

CHOLESTROL $\rightarrow$ liver, intestine, skin, adrenal cortex, Reproductive tissue.

2 Acetyl CoA - also called animal sterol.

CoA-SH $\xleftarrow{\text{Thiolase}}$

Acetoacetyl CoA

Acetyl CoA $\xleftarrow{\text{HMG CoA synthase}}$

CoA-SH

(HMG CoA) B

β Hydroxy β Methyl glutaryl CoA

2 NADPH + 2H^+

2 NADP $^+$

CoA-SH

HMG CoA reductase
Rate limiting enzyme (RLE)

$\oplus$ Insulin
 $\ominus$ glucagon, AMP, statins

Mevalonate (6C)

ATP $\xrightarrow{\text{Mg}^{2+}}$ ADP $\xrightarrow{\text{Mg}^{2+}}$ Mevalonate kinase

(helps to reduce cholesterol level in our body)

5-phosphomevalonate

ATP $\xrightarrow{\text{ADP}}$ Phosphomevalonate kinase

ATP $\xrightarrow{\text{ADP}}$ kinase

Co $_2$, Pi $\xleftarrow{\text{Pyrophosphomevalonate decarboxylase}}$

6 $\times$ Isopentenyl pyrophosphate (5C)

H $^+$ + NADPH $\xrightarrow{\text{Mg}^{2+}, \text{Mn}^{2+}}$ NADP $^+$ $\xrightarrow{\text{Squalene synthase}}$

PPi

Squalene (30C)

NADPH + H $^+$ $\xrightarrow{\text{epoxidase}}$

NADP $^+$ $\xrightarrow{\text{Hydroxylase}}$

O $_2$ $\xrightarrow{\text{cyclase}}$

H $_2$ O

Lanosterol

H $_2$ O $\xleftarrow{\text{NADPH, O}_2}$ $\xrightarrow{\text{A series of Rxn (about 19)}}$ $\xleftarrow{\text{NADP}^+}$ Cholesterol (27C)

enzymes - cytosol
- Amphipathic in nature
i.e. hydrophilic + hydrophobic

Hypercholesterolemia

- $\uparrow$ plasma cholesterol ($>200\text{mg/dl}$)
observed in:-
i) Diabetes Mellitus
ii) hypothyroidism
iii) obstructive jaundice
iv) Nephrotic syndrome

Control:-
i) consumption of polyunsaturated fatty acid
ii) plant sterols
iii) dietary fiber $\rightarrow$ less cholesterol absorption from intestine.
iv) avoid high carbs diet.
v) little red wine consumption.

Hypocholesterolemia

$\rightarrow$ less plasma cholesterol level.
observed in:-
i) hyperthyroidism
ii) pernicious anemia
iii) malabsorption syndrome
iv) hemolytic jaundice.

HMGR enzyme present in cytosol and in mito.

cholesterol synthesis $\uparrow$ ketone synthesis

Regulation

compactin, lovastatin (competitive inhibitors)

Insulin
Thyroxine
(enzyme dephosphorylated)

HMG CoA

$\oplus$

Mevalonate

$\downarrow$

Cholesterol

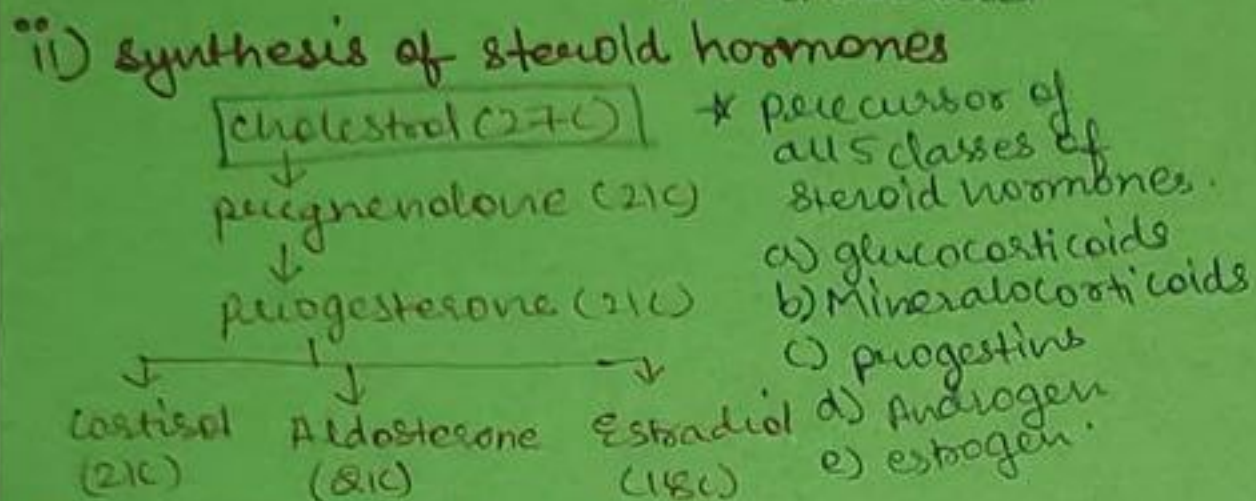
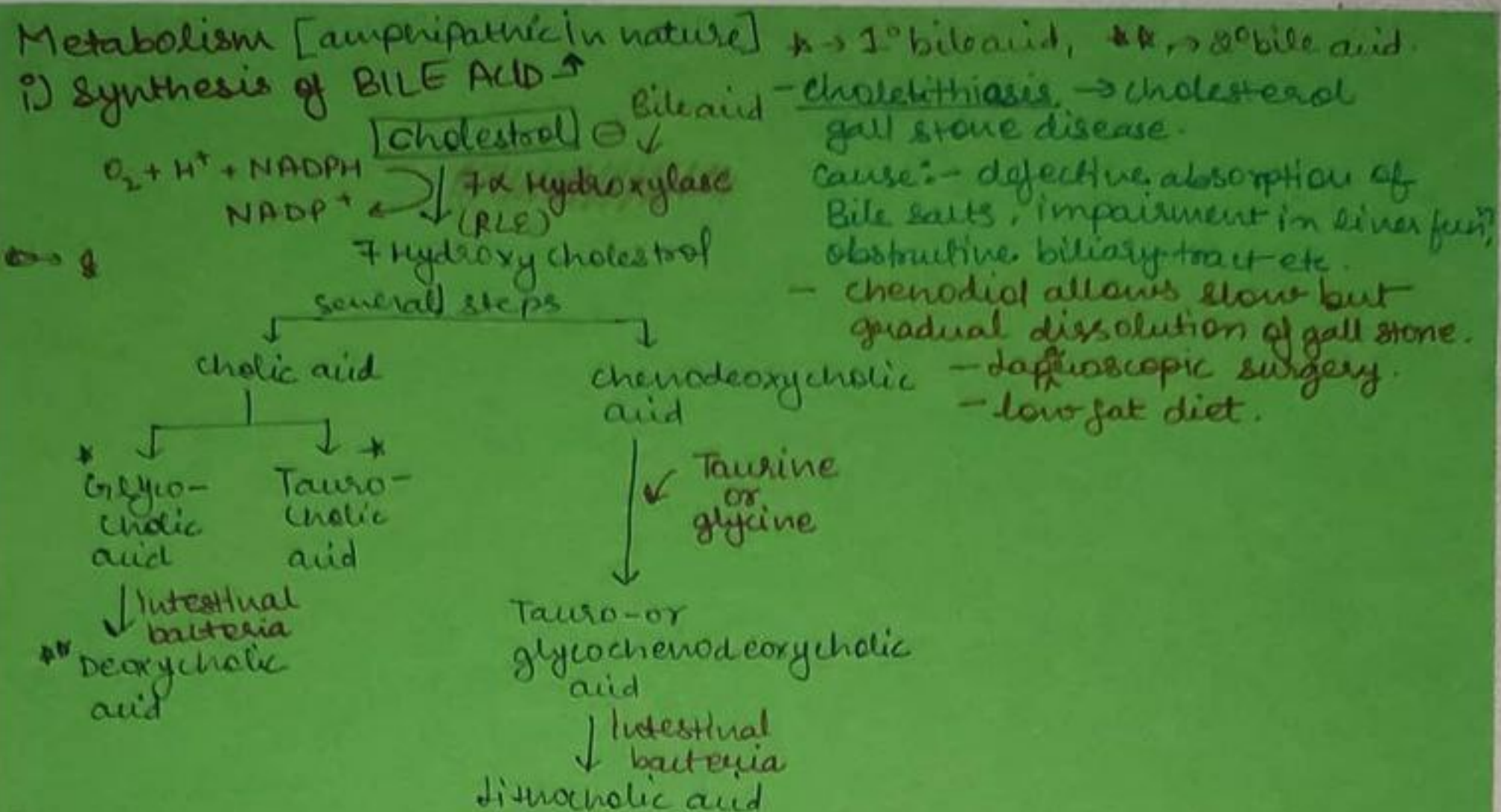
HMG CoA reductase $\ominus$

$\uparrow$ Translation mRNA

$\uparrow$ Transcription DNA

glucagon, glucocorticoids (phosphorylated)

Purpose:- cellular homeostasis
precursor for bile acids, hormone steroid, vit D.



iii) Synthesis of vitamin D.

