

WELCOME

Updated Management of NAFLD

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DARK NIGHT



SUN RISE

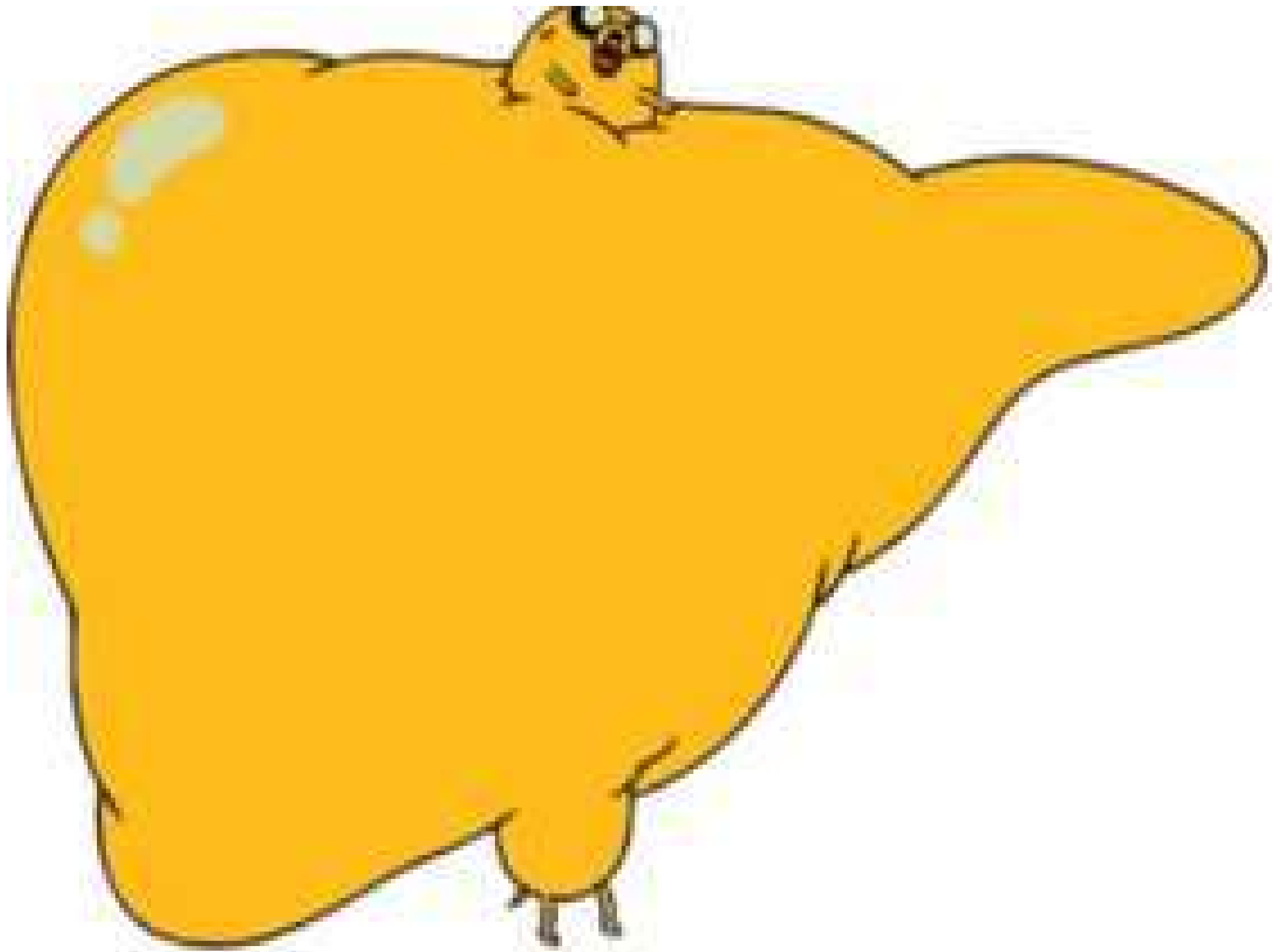


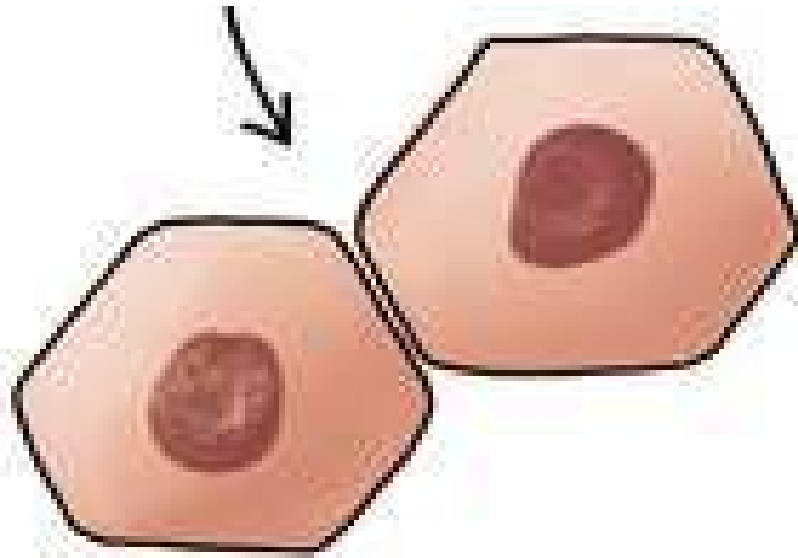
SUNNY DAY

■ ■ ■ ■ ■ ■ ■ ■ ■ ■ Changing life style

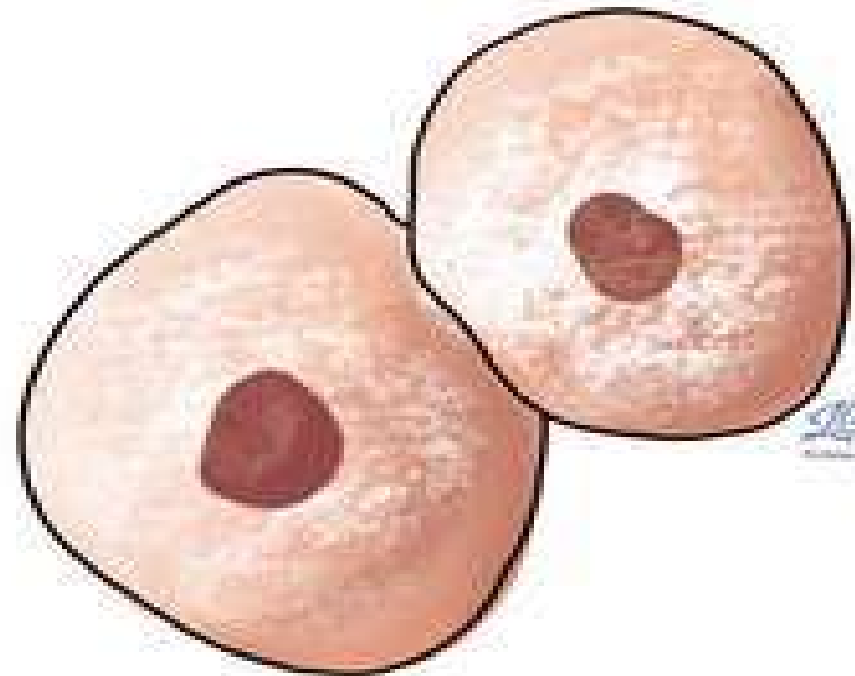
GENE ↔ IR







NORMAL, HEALTHY
HEPATOCYTES



BALLOONING HEPATOCYTES

- Man is obese
Liver large
- Cells are ballooned
Thing fibrous

..... NAFLD

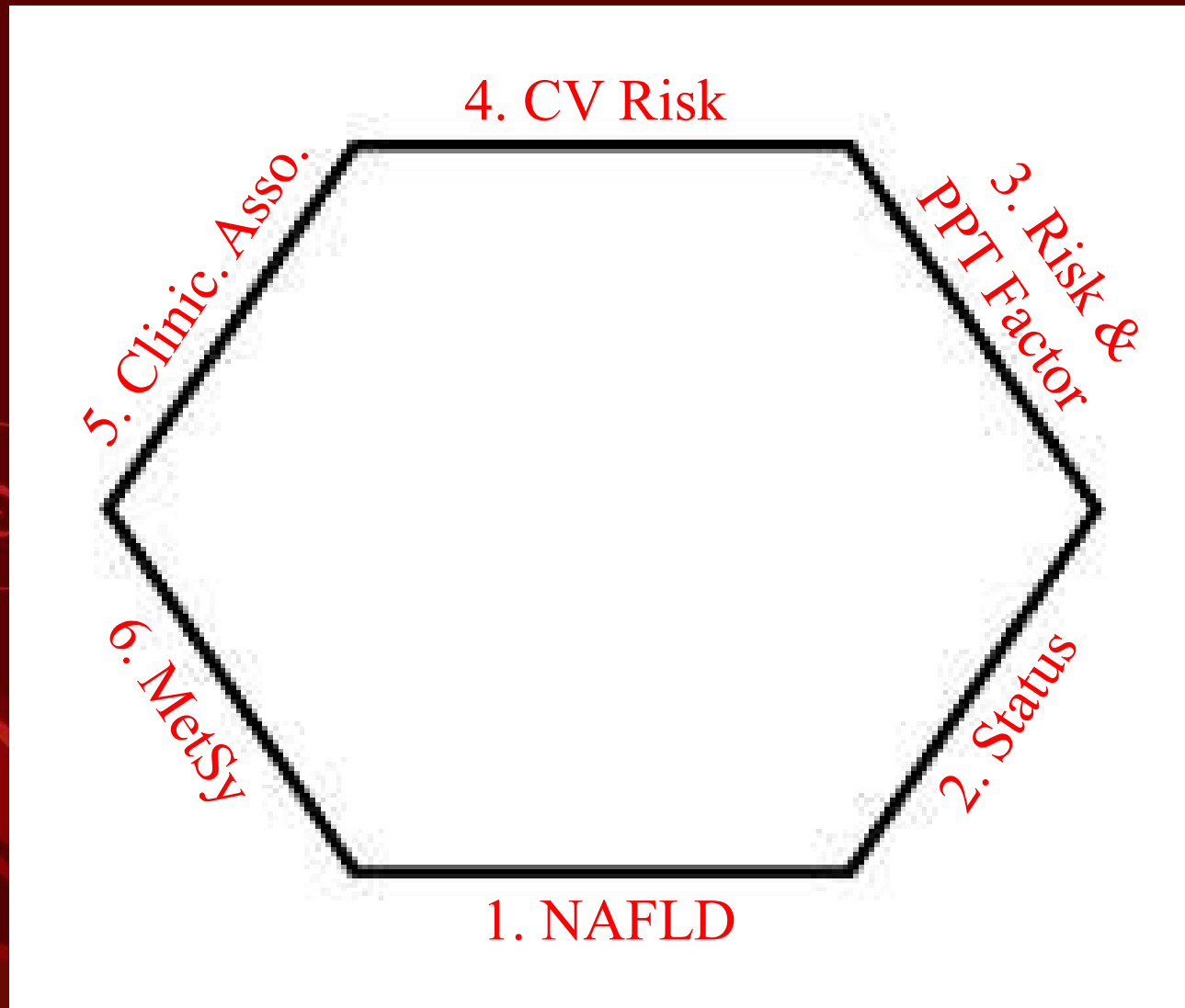
Management of NAFLD

Evaluation

Treatment

- NAFLD - Non alcoholic fatty liver diseases
- NASH - Non alcoholic steatohepatitis
- NAS - NAFLD activity score
- NFS - NAFLD fibrosis score
- NAF - No advanced fibrosis
- LR - Low risk
- IR - Indeterminate risk
- HR - High risk

Evaluation of NAFLD



1. NAFLD

1. Burning problem

In USA 25% of adult have NAFLD

20% of NAFLD patient have NASH

(5% of adults in the USA)

2. Hepatic manifestation of metabolic syndrome

3. Most common cause of abnormal LFT

4. cryptogenic cirrhosis; NAFLD cirrhosis

5. It includes

Steatosis → Steatohepatitis → Fibrosis → Cirrhosis

SUSPICION of NAFLD

1. Radiological evidence of steatosis
2. Abnormal liver biochemistry
3. Metabolic syndrome
4. Exclusion of alternative diagnosis

Pathogenesis

First Hit

Normally fat present in less than 5% of liver weight

Fat in liver depends on

Import & Synthesis

Export & Catabolism



If ratio favors import & synthesis fat deposits in liver.

Second Hit

Oxidative stress

Direct lipotoxicity

Endoplasmic reticulum stress

Gut-derived endotox

Cytok release (tnf - α)

Immune mediated

Pathology

1. Ballooning
2. Hepatocyte injury
3. Inflammation
4. Varying degree of fibrosis
5. Cirrhosis
6. Hepatocellular carcinoma

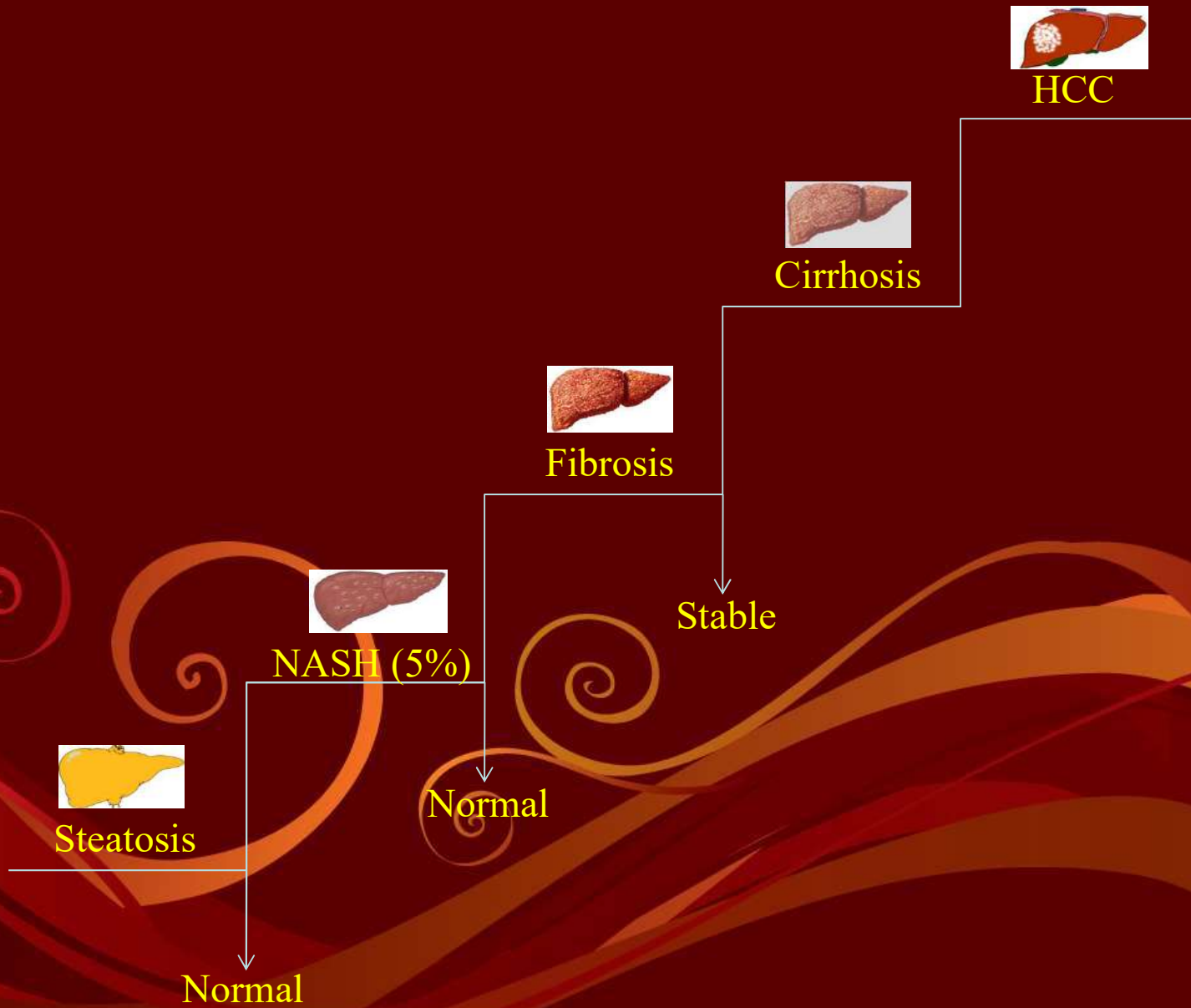
Fibrosis cirrhosis

1. Pericellular
2. Progress to cirrhosis

Pathology of Steatosis

1. Macro vesicular lipid accommodation
2. Occurs in >5% of hepatocyte
3. Begins around central veins

2. Status of NAFLD



NASH

Diagnosed by NAS (NAFLD activity score)

- NAFLD activity Score (NAS)

Steatosis	(0-3)
Lobular inflammation	(0-3)
Balloon degeneration	(0-3)
<hr/>	
Total NAFLD activity score	(0-8)

- If $NAS \leq 5$ – No NASH
- If $NAS > 5$ - NASH

Fibrosis & cirrhosis

- Assessment of fibrosis & cirrhosis

NFS (NAFLD fibrosis score)

Fibroscan

Liver biopsy

Assesment of status

Initial diagnosis of NAFLD



NFS (NAFLD fibrosis score)



Fibroscan (transient elastography)



Liver biopsy

What is NFS ? (non invasive process)

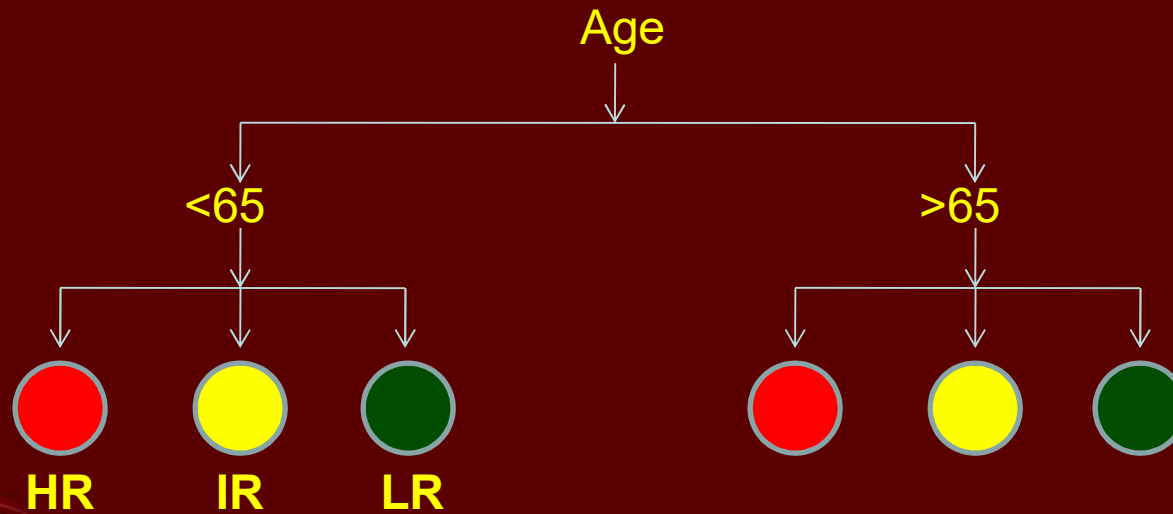
assessed by

1. Age
2. BMI
3. IFG/DM
4. AST / ALT ratio
5. Platelet count
6. Albumin level

Formula for NFS

$$\begin{aligned} & -1.675 + 0.037 \times \text{Age} \\ & + \\ & 0.094 \times \text{BMI} \\ & + \\ & 1.13 \times \text{IFG / DM} \\ & + \\ & .99 \times \text{AST / ALT} \\ & - \\ & 0.013 \times \text{Platelet count} \\ & - \\ & .66 \times \text{Albumin level} \end{aligned}$$

Threshold

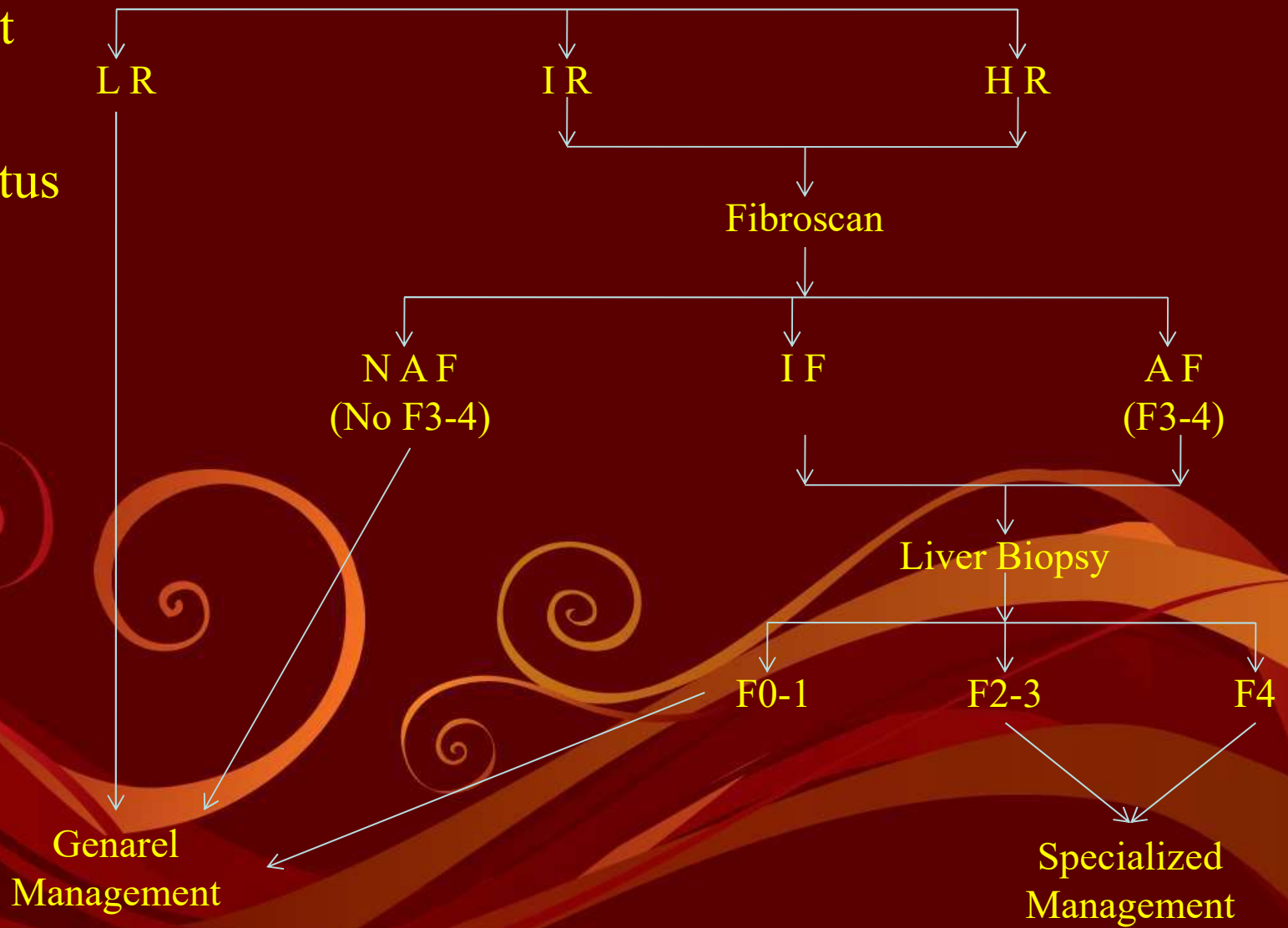


LR = <1.455
IR = -1.4552 to $.676$
HR = $>.676$

LR = <0.12
IR = 0.12 - $.676$
HR = $>.676$

NFS

Flow chart
To
Confirm status



3. Risk & PPT Factor

Risk Factor

1. Age over 45
2. Sex
 - Higher in men than in women during reproductive age
 - After menopause higher in women
3. Genetic
4. Insulin Resistance

PPT Factor

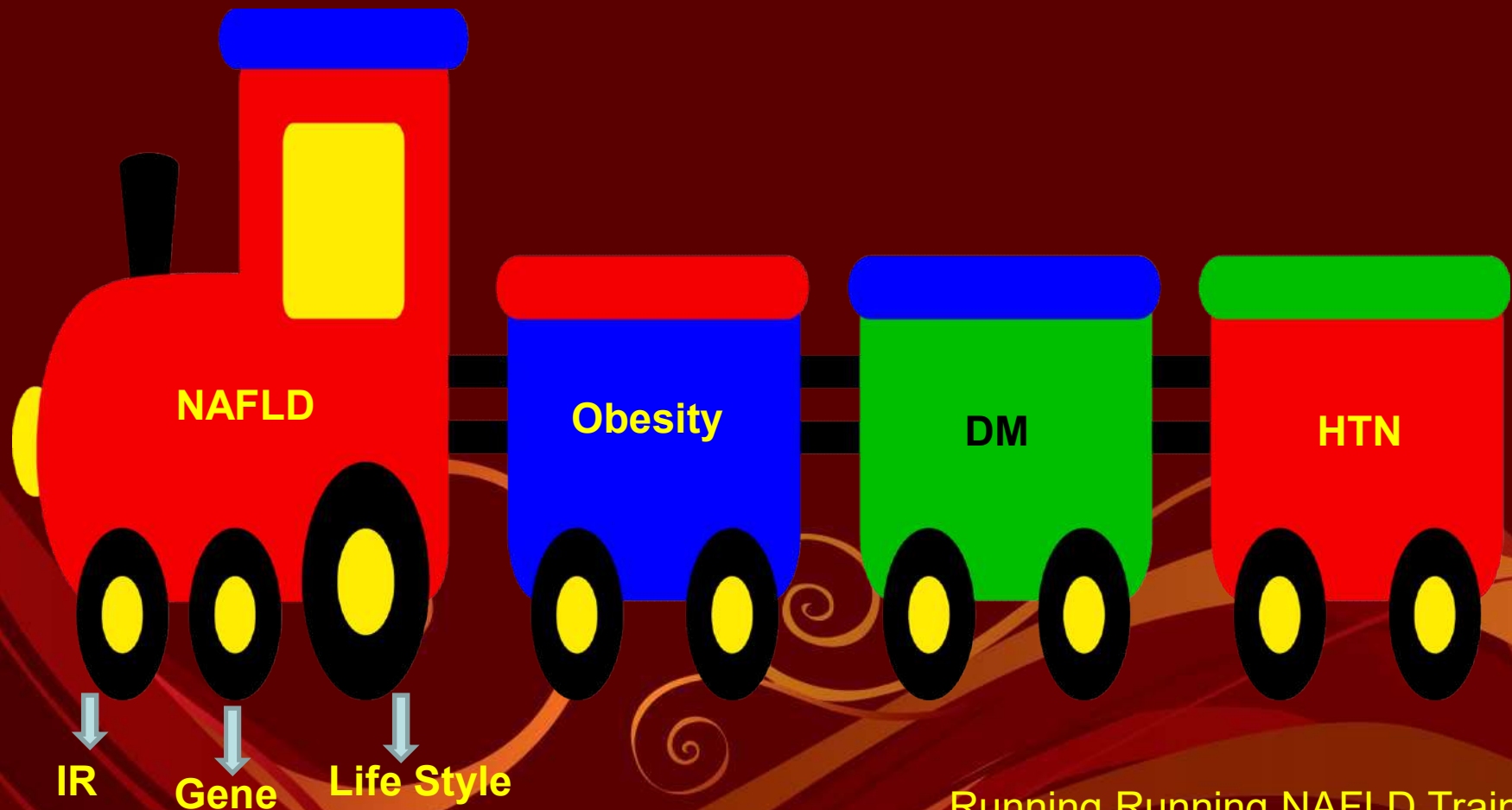
1. Changing dietary pattern
2. Sedentary Life style
3. Micro biota

4. Cardiac & Vascular Risk

1. Hypertension
2. Coronary heart disease
3. Cardiomyopathy and
4. Cardiac arrhythmias
5. Ischemic stroke

5. Clinical Association

Common



NAFLD Train

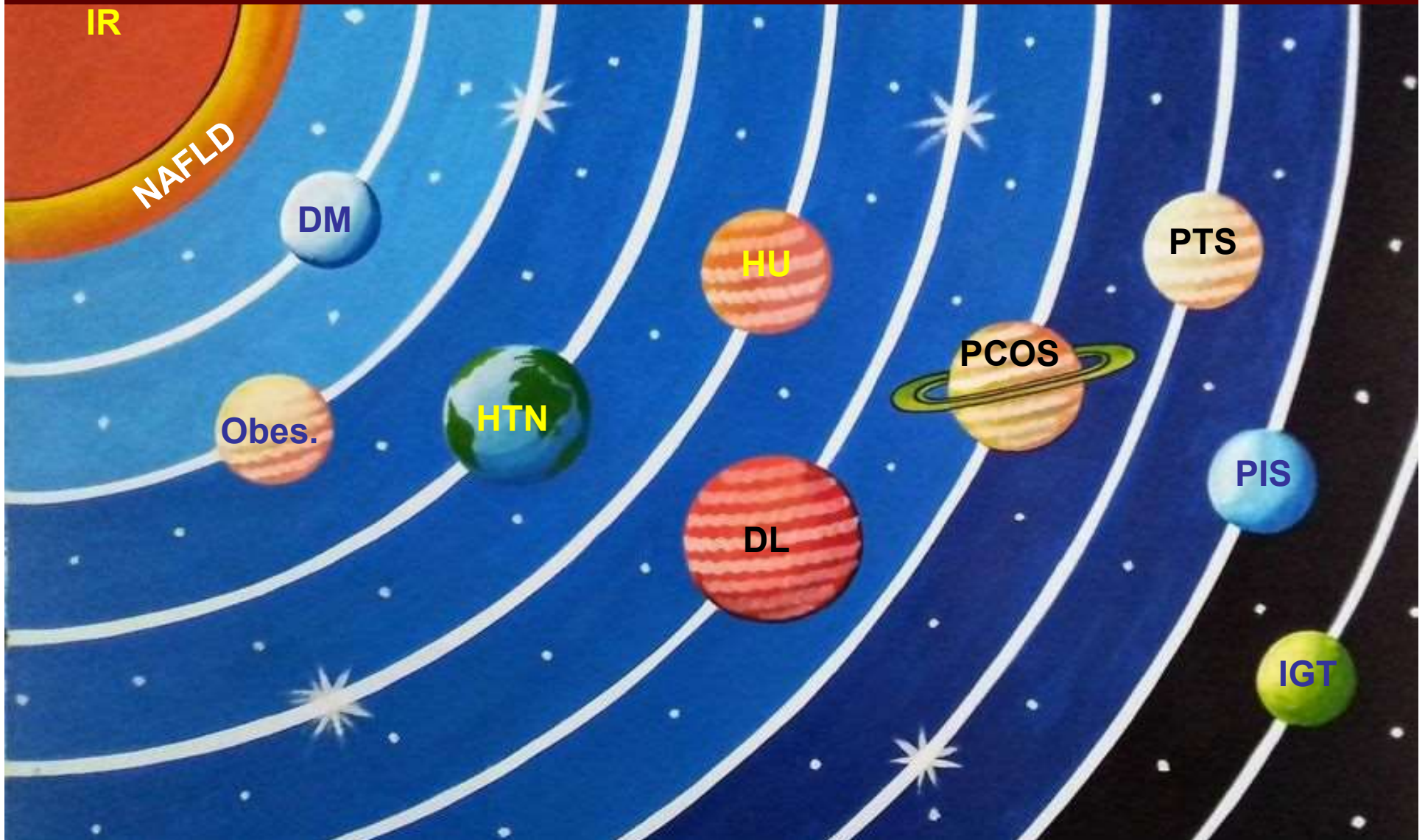
Running Running NAFLD Train
Gene is core and IR main
Change of diet makes speed more
If not treated life is bore

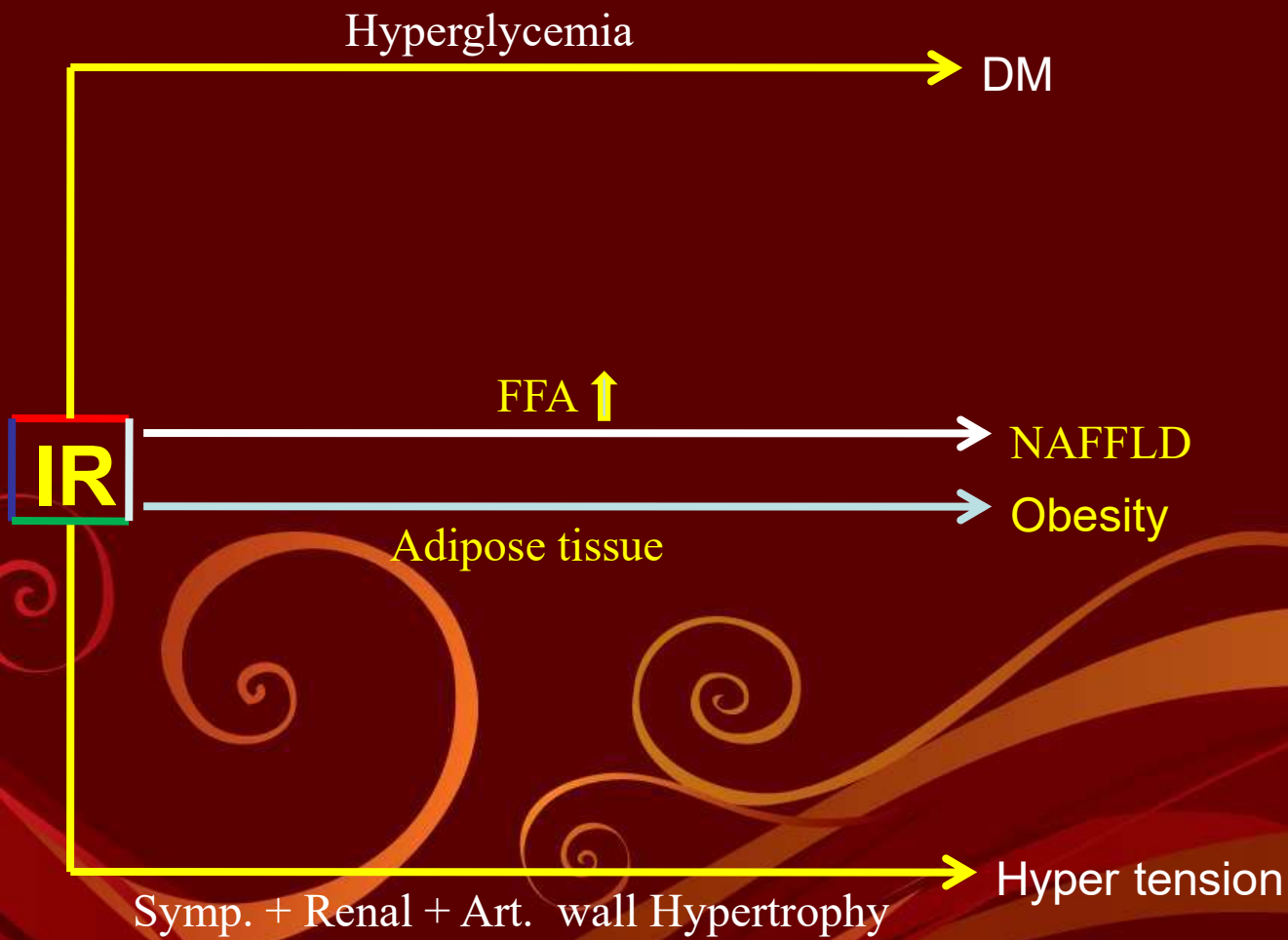
Uncommon

1. Polysistic Ovary syndrome
2. Small-bowel bacterial overgrowth
3. Hypothyroidism
4. Hypopituitarism

6. METABOLIC SYNDROME

NAFLD World





Investigation

1. Complete blood count
2. Liver function test
3. USG of W/A
4. Lipid profile
5. Blood sugar estimation
6. ECG
7. Echo
8. S / Uric acid
9. Fibroscan of liver
10. Liver biopsy

USG of W/A

Sonological Grading

Grade	Echogenicity	Comment
Grade 0	Normal Echogenicity	No Steatosis <5%
Grade 1	Higher than right renal cortex	Mild steatosis 5%-33%
Grade 2	Impaired echogenicity of the vein wall	Moderate Steatosis >33%-66%
Grade 3	Impaired visualization of the posterior hepatic parenchyma	Severe Steatosis >66%

Fibroscan of Liver

Specialized ultrasound
sometimes used instead of liver biopsy
to find out fat and scar tissue in the liver

Liver Biopsy

- Indication :- Fibroscan - Advance fibrosis (F3-4)
Indeterminate fibrosis
- Liver biopsy yeilds :-
NASH / fibrosis / both NASH and fibrosis / cirrhosis / HCC

- **Fibrosis** (MASSON – TRICHROME stained slide)

0 – No fibrosis

1 – Perisinusoidal fibrosis

2 – Perisinusoidal + portal / periportal fibrosis

3 – Bridging fibrosis

4 – Cirrhosis

- **Cirrhosis**

Fibrosis grade 4 is cirrhosis

Treatment

- Aim of Treatment

1. To reduce intrahepatic fat
2. To reduce NAFLD score
3. Histological improvement
4. To combat co morbidities

- **Modalities of treatment**

1. **Counseling**
2. **Lifestyle modification**
3. **Drug therapy**

- **Counseling**

1. Reasoning

2. Motivation

3. Determination

Life style modification

1. Exercise
2. Dietary modulation
3. Weight reduction
 - Low calorie intake
 - More calorie burn

4. Stop smoking
5. Water instead of sweet drinks
6. Sound and timed sleep with appropriate duration

Exercise regularly

1. At least 150 minutes/week

2. Moderate intensity activity (Walking/cycling)

- ❖ improve NAFLD, even without loss of weight

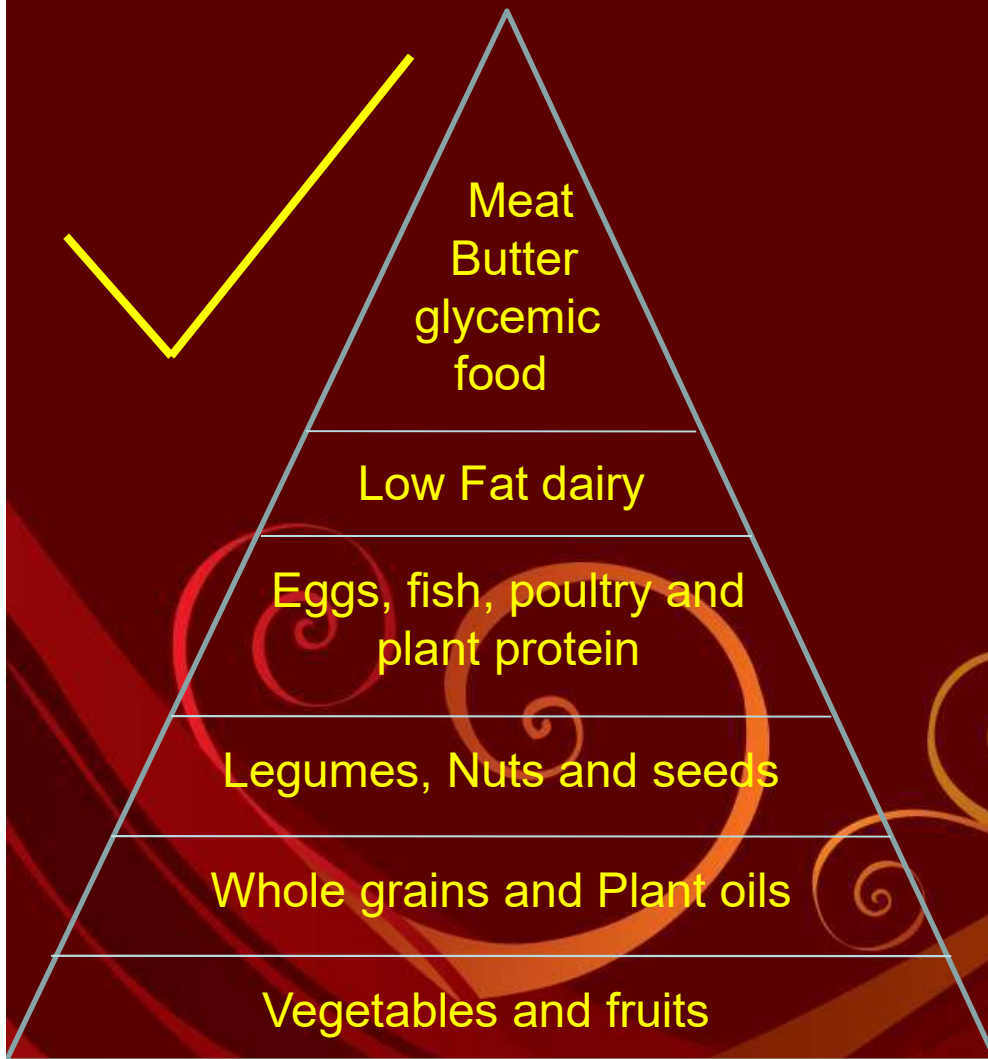
Dietary modulation (Mediterranean Diet)

1. Whole grain
2. Vegetables
3. Fruits
4. Less carbohydrate
5. Moderate protein
6. Low fat, sugar and salt
7. Water instead of sweet drinks

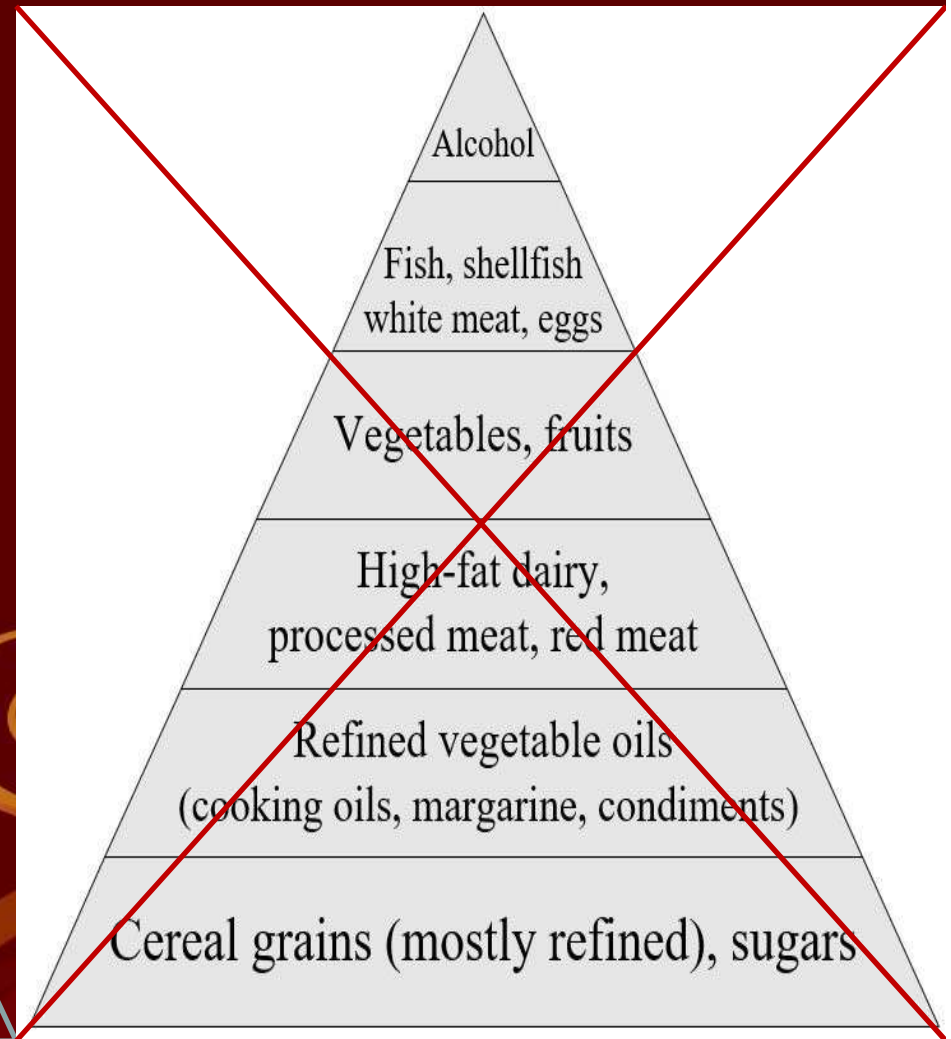
Mediterranean Component



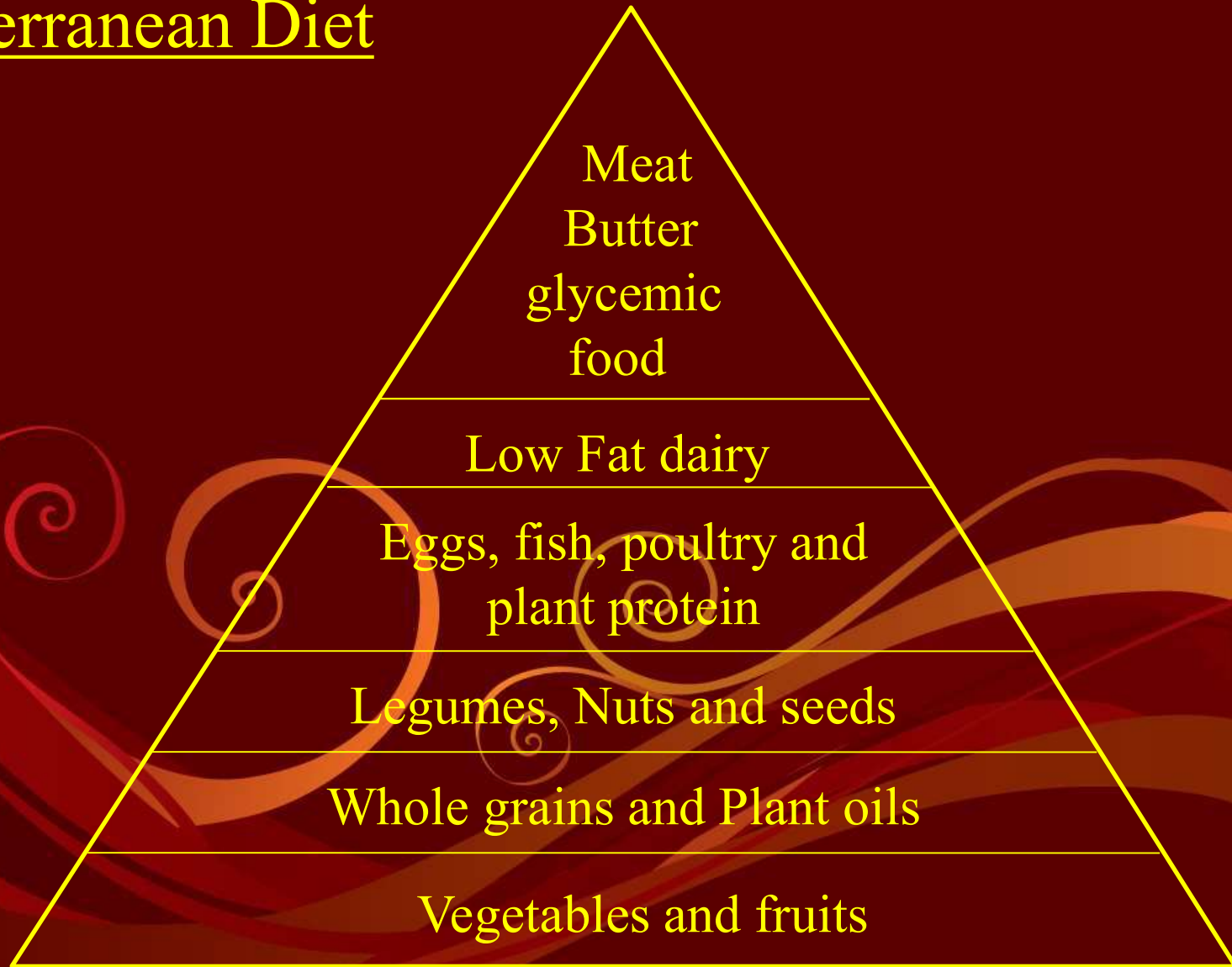
Mediterranean Diet



Western Diet



Mediterranean Diet



Food for Life

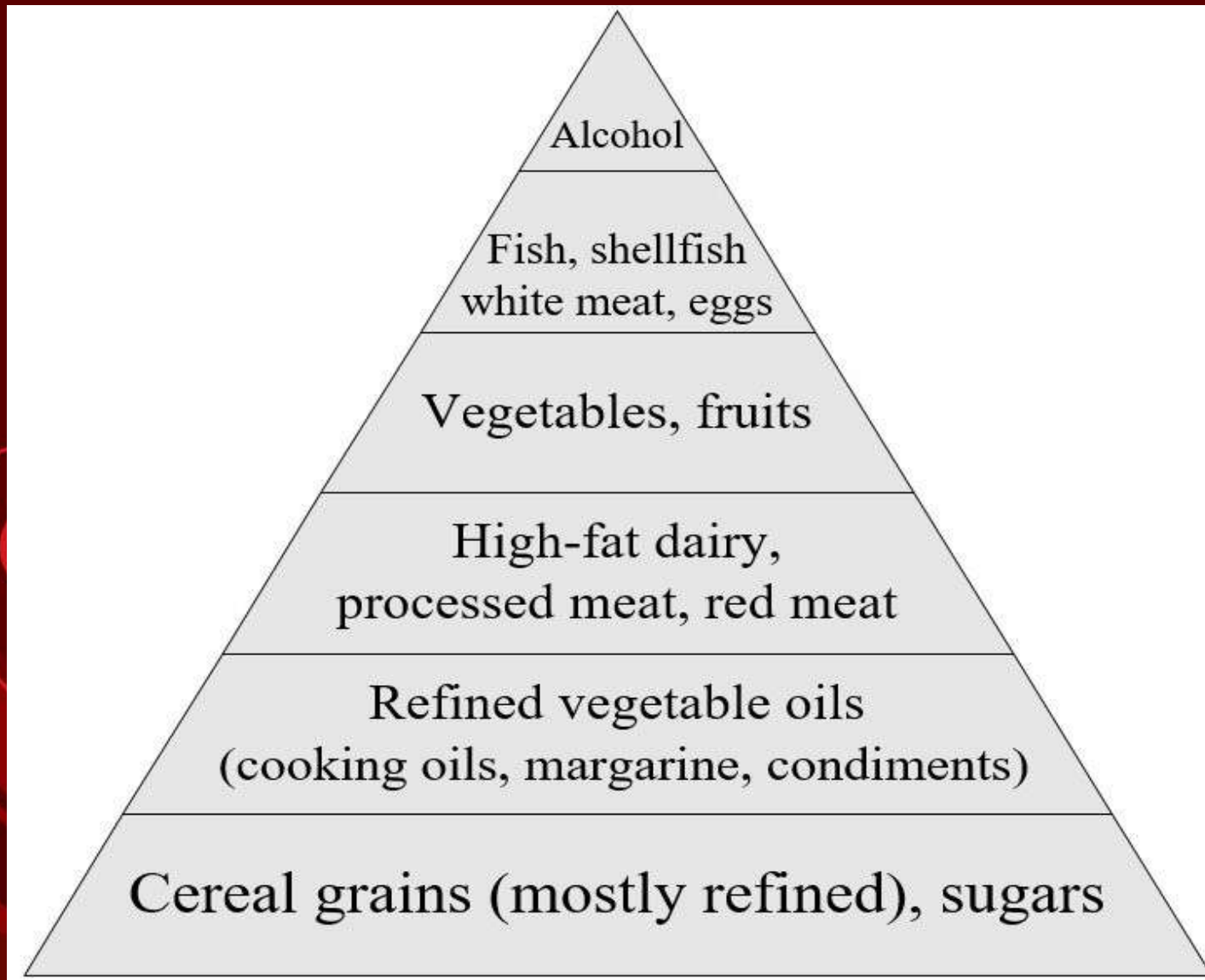


**Less curb, more herb,
slim and superb**

**More Move, Less eat,
Make your body fit**

**Less meat, Less fat,
nice your architect**

Western Diet



Western Component

What alluring !



Image credit: iStockphoto.com/Carlomagno

Life for Food !

**Oh ! What charm !
Occupying large
portion of the world !**



- **Weight Reduction**

1. 1kg / week improve both NASH and NAS
2. 1.6kg / week worse and the situation

Pharmacological Treatment

No pharmacology agents are currently licensed specifically for NASH therapy

Aims of drug therapy

1. To reduce NASH fibrotic activity
2. To control associated metabolic disorder

Following drugs are sometime used with question

1. Ursodeoxycholic acid
2. Obeticholic acid
3. Metformin
4. Vitamin-E
5. Pentoxifylline
6. Angeotensin receptors blockers
7. N-3 polyunsaturated fatty acids

Ursodeoxycholic acid

1. American guidelines do not recommend

Obeticholic acid (OCA)

1. Is a semi synthetic bile acid analog
2. Used in primary biliary cholangitis
3. 25 milligram per day for 18 month result in a highly statistically significant improvement of NAFLD activity score. 45% of treated add group show this result. It increase insolence sensitivity decrease marker of liver damage

Metformin

American guideline for NAFLD don't recommend

Vitamin-E

American guideline recommend non diabetic patient and biopsy proven NASH

Pentoxifylline

1. Inhibits synthesis of TNF- α
2. Help resolution of the NASH

Following drugs are also under study

- TSHB against – Thyroid hormone receptor bet
- Lipogenesis inhibitors
- ACC inhibitors (Acetyl CO-A Carbaxylose)
- FASN inhibitors (Fatty Acid Synthase)
- SCD inhibitors (Stery1-CO-A Ceseturax)

Last but not the least

1. Metabolic syndrome
2. Hepatic presentation
3. Genetic and Insulin resistance
4. Life style changes
5. No universal acceptance of drugs
6. Life style main stay
7. Counseling - RMD



Drugs

**Mediterranean
Food**

Lastly

We are waiting for universal drugs.

Looking forward
day and night
Full of pain
with log in fight.

We are tired
not with sleep
One by one goes
All hope slip.

নিশিদিন বসে আছি শুধু পথপানে চেয়ে

সহে না যাতনা

দিবস গণিয়া গণিয়া বিরলে

দেহে বল নাই চোখে ঘুম নাই

একে একে সব আশা ঝরে ঝরে পড়ে
যায় ।

Wait and wait for
several years
Drugs for NAFLD
Will appear.

কবে হবে অপেক্ষার পালা শেষ
কবে আমি পাইবো যে তারে



THANK YOU

