# M2 TEACHING
# UNDERSTANDING PHARMACOLOGY

## USING CVS SYSTEM AS AN EXAMPLE

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# TODAY'S OBJECTIVE

**Pharmacology often seems like an endless list of mechanisms and side effects to memorize.**

- **To realise that a drug's effects and side effects may largely be understood by exploring its mechanism in relation to physiology and pathophysiology**
- **To integrate physiology, pathology, pharmacology, and clinical exam.**
- **To illustrate the advice of 'understand not memorize' and 'think of a patient'**

**Key goal is not to teach content, but to teach an approach you can apply to all other systems.**

# TODAY'S TOPICS

**Will cover:**

- **Drugs used in heart failure**
- **Drugs used in hypertension**
- **Drugs used in diabetes**

**Also important in CVS drugs but not taught to you yet:**

- **Anti-platelet agents and anticoagulants.**

# APPROACH

- **Understand the disease's natural history and impact, and hence the GOALS of treatment ('Why')**

  What is 'symptomatic treatment' and when do we use it?

- **Understand the disease pathophysiology and hence the PRINCIPLES of treatment ('What')**
- **Understand the pharmacological mechanisms used to achieve the goals, and hence the 'logical' effects, side effects, contraindications, and drug interactions.**
- **Fill in the remaining 'idiosyncratic' effects and side effects (these do not logically follow from its mechanism)**
- **Address not only the disease itself, but also its complications and potential complications – intervene early if indicated**

# HEART FAILURE

**Case:** Chronic heart failure - systolic dysfunction due to old infarct

## Natural history & impact

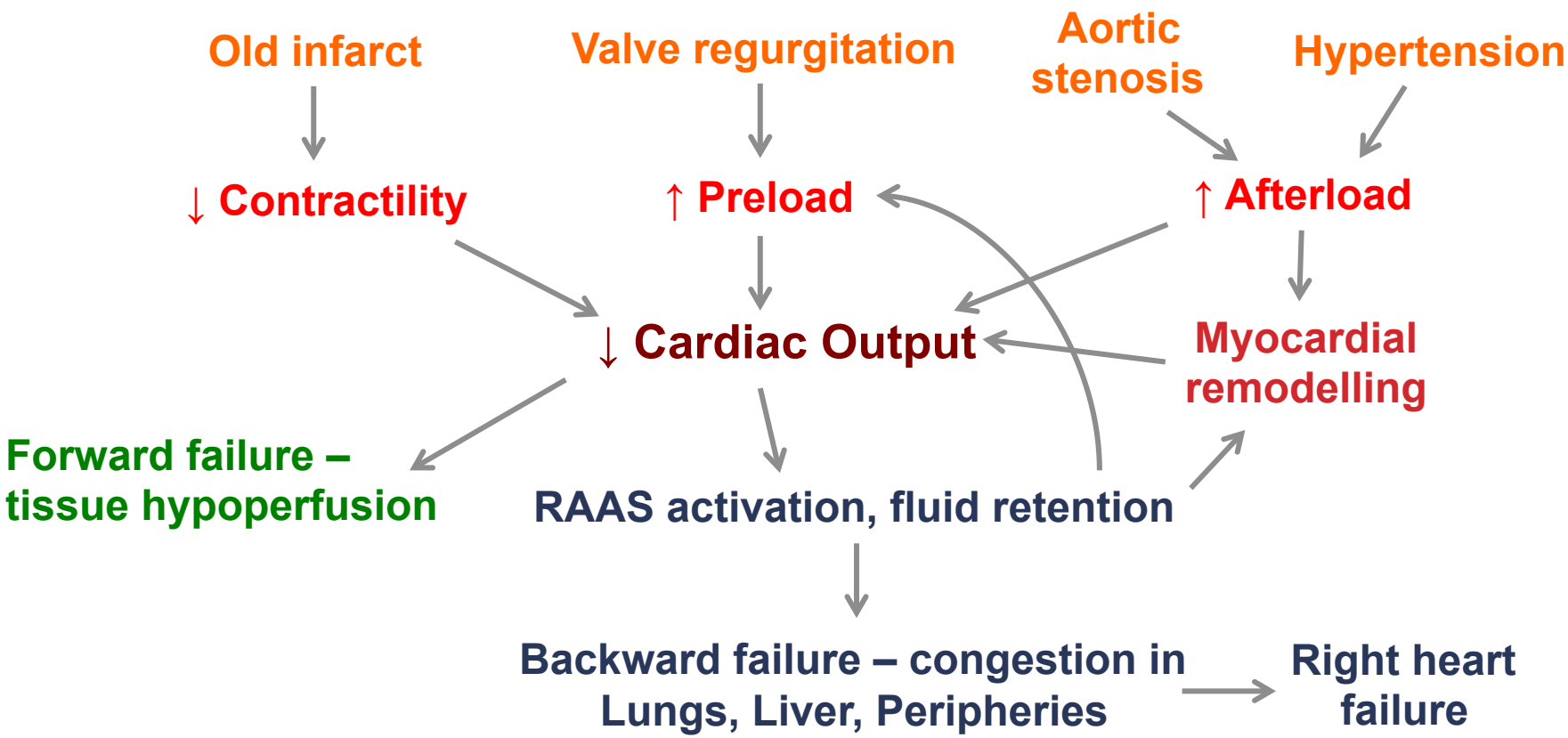
- Symptoms of heart failure can be debilitating e.g. dyspnoea
- Heart failure progresses (Why?)
- Risk of re-infarct (Why?)

## Principles of management:

- Symptom control: dyspnoea, orthorpnoea etc
- Retarding disease progression
- Preventing re-infarct: investigate and treat the underlying cause of heart failure

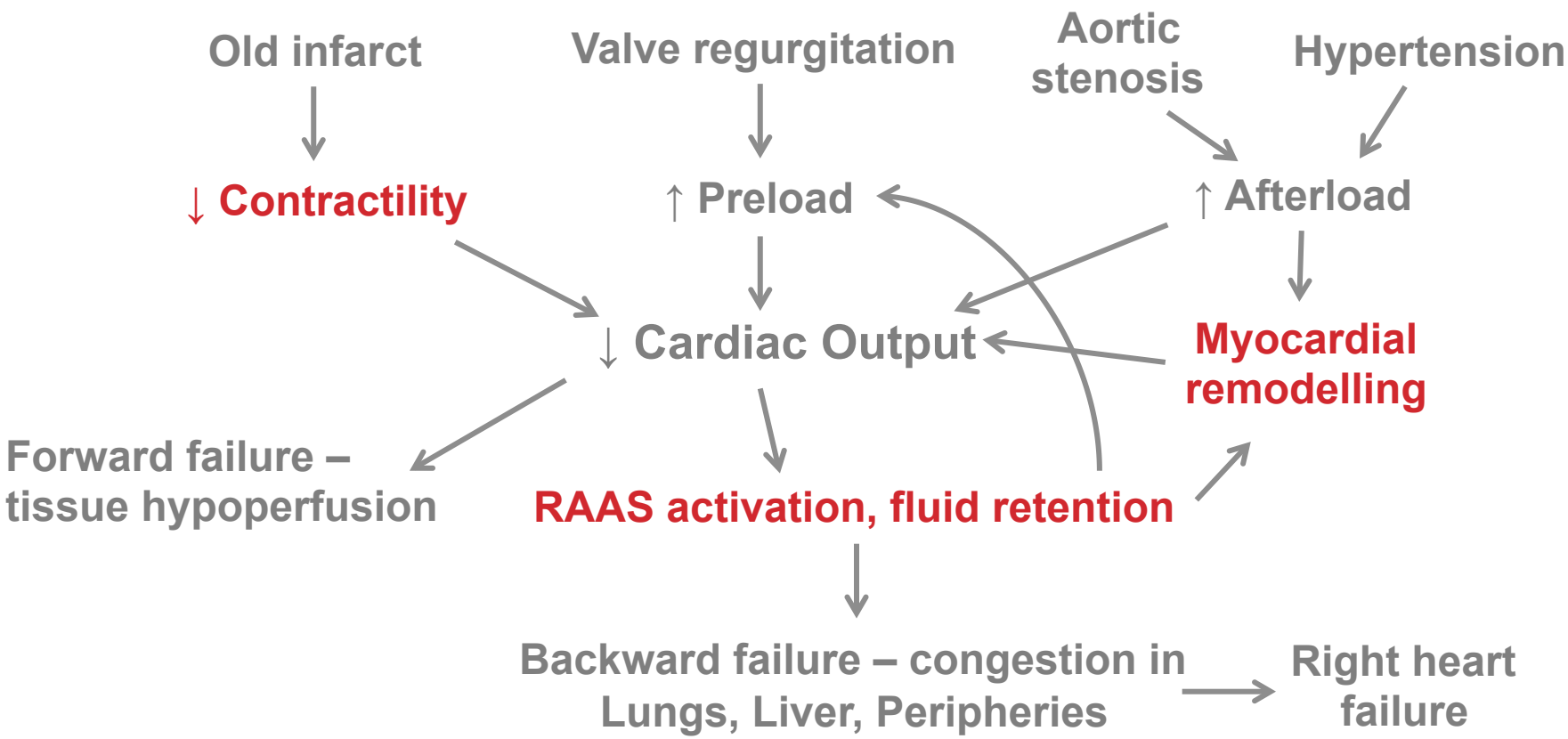
# HEART FAILURE

**Its clinical presentation directly follows from its pathophysiology:**
**Consider Left Heart Failure** (simplified schema)



# HEART FAILURE

**Understand PRINCIPLES of treatment:** inhibit the vicious cycle that causes heart failure to progressively worsen.



# HEART FAILURE

**Inhibits fluid retention: improves symptoms, inhibits remodelling with evidence-based survival benefit**

- **ACE-I or ARB**
- **Aldosterone antagonists**

**Inhibits remodelling: proven survival benefit**

- **Beta-blockers:** some (not all) are evidence-based.

**Improves symptoms but NO survival benefit**

- **Diuretics:** improve symptoms by reducing fluid overload
- **Digoxin:** improves symptoms and reduces readmissions
- **Inotropes:** in intractable cases

# HEART FAILURE

## Treating the underlying cause:

**In this case ischemic heart disease**

- **Anti-platelets**
- **Risk factor control: lipids, BP, and blood sugars**
- **Revascularization**

## Notes & reminders:

- **Management has to be tailored to the patient. Not all heart failure is equal, not always due to old infarct.**
- **Not all management is pharmacological**
- **Must also look out for and manage complications (of disease and of treatment)**

# HEART FAILURE

**Enalapril and frusemide.**

- **How do you expect him to benefit**
- **What do you have to monitor?**

**What if:**

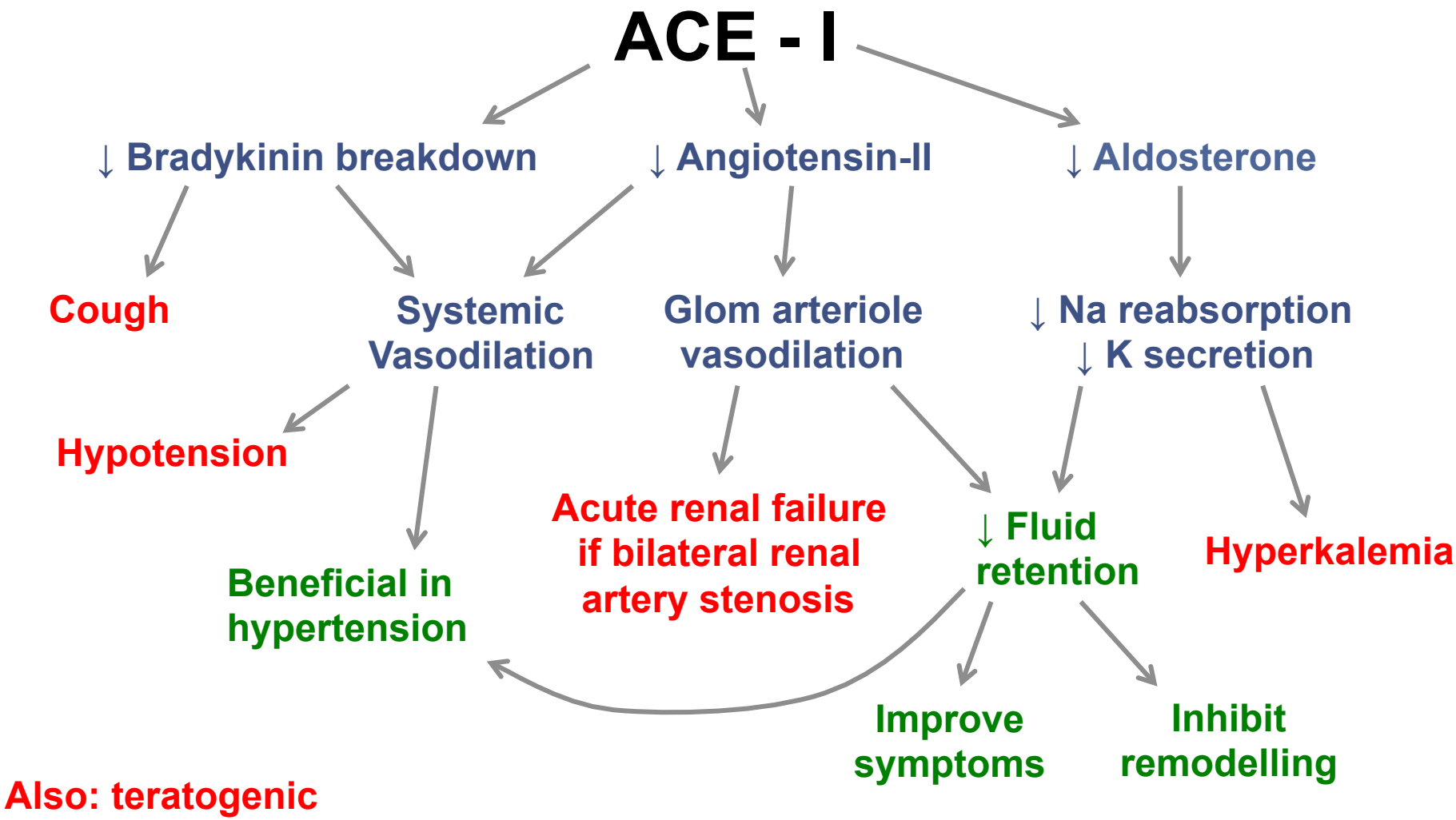
- **Now comes in with palpitations**
- **Has chronic cough for 2 months**
- **Complains of giddiness, especially on waking up.**
- **Poor urine output and serum creatinine rises.**
- **6 months later - Elevated JVP, basal crepitations, lower limb edema**

# HEART FAILURE

**Understand physiological role of ACE:**

- **Physiological response to hypovolemia. Heart failure is perceived as a state of relative hypovolemia (why?)**
- **RAAS axis: Angiotensin-II & Aldosterone production**
- **↓ Fluid excretion: glomerular arteriole dilation (angiotensin II) and ↑ Na reabsorption (aldosterone)**
- **Sympathetic stimulation (angiotensin II) causing vasoconstriction**

# HEART FAILURE




Also: teratogenic

# HEART FAILURE

**Patient is started on Enalapril and frusemide.**

- **How do you expect him to benefit**
- **What do you have to monitor?**

**What if:**

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# ESSENTIAL HYPERTENSION

## Natural history & impact

**Usually asymptomatic but long term danger**

- **Heart – hypertrophy predisposing to MI or heart failure**
- **Brain – stroke**
- **Kidney – glomerulosclerosis, proteinuria**

## Principles of management:

- **Ask "Is there really hypertension"**
- **Nonpharmacological – diet, salt restriction, exercise, etc.**
- **Pharmacological**
- **Control other cardiovascular risk factors**

# ESSENTIAL HYPERTENSION

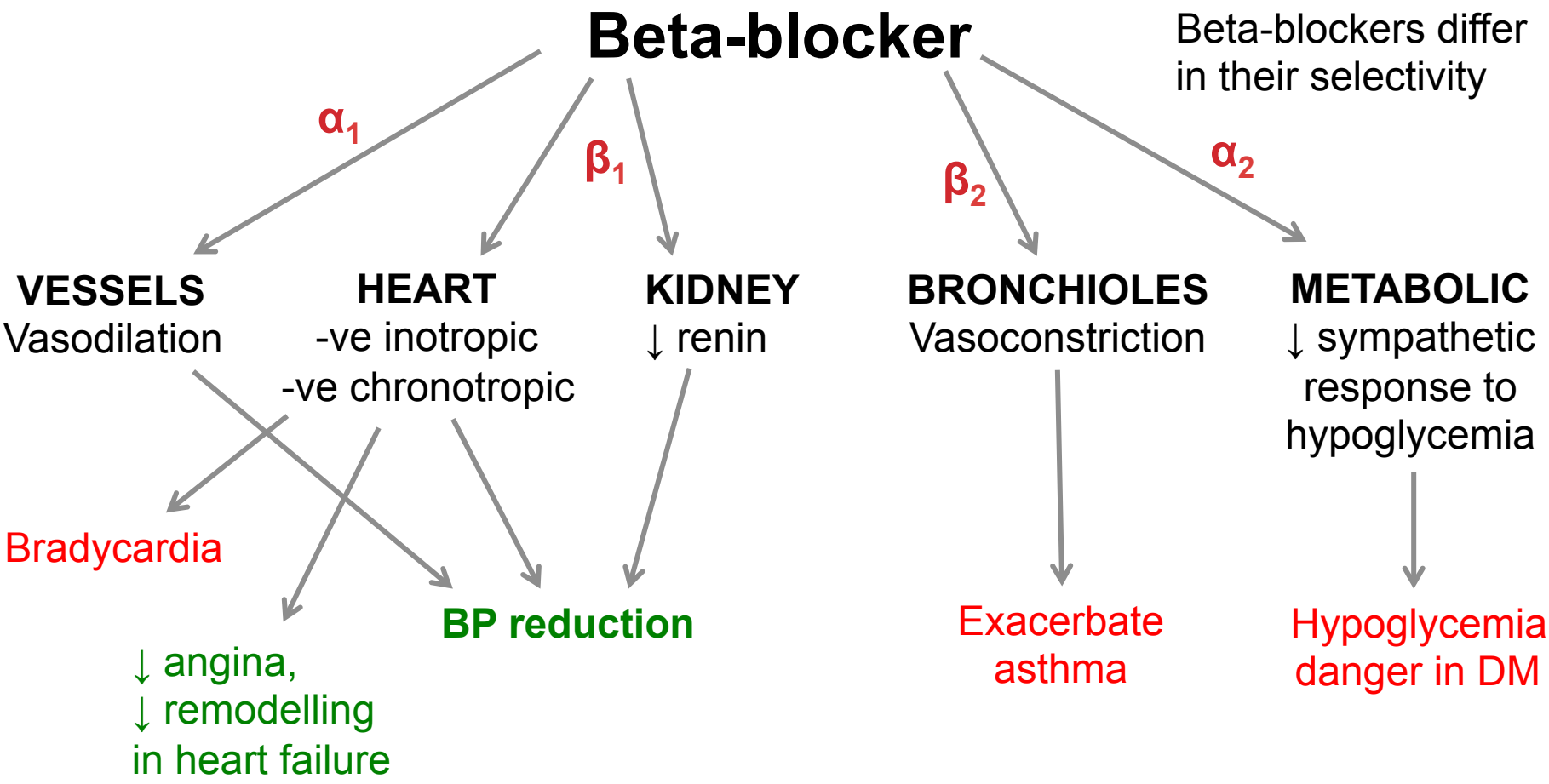
**Therapeutic options:**

- **A: ACE-I or ARB**
- **B: Beta-blocker**
- **C: Ca-channel blocker**
- **D: Diuretics**

**Notes:**

- **BP drugs are synergistic, usually >1 required**
- **Achieving target BP more important than specific drug used. Hence, presence of comorbids is used to choose the BP drug.**
- **Malignant hypertension and hypertension in pregnancy are separate entities**

# ESSENTIAL HYPERTENSION



# ESSENTIAL HYPERTENSION

**Choice of anti-hypertensive agent based on comorbidity:**

| | ACE-I | Beta-blocker | CCB | Diuretic |
|---|---|---|---|---|
| DM | | | | |
| Asthma | | | | |
| CCF | | | | |
| Angina | | | | |
| Pregnancy | | | | |
| Arrhythmia | | | | |
| Gout | | | | |
| ↑ K | | | | |

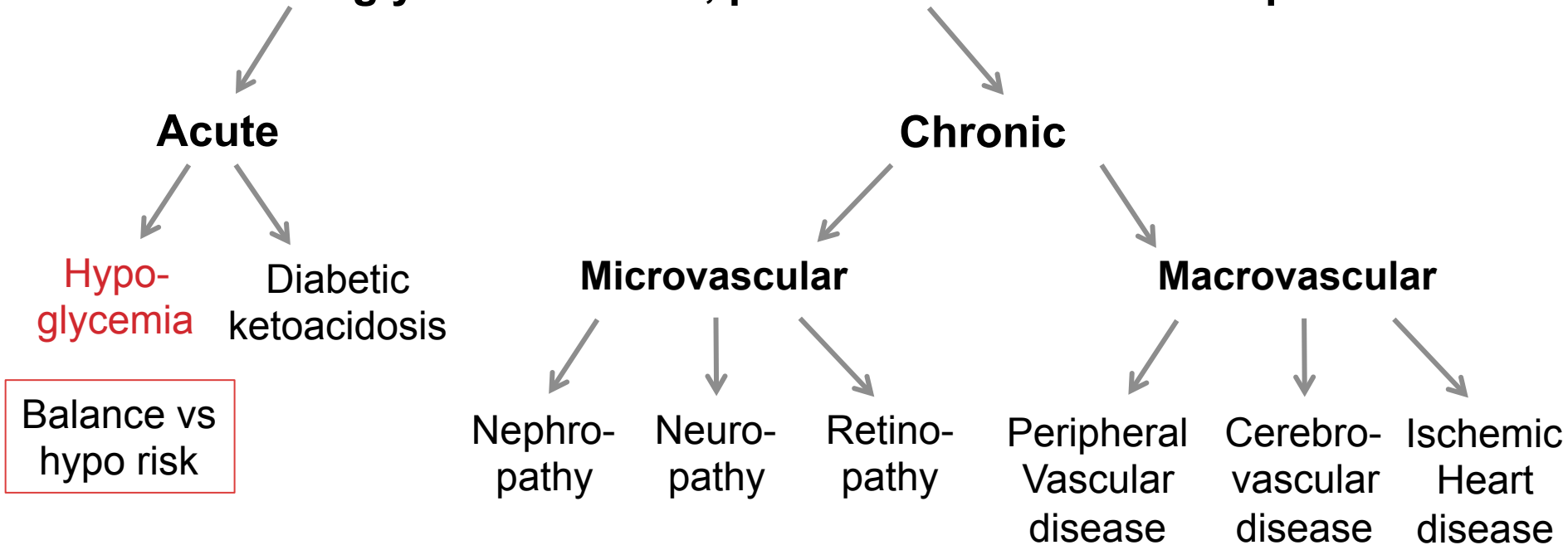
# ESSENTIAL HYPERTENSION

**Choice of anti-hypertensive agent based on comorbidity:**

| | ACE-I | Beta-blocker | CCB | Diuretic |
|---|---|---|---|---|
| DM | ↓ proteinuria | Hypo danger | | ↑ Glucose |
| Asthma | | Exacerbates | | |
| CCF | ↓ remodelling | ↓ remodelling<br>May worsen severe CCF | Non-DHP may worsen | Relieves symptoms |
| Angina | | ↓ $O_2$ demand | ↓ $O_2$ demand | |
| Pregnancy | Teratogen | Careful | | |
| Arrhythmia | | Helps tachys<br>Worsen blocks | | |
| Gout | | | | May worsen |
| ↑ K | Will ↑ K | | | K-losing help<br>K-sparing ↑ K |

# DIABETES

**Goal: Good glycemic control, prevent downstream complications.**




**Principles:**

- **Type 1: absolute insulin insufficiency, absolute replacement.**
- **Type 2: natural history is progressive beta cell failure.**

# DIABETES

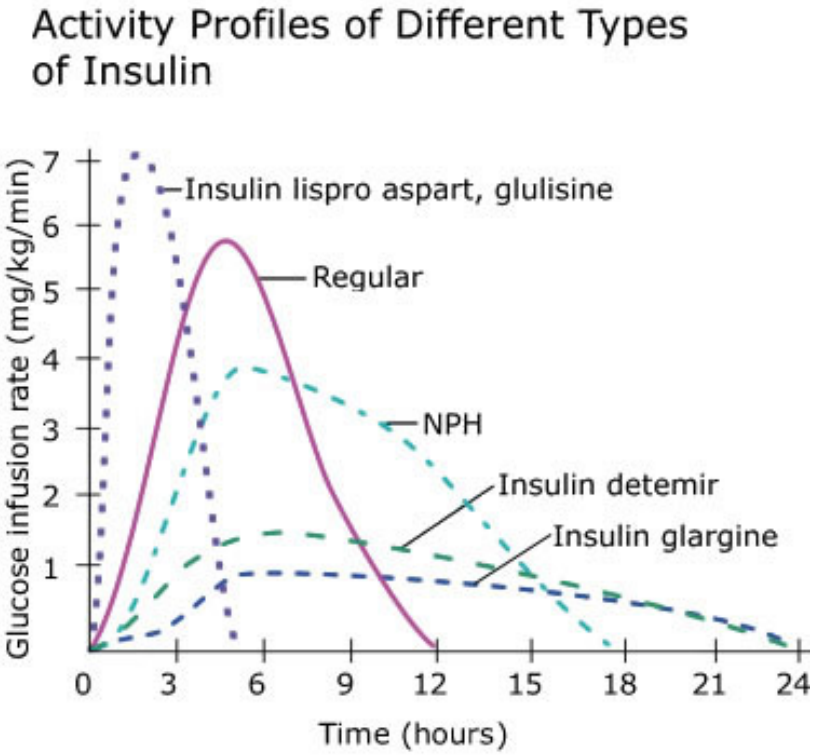
## Key thrusts of pharmacological management of DM:

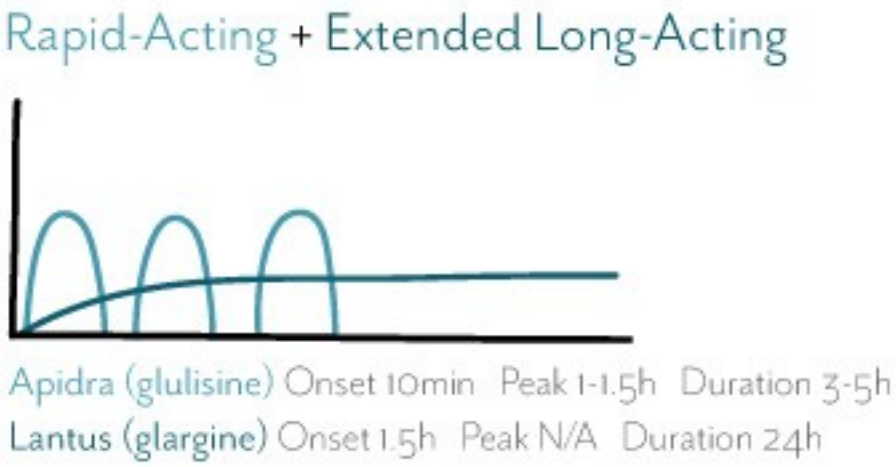
- **Increase sensitivity to insulin (metformin).**
  - Works when beta cells are intact
  - Unlikely effective in T1DM, or late T2DM
- **Increase amount of insulin**
  - Increase endogenous secretion (secretagogues)
  - Give exogenous insulin
- **Why are there so many different types of insulin?**

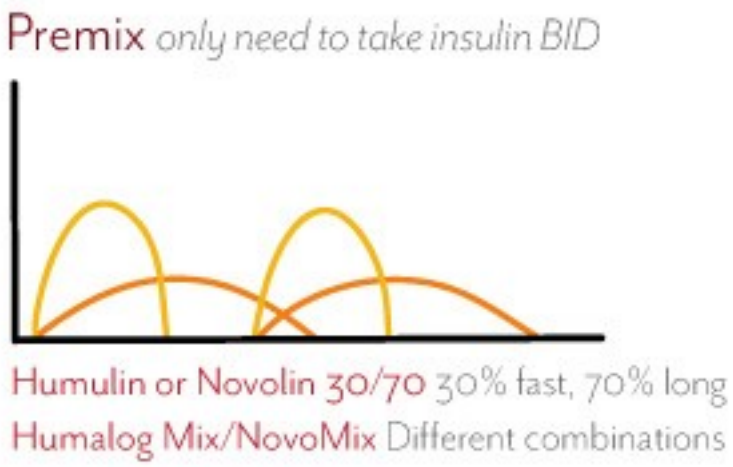
# DIABETES

Having different insulins allow us to choose different dosing regimens

Source
- http://sketchymedicine.com/
- http://dtc.ucsf.edu/types-of-diabetes/type1/treatment-of-type-1-diabetes/medications-and-therapies/type-1-insulin-therapy/types-of-insulin/



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