intensive therapy
- Further randomisation of hypertensive patients to less tight vs tight blood pressure control

Results

- Better blood glucose control reduces the risk of any diabetic endpoint by 12%
- Major diabetic eye disease reduced by 25%
- Non significant reduction in MI, and diabetic related death
- Increase in incidence of hypoglycaemia and weight gain
- No adverse effect on cardiovascular outcomes


Type
Diabetes
1

Case study 1

Master CM

- 7 years old and has been sick with a chest infection
- Other symptoms develop:
  - dehydrated
  - fatigue and malaise
  - nausea/vomiting
  - abdominal pain
  - polydipsia
  - polyuria
  - polyphagia
  - weight loss
  - fever

What do you think is happening?

What other things can we look for and do?

- altered mental status without evidence of head trauma
- tachycardia and tachypnoea
- low blood pressure
- limbs poorly perfusion
- acetone odour of the breath

Tests

- BSL 20mmol/L
- K 4.5mmol/l, HCO_3 9mmol/L
- Urinalysis +ve for ketone and glucose

What is happening?

Diagnosis:

Diabetic Ketoacidosis (DKA) and Type 1 DM

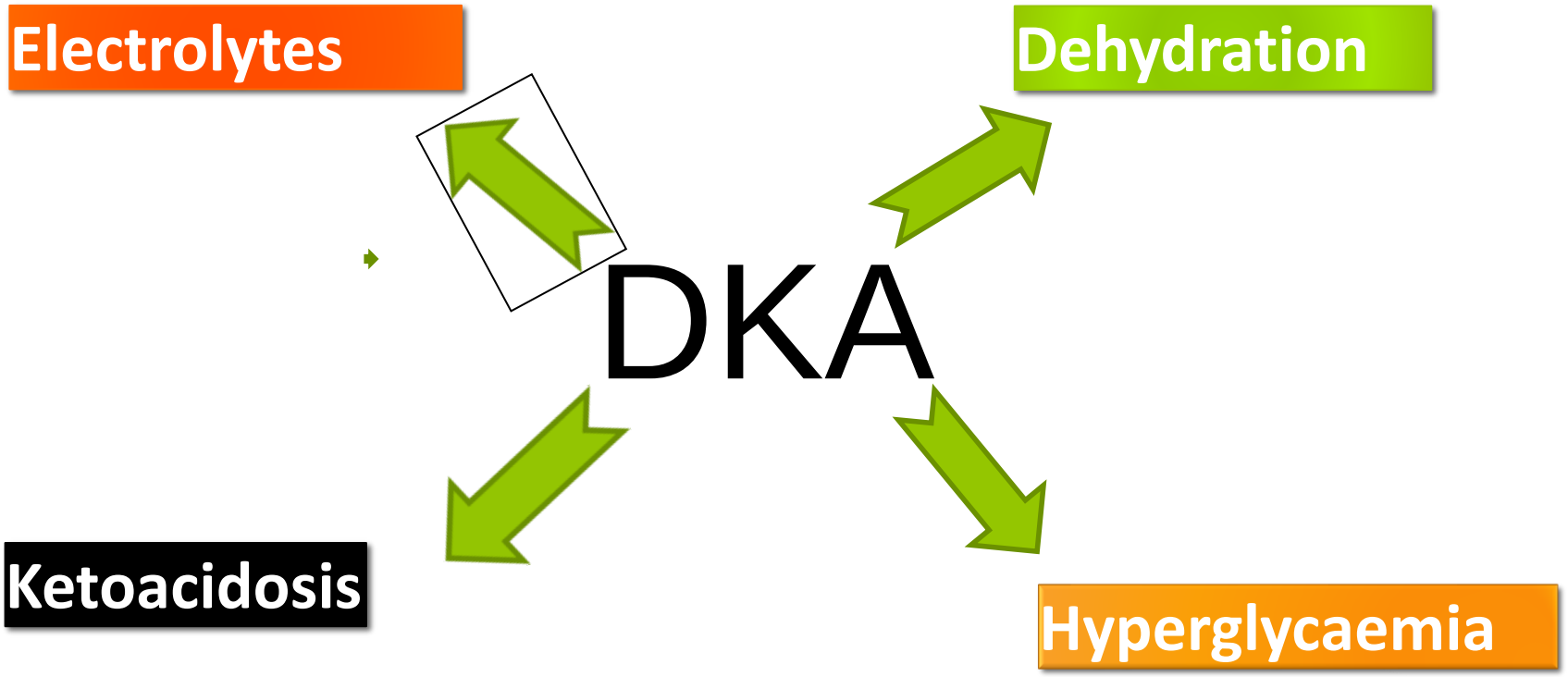
- inadequate serum insulin to allow glucose from the blood into the cells to be used for energy or stored as fat
- cells use stored fatty acids for energy liberating ketoacids as the main energy source
- 4 issues occur as a result in this metabolic state which need treating separately
- medical emergency 3-5% mortality risk

Diabetic ketoacidosis DKA

- **Occurs**
  - at onset of T1DM
  - during illness or stress
  - with persistent high glucose concentration

- **Caused by stresses such as:**
  - infection
  - inappropriate withdrawal of insulin
  - acute myocardial infarction
  - trauma In adolescents,
  - omission of insulin (common cause in adolescents)

The 4 problems



Managing ketoacidoses

- **Patients with DKA are:**
  - Deficient in insulin - need insulin(short-acting) infusion
    - opens potassium channels in the cells to drive potassium intracellularly
    - helps correct acidosis
  - Acutely dehydrated - rehydrate(normal saline)
  - Need substantial potassium replacement
    - Acid in the blood is buffered in the cell -as H+ goes in, K+ comes out and is removed by the kidney -total body potassium is depleted but the blood potassium may be high
- Need to monitor urine ketones
- Monitor BSLs hourly – If BSL <14 give Glucose

Case study 1

Master CM is admitted to hospital and given

- Insulin infusion using neutral insulin 0.05-0.10 U/kg/h
- Normal saline IV
- Potassium IV

When recovered, insulin is started as basal-bolus

Insulin aspart - tds just before meals

Insulin glargine at bedtime (approx 50% of daily dose)

Total daily dose to start = 0.7 to 1 unit/kg

(?too young to consider insulin pump)

Activity

What information does patient need about:

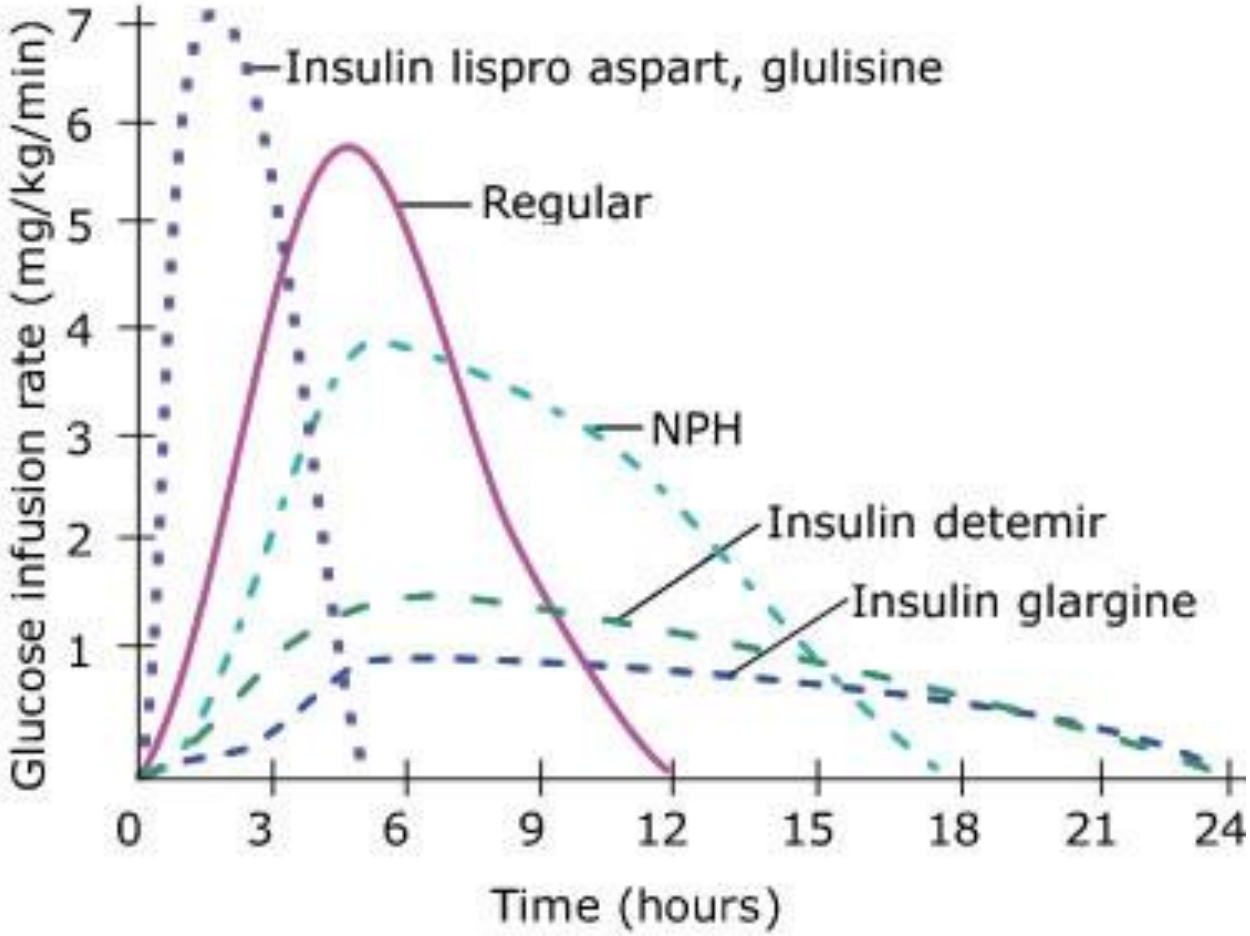
- Insulin
- Blood sugar tests
- Hypoglycemia and treatment
- Diet
- Treatment in acute illness

What information does patient need?

Insulin

- How it works?
- How it will help?
- Is it long term?
- How is it injected?
- Where to inject?
- Why 2 insulins?
- Storage

Activity Profiles of Different Types of Insulin



What are the advantages of newer insulins?

Ultra-short acting (aspart, lispro, glulisine)

- Can be given immediately before meals
- May reduce frequency of hypoglycemia

Glargine

- May decrease nocturnal hypoglycaemia compared with once daily isophane insulin in patients with type 2 diabetes but more painful injections

Detemir

- may cause less weight gain than isophane insulin but more local reactions

What information does patient need?

Blood sugar tests

- How they work?
- Why do we need them?
- How will they help?
- How do you do it?
- Where do you do it?

Blood tests – why we need them?

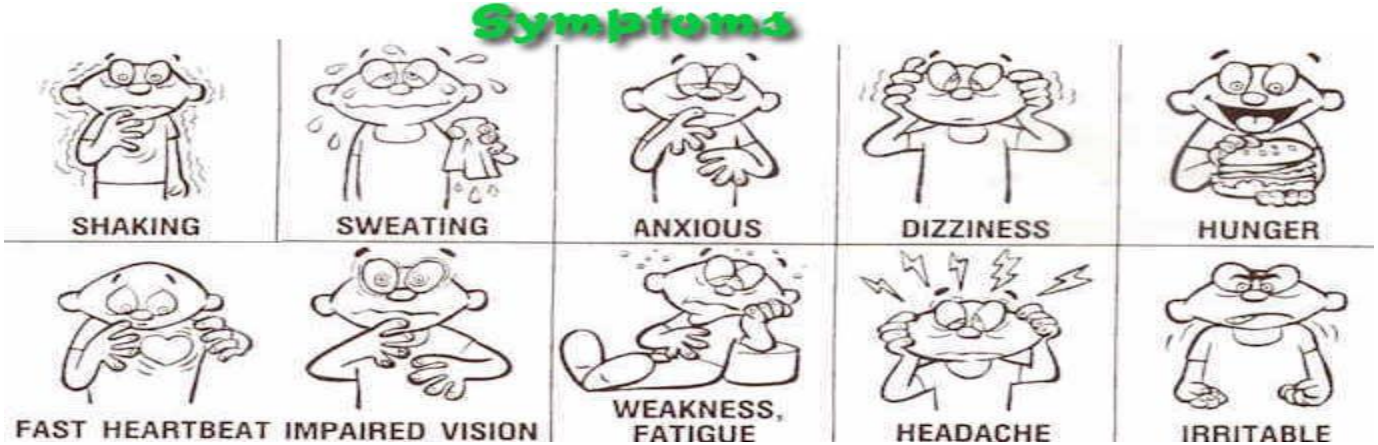
Can assist in

- self-adjustment of diet, exercise or insulin dosage
- identifying and treating hyperglycaemia and hypoglycaemia
- assisting the health professional in modifying treatment
- motivating the patient to become more involved in self-management
- VIP in children to avoid hypoglycemia as has effects on cerebral development

What information does patient need?

Hypoglycemia – signs and symptoms

- Feeling shaky, sweaty or tired
- Feeling hungry or confused
- Tachycardia
- Blurred vision or headache
- Tingling or numbness around lips



What information does patient need?

Hypoglycemia – how to treat in children

- 1 glass of oral glucose solution OR 180 mL of juice (a small glass or box of juice) or sweetened soft drink OR 1 tablespoon of honey OR 1 tablespoon of glucose gel

If unconscious

- **glucagon** 0.5 mg (weight less than 25 kg) or 1 mg (weight 25 kg or more) SC or IM. Follow by oral feeding ONLY when conscious

What information does patient need?

Diet

- consider the child's usual appetite, food intake pattern and level of exercise
- healthy eating principles of three balanced meals per day with appropriate healthy snacks.
- focus on decreasing the intake of sweetened soft drinks and saturated fat while increasing the intake of fruit, vegetables and dairy products.
- Specialist advice on nutritional management re carbohydrate amount, type and distribution over the day, taking into account the insulin regimen

Acute illness

- An insulin dose must never be omitted in type 1 diabetes, even if the illness is accompanied by nausea, vomiting or marked anorexia, as this could lead to diabetic ketoacidosis.
- Acute illness in a person with diabetes is usually associated with increased secretion of counter-regulatory hormones such as glucagon, cortisol and adrenaline

Case study 1

Mr CM

- Now 20 year old
- Insulin lispro TDS cc and insulin glargine at night
- His glucose levels have been ‘all over the place’ and he wants advice re his glucose meter:
  - Check reagent strips in date
  - Check no obvious residue on meter window
  - Has meter been calibrated with strips
  - Check against standard reagent solutions

Case study 1

When should he measure his blood glucose?

- Blood sugar levels should be done before meals and at night

What other monitoring tests may be used?

- HbA_{1c}- long term control
- Urine ketones-during periods of acute stress/illness

What else should we consider?

Risk factors

- Smoking
- Hypertension
- Obesity
- Dyslipidemia

Important to address these risk factors to address diabetes-related morbidity and mortality

Case study 1

What else should we consider?

- Is he using his insulin properly?
- Is his diet appropriate?
- Is he getting regular checks eg eyes, feet
- Does he have any evolving symptoms
- Discuss DKA and symptoms
- Is he looking after himself?

- **Make the most of this opportunity!!!!!!!**


TYPE
2
DIABETICS

Activity

- **What are the priorities for the management of Type 2 diabetes?**
- **Management plan ideas**

Priorities for management in T2DM

Priorities for the management of diabetes are:

- to relieve symptoms of hyperglycaemia
- to avoid acute complications of hyperglycaemia, such as diabetic ketoacidosis and hyperosmolar nonketotic coma
- to avoid hypoglycaemia
- to reduce risk of long-term end-organ complications by addressing risk factors
- screen for retinopathy, neuropathy, albuminuria

Case Study 2

Mrs SW

- 45 years, overweight, with hypertension
- New diagnosis of T2DM
- Dr has advised to lose weight by:
  - dieting
  - exercising
- Medication
  - hydrochlorothiazide 25mg mane
  - atenolol 50mg mane

Case study 2

Comment on these medications in relation to her diabetes

- thiazides can ↑BSL's
- beta blocker reported as increasing and decreasing blood glucose
- beta blockers can mask signs of hypoglycaemia

Would you recommend any change in therapy-if so why?

- ACE inhibitor first line if microalbuminuria or LVF is present

Activity

What risk factors do we need to consider?

Check risk factors

- BP
  - Target <130/80
- Cholesterol
  - Target LDL<2
- Diabetics increased risk CHD
- Smoking status
- Treat albuminuria if present
- Consider aspirin if cardiac symptoms are present

Case study 2

One month later:

- Mrs SW returns with a prescription for Metformin 850mg tds

Comment on the choice of anti-diabetic agent and dose

- Agent of choice in overweight patient – will reduce incidence of diabetes-related events and mortality
- Dose too high for initial therapy – discuss with doctor (usual starting dose is 500mg)

Choice of agent ()

Factors influencing choice of antihyperglycaemic drug for type 2 diabetes (Box 18.6) [NB1]

Patient-related factors

degree of hyperglycaemia

risk of hypoglycaemia

weight

comorbidities (eg kidney or liver impairment, cardiovascular disease)

patient preference—impact of drug-related factors

patient life expectancy

Drug-related factors

efficacy in lowering blood glucose concentration

potential nonglycaemic effects (eg cardiovascular benefits for patients with established cardiovascular disease, slowing progression of kidney disease)

risk of inducing hypoglycaemia

effect on patient weight

contraindications to use and adverse effects

ease of use—complexity of dosage regimen and route of administration

cost

Metformin

- Requires insulin for its action
- Increases insulin sensitivity
- Inhibits hepatic glucose production
- Increases peripheral uptake of glucose
- Delays glucose absorption from GI tract
- Uses anaerobic pathways
- Produces lactic acid
- Use with caution in renal disease

Metformin

- Reduces HbA_{1c} by 1-2%
- Reduction of microvascular complications
- Reduction of macrovascular complications
- No hypoglycaemia
- Beneficial effect on body weight profile
- Useful in obese patients
- Improved lipid profile
- Preferred initial drug therapy

Activity

- **How would you counsel Mrs SW about metformin?**

How would you counsel metformin?

- Reduces glucose production and increases glucose sensitivity
- GIT upset, taste disturbance, diarrhoea, vomiting,
  - dose limiting
  - take with food
- Won't cause hypos
- Explain lactic acidosis –
  - occurs with high dose and renal impairment
  - precipitated by dehydration, severe infection, surgery, liver and heart failure, alcohol abuse
  - symptoms are anorexia, nausea, vomiting, abdominal pain, cramps malaise and weight loss
- Maintain a healthy diet and take exercise
- Reduces vitamin B_{12} absorption

Metformin-Lactic Acidosis

- Rare but serious adverse effect of metformin (0.03 per 1000 patient years)
- Cochrane-no evidence of increased risk from clinical trial data
- Contraindicated in patients at risk:

- Impaired renal function
- CrCl<30ml/min(?<20m/min)
- Severe hepatic disease
- Acute CHF
- Recent MI
- Respirator insufficiency
- Severe dehydration
- Use of iodinated contrast
- Acute /chronic alcoholism
- Septicaemia
- Patients undergoing surgery
- Very elderly
- Presence of acute or chronic metabolic acidosis
- History of lactic acidosis

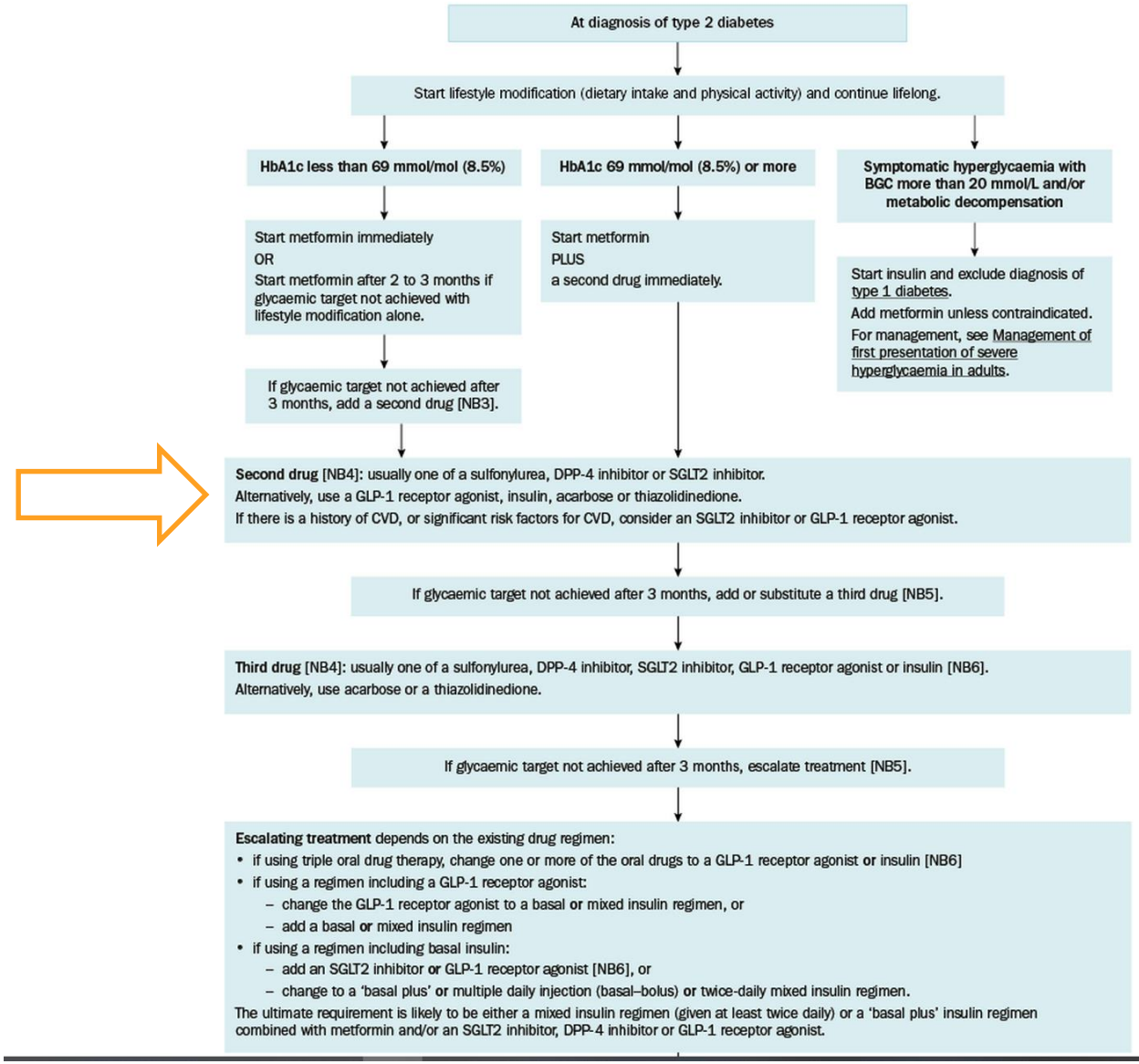
Case study 2

Activity

Six months later, Mrs SW returns and tells you her sugar levels are still too high

What are her 2nd line options?

Suggested approach to glycaemic management for adults with type 2 diabetes (Figure 18.1) [NB1] [NB2]



Sulfonylureas

- Inulin secretogue
- Reduce microvascular but not macrovascular complications
- Alternative if metformin contraindicated or not tolerated
- Avoid longer acting (glibenclamide) in elderly / renal and hepatic impairment
- HbA_{1c} ↓ ~ 1%
- Hypoglycaemia
- Weight gain

Other options (little mortality data for orals)

Class	Action
Thiazolidinedione (glitazones)	increases insulin sensitivity and decreased hepatic glucose output (rosiglitazone/pioglitazone)
Dipeptidyl Peptidase-4 inhibitors (DPP-4 inhibitors, gliptins)	increases incretin hormone - increases insulin secretion and glucagon production reduced (sitagliptin, vildagliptin, linagliptin)
Synthetic analogues of glucagon-like peptide-1 (GLP1 analogues)	increases insulin secretion , and suppresses inappropriate glucagon production (exanitide)
Sodium glucose co-transporter 2 (SGLT2) inhibitors	Increase renal excretion of glucose (canagliflozin, dapagliflozin, empaglifazin) May have some benefit to ll cause mortality and adverse cardiac events
Insulin	

Common side effects and tolerability concerns associated with non-sulfonylurea oral glucose-lowering medicines (MedicineWise News July2016 NPS)

Class of oral glucose-lowering medicine	Tolerability and side effect profile
DPP-4 inhibitors	•Common adverse effects include headache, musculoskeletal pain, mild gastrointestinal disturbance and nasopharyngitis.[1, 4] •Pancreatitis and joint pain have been reported in post-marketing experience.[21-23] •Well-tolerated and not associated with weight gain or hypoglycaemia.[25]
SGLT2 inhibitors	•Common adverse effects include genital and urinary tract infections.[1, 4] •Associated with modest weight loss, generally do not cause hypoglycaemia unless used with a sulfonylurea or insulin.[1, 4]
Acarbose	•Common adverse effects include bloating and flatulence that can be difficult to tolerate.[1] •Limited role in therapy.[4]
Thiazolidinediones	•Associated with more serious and severe adverse effects.[1] •These include heart failure, bladder cancer, increased risk of non-axial fractures in women.[1] •Also associated with weight gain and fluid retention.[1] •Not generally recommended as initial choice for dual or triple therapy.[1]

Case study 2

Six months later:

Dr has given her a script for Gliclazide SR 30mg mane

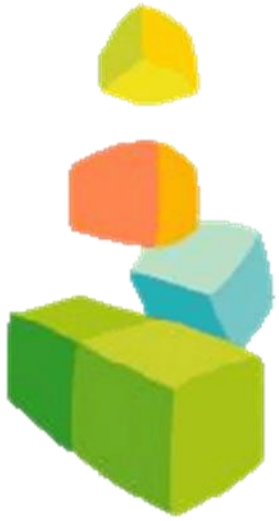
- She wants to know should she stop her Diabex or take both together
- What would you tell?
  - Drugs have different modes of action
  - It is common to take both types together

Case study 2

- When should she take it in relation to meals?
  - Drugs should be taken with food to minimise GIT effects
  - Food must follow the sulphonylurea or else risk or hypoglycaemia

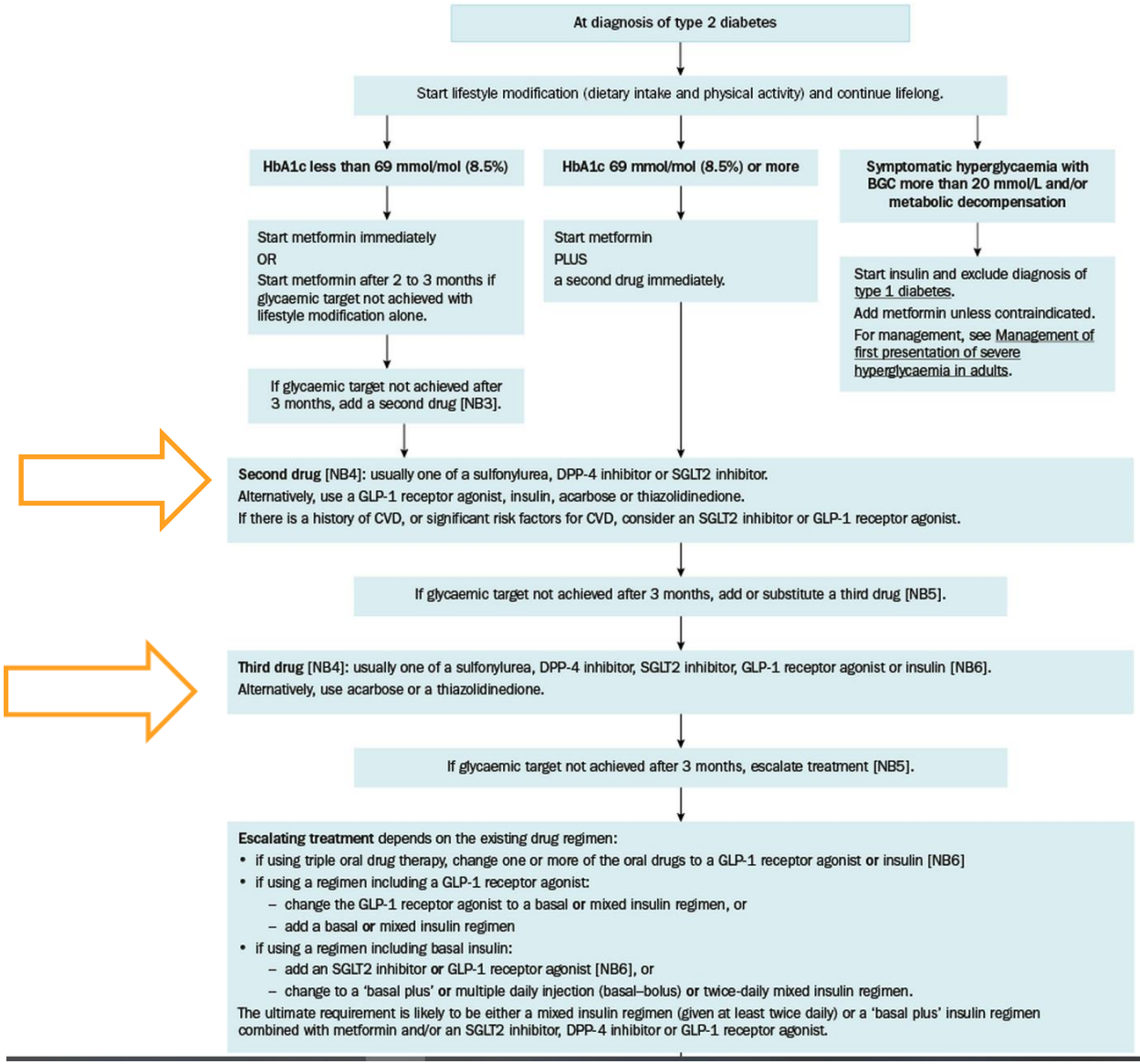
Case study 2

Activity



- After another 18 months Mrs SW's diabetes is still not well controlled
- What are her 3rd line options?

Suggested approach to glycaemic management for adults with type 2 diabetes (Figure 18.1) [NB1] [NB2]



3rd line options

Insulin:

- Can be used at any stage
- Pregnancy, breastfeeding and surgery
- Good if BSLs are very high or metabolic decompensation
- High dose steroids
- Risks of hypoglycaemia and weight gain

Synthetic analogues of glucagon-like peptide-1 (GLP1 analogues):

- Obese patients or desire to lose weight
- Slightly superior to orals
- Low risk of hypos
- Beneficial effect on blood pressure, mild increase in HR
- Causes nausea and vomiting, increase risk of pancreatitis

Controlling other risk factors

- Hypertension – aim 130/80
- Microalbuminuria - ACEi
- Cardiovascular prevention including cholesterol lowering agents

Managing hypertension

- Tight BP control achieves greater reduction in diabetes complications and mortality than less tight BP control
- ACEi, thiazide diuretics, and beta blockers all reduce CV mortality and morbidity in people with diabetes and hypertension
- BUT thiazides inc BSL AND beta blockers may mask symptoms of hypoglycemia
- ACEi usually 1st line treatment
- Watch for different side effects

Evidence

- **UKPDS**: intensive blood pressure control reduced diabetic death, macrovascular disease and microvascular disease.. No difference seen between captopril and atenolol in cardiovascular events

- **HOT** study: reducing diastolic BP to 80mmHg ↓ major cardiovascular events in diabetics

- **MICRO-HOPE**: Ramipril beneficial in reducing cardiovascular events and overt nephropathy in diabetics
- FACET: ACE inhibitors □ cardiovascular events compared to calcium channel blockers

- Most patients require combination therapy to achieve targets

Choice Of Agent

- Most important thing is to ↓ BP
- Depends on patient
- Compelling indications (WHO-ISH/NHF)
  - Angina — ß blockers, CCB's
  - Post MI — ß blockers, ACEIs
  - Heart Failure — ACEIs, ARAs, thiazide diuretics, ß blockers
  - Diabetics with nephropathy — ACEIs, ARAs

Kidney damage-proteinuria

- Improvement in BSL control and reducing in BP reduce progression to renal disease
- In normotensive patients with microalbuminuria, ACEi reduce progression to overt nephropathy
- Losartan prevents progression of renal disease in T2DM patients with hypertension and proteinuria or microalbuminuria

Cardiovascular prevention

- Consider low dose aspirin in patients with high risk of CV disease (risk vs benefit)
- Consider statins in patients with LDL>3.4mmol/L or with combined CV disease
- Read MJA 2009;190: 614-615

Dyslipidaemia-Evidence

- Cardiovascular mortality increased 2-4 times in diabetics (MRFIT)
- Most common lipid profile: ↑ TG & LDL, ↓ HDL,
  - Statins first line, may need fibrates to ↓ TG
- Heart Protection Study: 5963 patients with diabetes
  - 49% no vascular disease
  - Near normal lipids
  - Simvastatin 40mg v placebo
  - Rate of 1st major vascular event ↓ by ~ 25%
- Also evidence for pravastatin and atorvastatin

Target Lipid Levels

- Total cholesterol <4mmol/L
- LDL-C <2.0 mmol/L
- HDL-C >1.0 mmol/L
- Triglycerides <2mmol/L
- Statin therapy if LDL > 2.5mmol/L in diabetic patients
- Fibrate therapy if TG > 2.0mmol/L in diabetic patients

Total cholesterol (mmol/L)

(Diabetes Australia)

Type 2 diabetes: goals for optimum management

Encourage all people with type 2 diabetes to approach/reach these goals	
Diet	Normal healthy eating. If concerns regarding cardiovascular risk, advise Mediterranean diet.
Body mass index (kg/m^2)	Therapeutic goal is 5–10% loss for people overweight or obese with type 2 diabetes. With BMI >35 and comorbidities or BMI >40, greater weight loss measures should be considered. Note that BMI is a difficult parameter to standardise between different population groups.
Physical activity	At least 30 minutes of moderate physical activity on most if not all days of the week (total ≥150 minutes/week).
Cigarette consumption	0 (per day)
Alcohol consumption	≤2 standard drinks (20 g) per day for men and women.
BGL	6–8 mmol/L fasting and 8–10 mmol/L postprandial. Ongoing self-monitoring of blood glucose is recommended for people with diabetes using insulin, with hyperglycaemia arising from illness, with haemoglobinopathies, pregnancy or other conditions where data on glycaemic patterns is required. Routine self-monitoring of blood glucose in low-risk patients who are using oral glucose-lowering drugs (with the exception of sulphonylureas) is not recommended.
HbA1c (mmol/mol; %)	Needs individualisation according to patient circumstances. Generally: • ≤53 mmol/mol (range 48–58) • ≤7% (range 6.5–7.5). Allowing for normal variation in test accuracy, HbA1c results which range between 6.5 and 7.5% would reflect this goal.
Total cholesterol (mmol/L) <4.0	Initiation of pharmacotherapy is dependent on the assessment of absolute cardiovascular risk (Refer to the Australian absolute CVD risk calculator). This requires using multiple risk factors, which is considered more accurate than the use of individual parameters. Once therapy is initiated the specified targets apply; however, these targets should be used as a guide to treatment and not as a mandatory target.
HDL-C (mmol/L) ≥1.0	
LDL-C (mmol/L) <2.0	
Non-HDL-C (mmol/L) <2.5	
Triglycerides (mmol/L) <2.0	
Blood pressure (mmHg) 130/80	
Urinary albumin excretion	Timed overnight collection (mcg/min): <20 Spot collection (mg/L): <20 Urinary albumin-to-creatinine ratio • Women (mg/mmol): <3.5 • Men (mg/mmol): <2.5
Vaccination	Consider immunisation against influenza and pneumococcal disease, and the dTPa vaccine.

Eye screening

- Patients with diabetes need regular eye screening to detect retinopathy

Normal vision

Vision with diabetic retinopathy

Neuropathic pain management

- Diabetes can damage the peripheral nerves, especially those in the legs and feet, causing pain as well as numbness and tingling
- Difficult to treat
- Tricyclics, gabapentin, pregabalin
- Protect feet and good foot care
- Can cause diabetic foot ulcers

Summary

- Diabetes will continue to be a major public health issue
- Prevention and lifestyle intervention should be the foundation of care
- Good control reduces complications
- Associated risk factors can be modified
- The pharmacist has a huge role to play in optimisation & monitoring of both diabetic and non diabetic medication