Metabolic Syndrome
“Is it an entity?”

Prof. Md. Rajibul Alam

MBBS, FCPS, MD, MACP
Professor of Medicine
Sir Salimullah Medical College &
Mitford Hospital

Metabolic Syndrome

Metabolic syndrome
(Syndrome X)

- Central obesity
- High blood pressure
- High triglycerides
- Low HDL-cholesterol
- Insulin resistance

Body Mass Index and Lipids

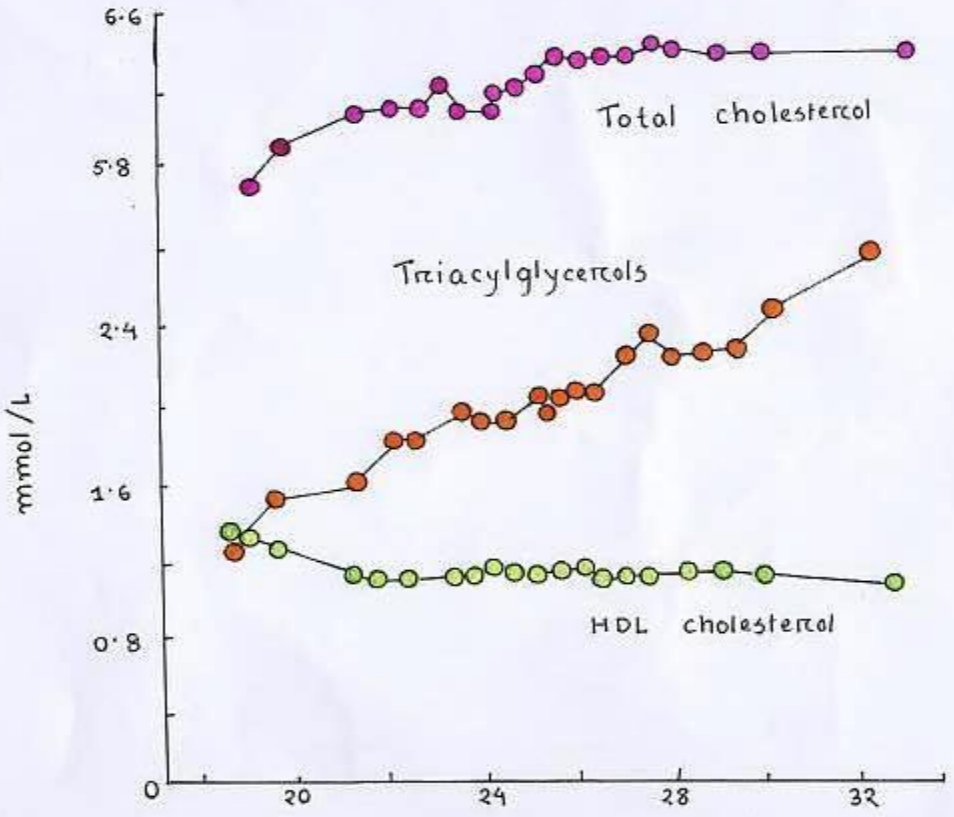
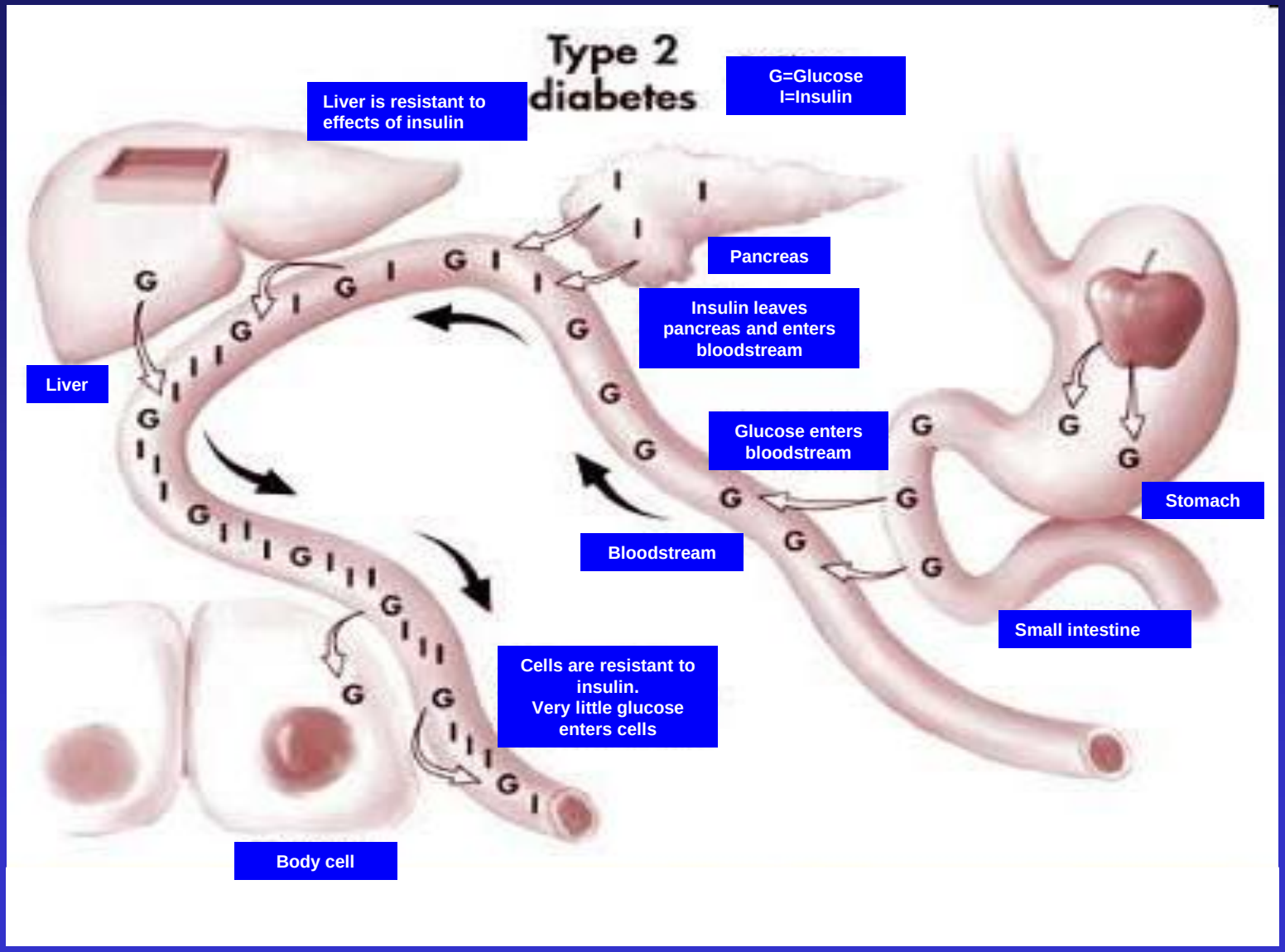


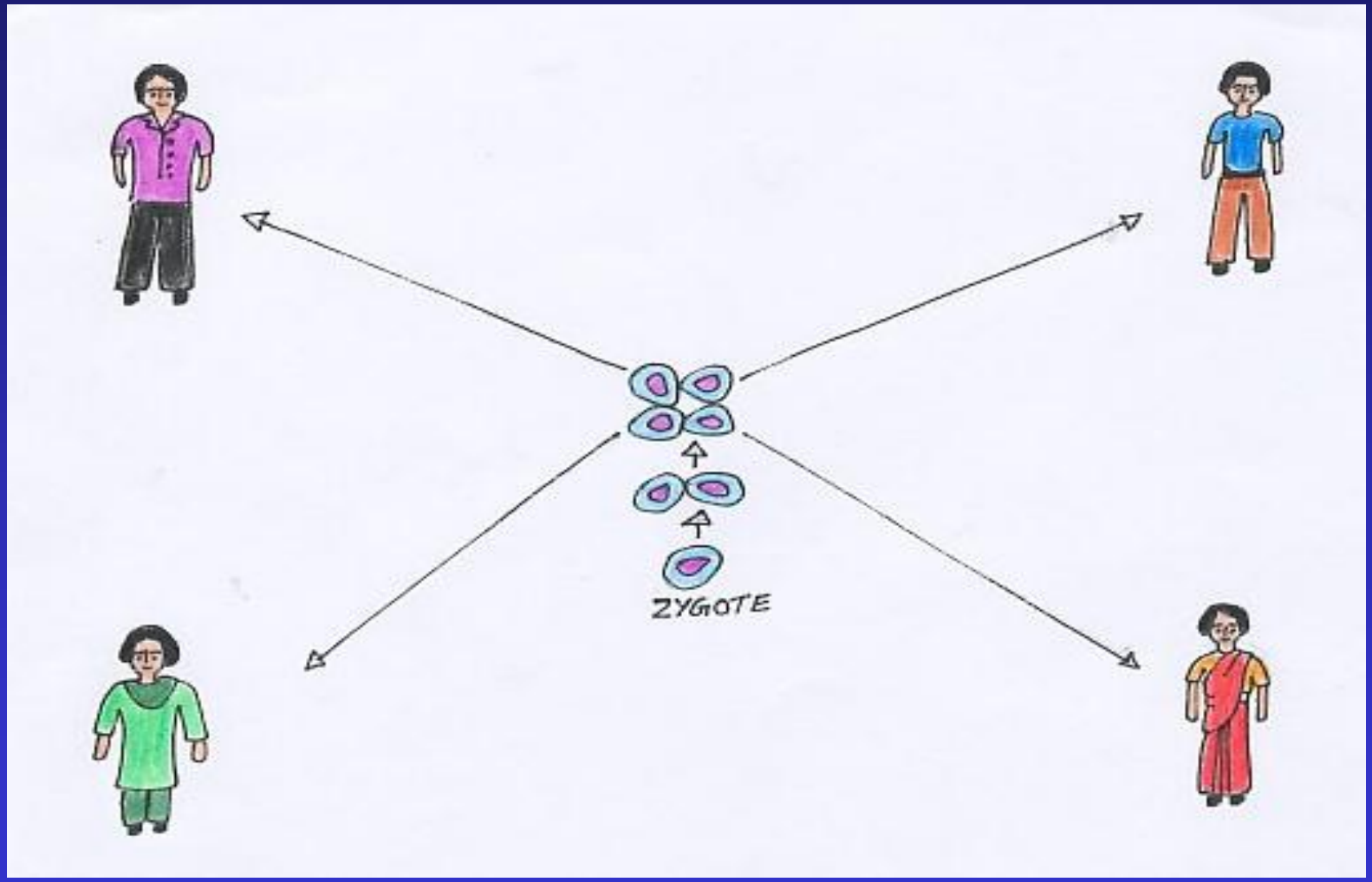
Fig: Body mass index and changes in blood lipids.

Insulin Resistance



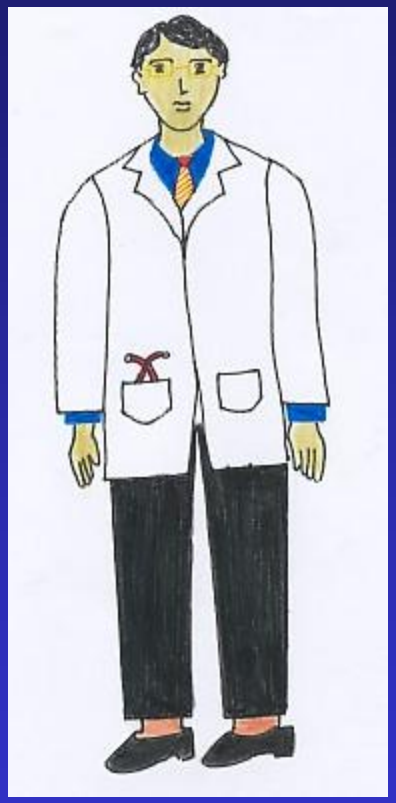
Is it an entity??

Components of Syndrome – Same Origin / Pathology?

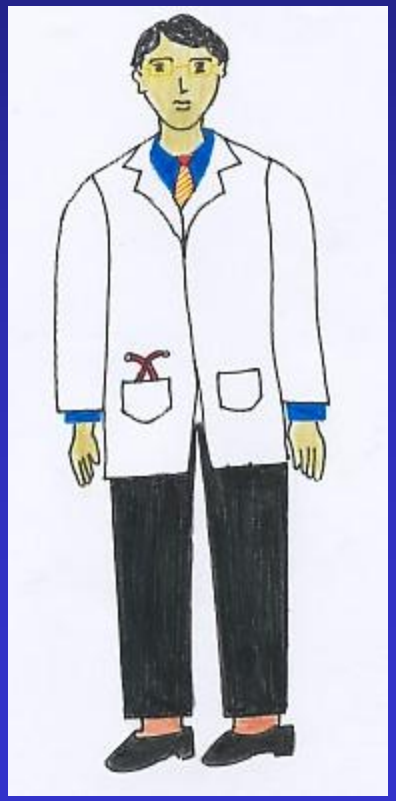


Components of Metabolic Syndrome-

Different Origin?



Component of Syndrome of Different Origin?



Definition of Syndrome

- Syn·drome

1. A group of symptoms that collectively indicate or characterize a disease, psychological disorder, or other abnormal condition.

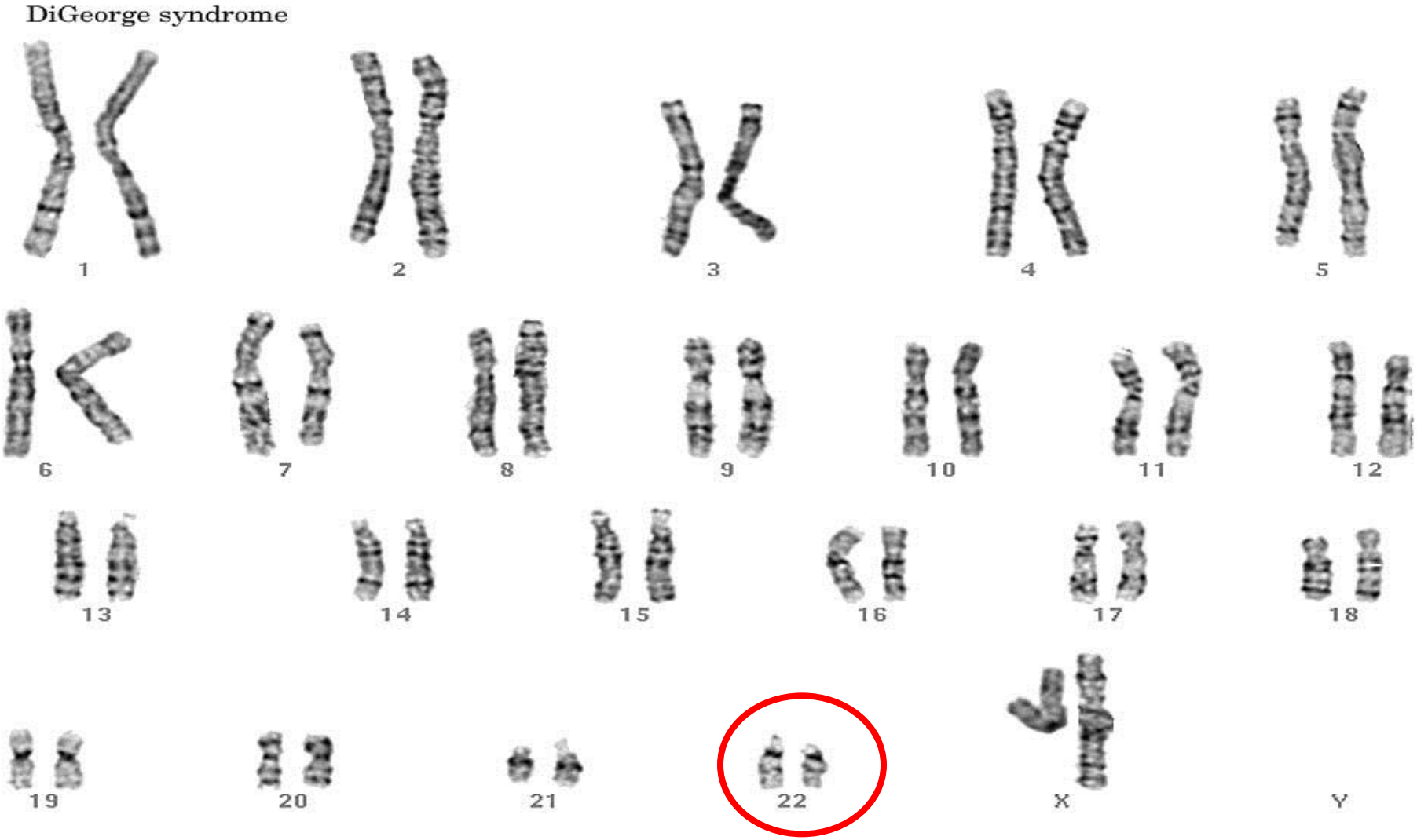
- Ref - The American Heritage® Dictionary of the English Language,

DiGeorge Syndrome

- ***DiGeorge Syndrome*** (*Angelo DiGeorge,1965*) is a set of symptoms which are part of 22q11.2 deletion syndrome.

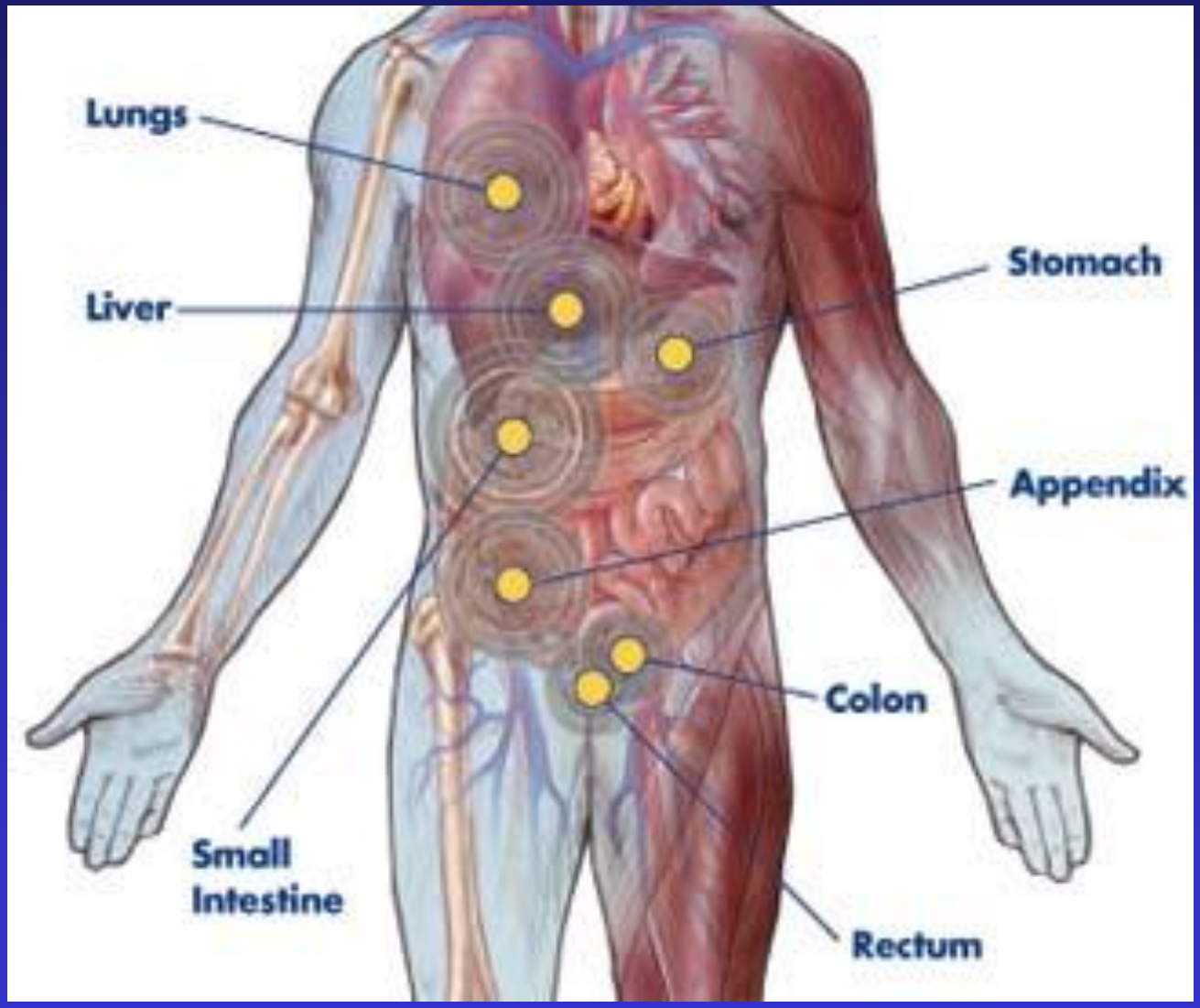
  - Thymic hypoplasia,
  - Hypo-parathyroidism, and
  - Recurrent infection.

Karyotype of DiGeorge Syndrome



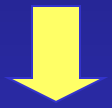
Light band missing at the pair of 22's

Carcinoid Syndrome



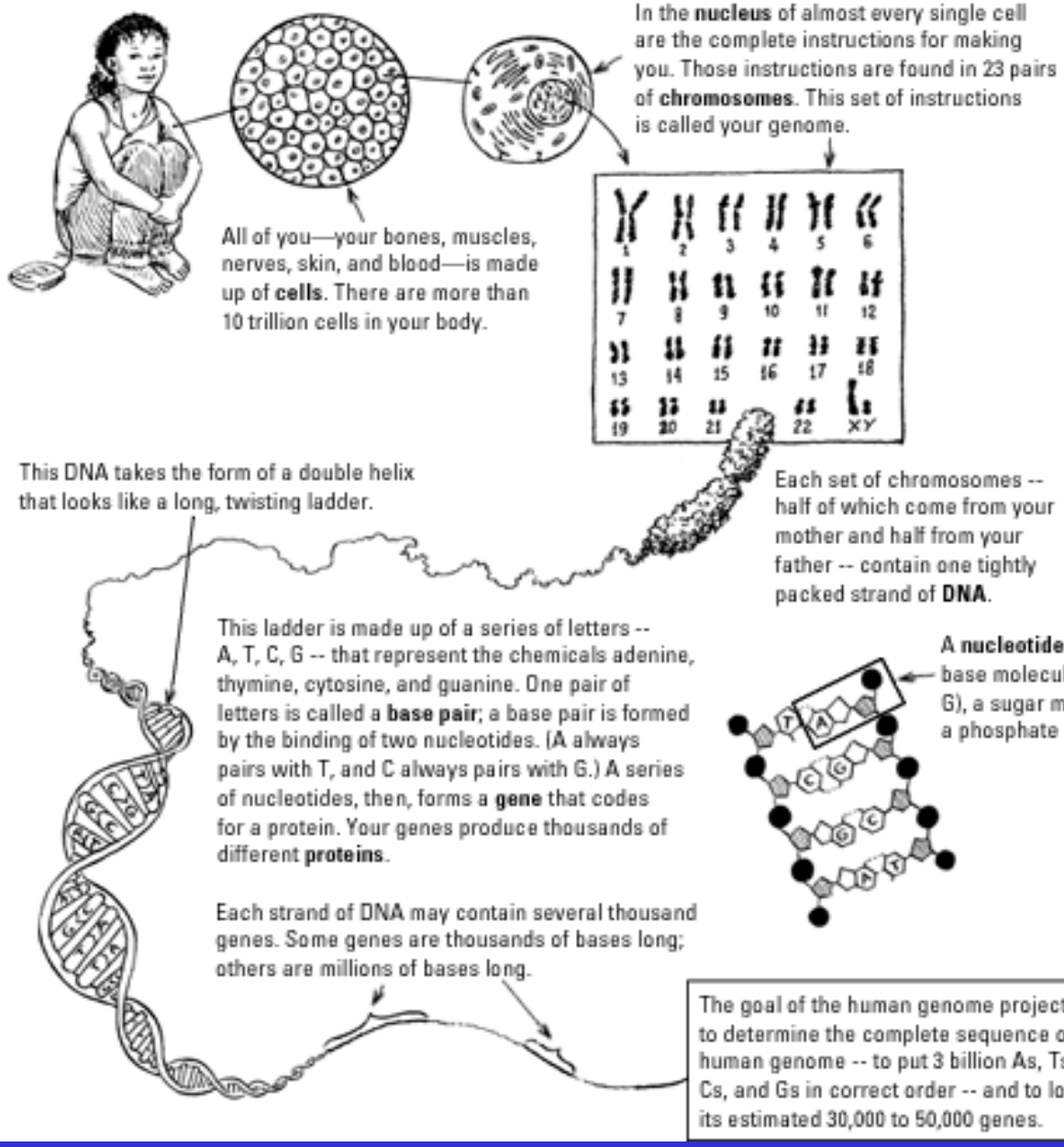
Nephrotic Syndrome

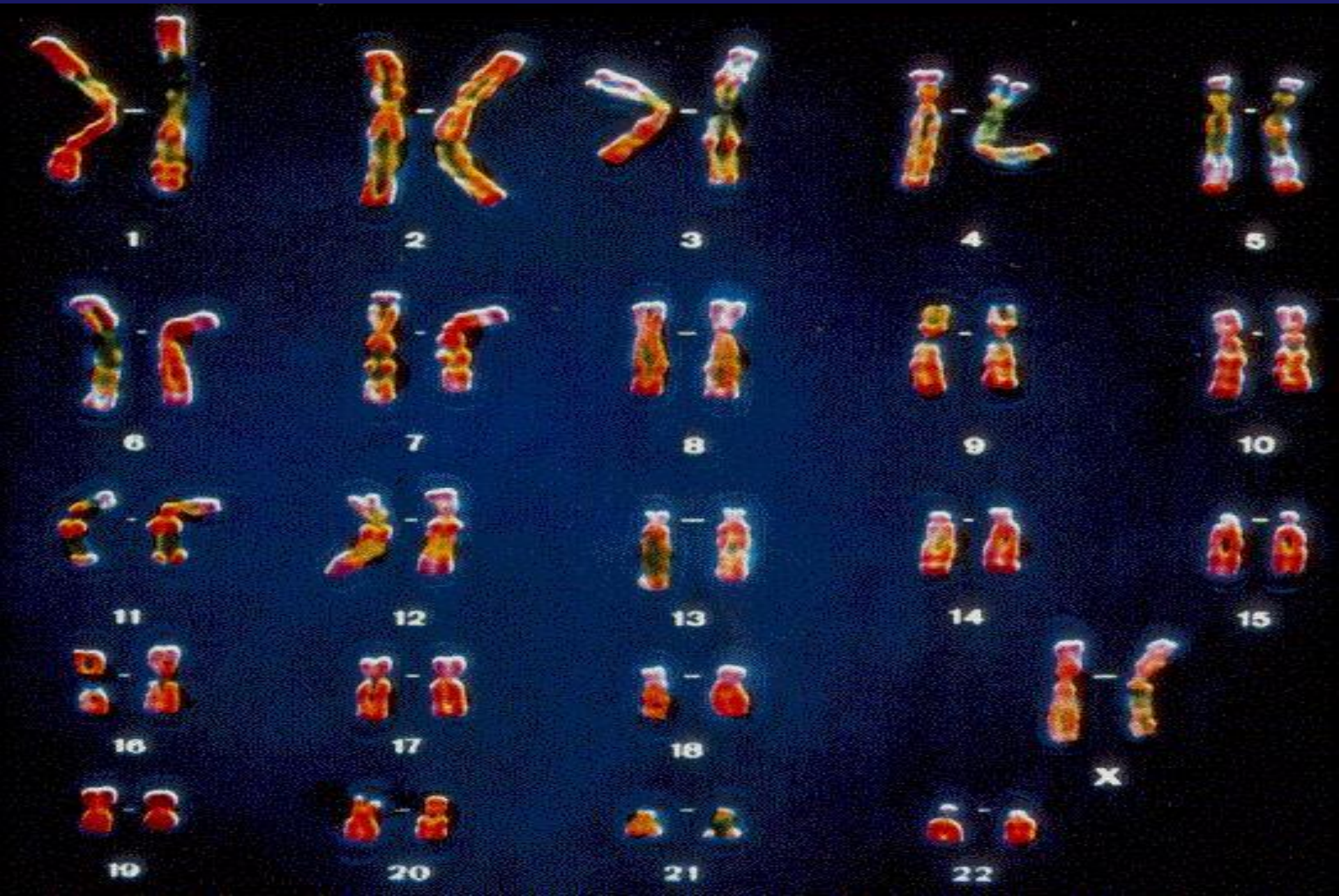
- A complex of symptoms, resulting from damage to the basement membrane of glomeruli.



  - Proteinuria
  - Hypoalbuminemia
  - Oedema, and
  - Hyperlipemia

Analysis of genetic structure of different components of Metabolic Syndrome


In the **nucleus** of almost every single cell are the complete instructions for making you. Those instructions are found in 23 pairs of **chromosomes**. This set of instructions is called your genome.
All of you—your bones, muscles, nerves, skin, and blood—is made up of **cells**. There are more than 10 trillion cells in your body.
This DNA takes the form of a double helix that looks like a long, twisting ladder.
Each set of chromosomes -- half of which come from your mother and half from your father -- contain one tightly packed strand of **DNA**.
This ladder is made up of a series of letters -- A, T, C, G -- that represent the chemicals adenine, thymine, cytosine, and guanine. One pair of letters is called a **base pair**; a base pair is formed by the binding of two nucleotides. (A always pairs with T, and C always pairs with G.) A series of nucleotides, then, forms a **gene** that codes for a protein. Your genes produce thousands of different **proteins**.
A **nucleotide** contains a base molecule (A, T, C, or G), a sugar molecule, and a phosphate molecule.
Each strand of DNA may contain several thousand genes. Some genes are thousands of bases long; others are millions of bases long.
The goal of the human genome project is to determine the complete sequence of the human genome -- to put 3 billion As, Ts, Cs, and Gs in correct order -- and to locate its estimated 30,000 to 50,000 genes.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Associations with Body Weight, BMI, Overweight, and Obesity

- **Body weight, BMI, overweight, and obesity were associated with DNA sequence variation in**

  - ABCG5 (88) , ACDC (89) (90) , ACE (91) , ADRB3 (92) (93) , AGRP (94) , APOC3 (95) , APOE (96) , AR (97) , CRHR1 (23) , CYP19A1 (98) , DRD4 (99) , GAD2 (100) , FABP1 (101) , GHRL (102) , GNB3 (103) , HTR2C (104) , IDE (105) , IL6 (106) (107) (108) , IL6R (109) , INS (110) (111) , IRS1 (112) , LEP (113) , LEPR (114) , MAOA (115) , MC4R (11) (116) , NPR3 (117) , NPY2R (118) , NR3C1 (119) , PLIN (120) , PON1 (121) , PPARD (122) , PPARG (123) (124) (125) (126) (127) (128) , PTPN1 (129) (130) PTPRF (131) , RETN (132) (133) , SGK (134) , SLC6A14 (135) , SORBS1 (121) , SREBF1 (136) , TNF alpha (137) , UCP2 (138) , UCP3 (139) (140) , and VDR (141) (142) (143) .

For the first time a locus on chromosome 21 has been identified in human based on a genome scan study

Gene for Hypertension

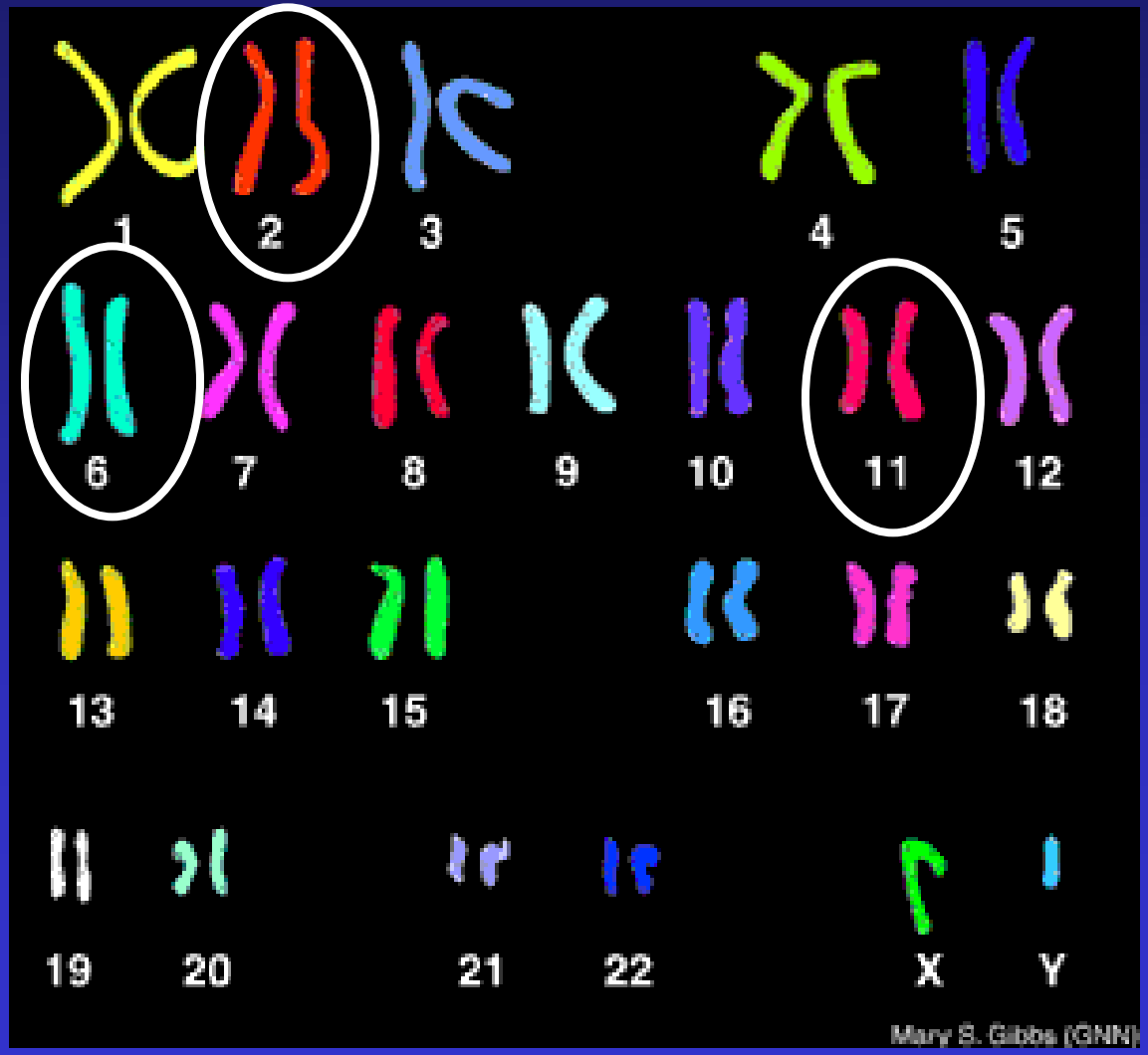
- No hypertension gene has been found for essential hypertension by virtue of linkage analysis in humans or animals

- A locus for blood pressure, fasting insulin, and leptin was found on chromosome 7q

Gene for Diabetes Mellitus: Type-1

Gene	***Locus***
HLA-DQB1	6p21.3
INS	11p15.5
CTLA4	2q31-35

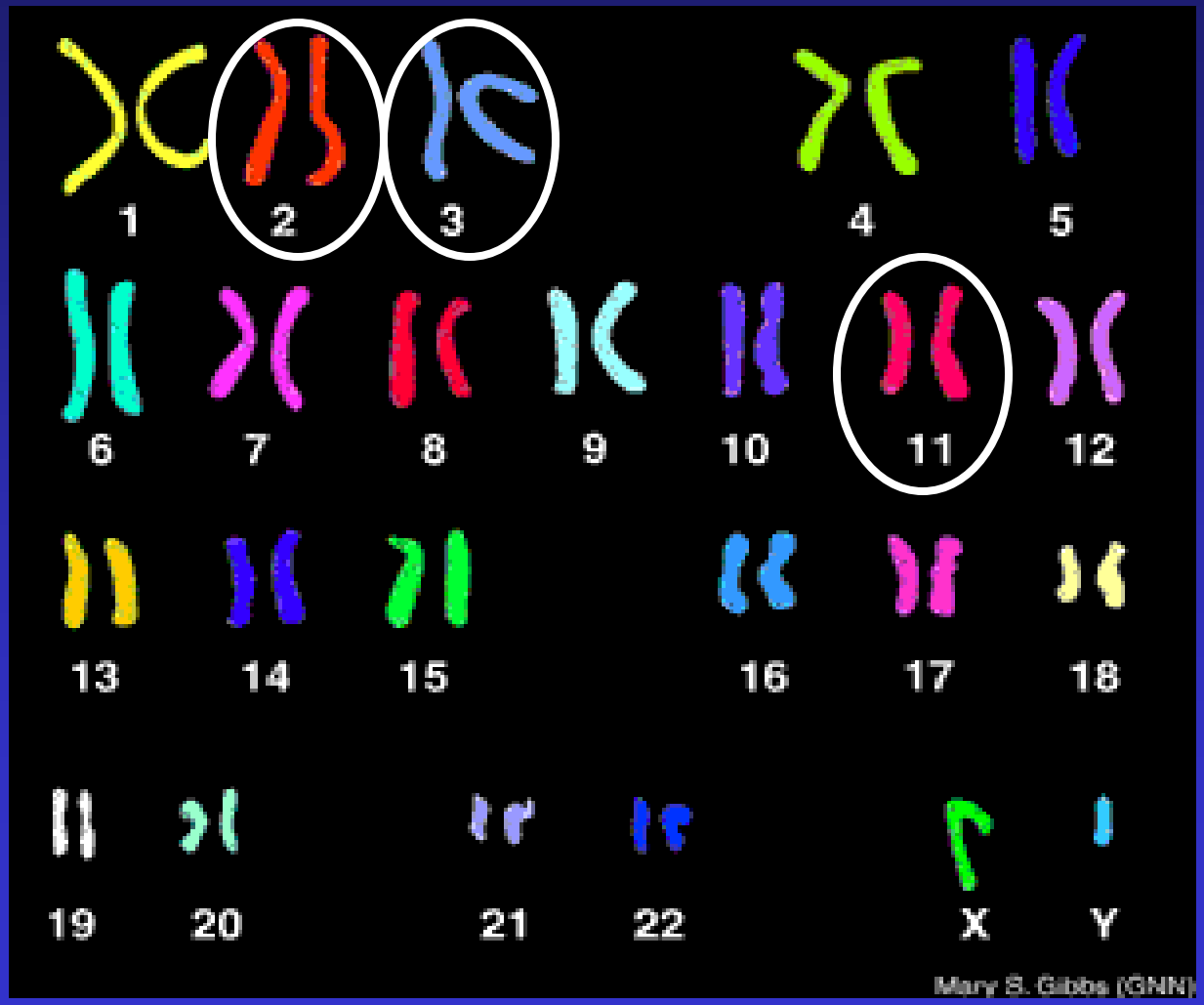
Gene for Diabetes Mellitus: Type-1



Gene for Diabetes Mellitus: Type-2

Gene	***Locus***
PPARy	3p25
ABCC8	11p15.1
KCNJ11	11p15.1
CALPN10	2q37.3

Gene for Diabetes Mellitus: Type-2



No uniform genetic background of metabolic syndrome/ components

Historical background of Metabolic syndrome

Historical background

During 1st world war

Karl Hitzenberger & martin Richter-Quittner (Austrian scientists)

- DM & HTN related

One year later

Kylin

- Expaneded definition
- Hypertension-hyperglycaemia-hyperurecaemia syndrome
  (hypertoni-hyperglycemi-hyperurikemi syndrome)

Albrink & Meigs

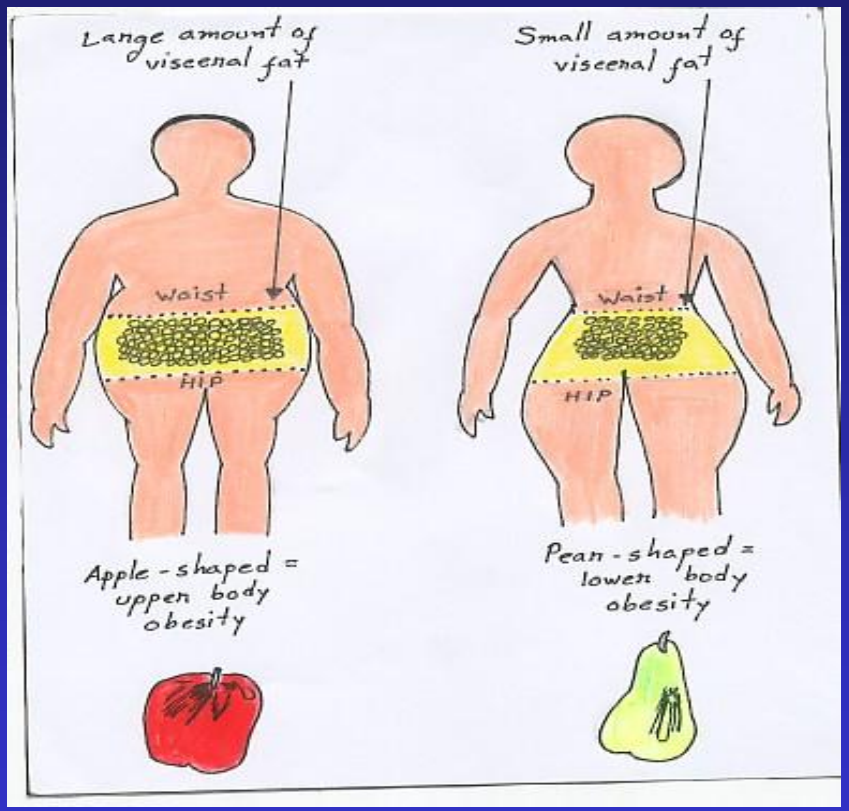
- Described relation between obesity & dyslipidaemia & hyperglycaemia

Historical background

1947

Vague

- **Distinguished android from gynaecoid form of obesity**
- **And connection between android obesity & DM,HTN, gout, atherosclerosis**



Historical background

1960

Yallow & Berson

- Obesity with or without DM is the cause of insulin resistence

Camus, France

- Metabolic trisyndrome(gout, DM, Hyperlipidaemia)

1967

Italian & German researchers

- Clustering of cardiovascular risk factors
  - (HTN, DM, Hyperlipidaemia & obesity)

Historical background

1981

Henefeld & Leonhardt

- Described metabolic syndrome
  - DM type 2 , HTN, obesity, gout, hyperlipidaemia, thrombophilia

1988

Gerald M.Reaven

- ‘Syndrome X’
  - IGT, low HDL, high VLDL, HTN, Hyperinsulinaemia

1989

Norman Kaplan

- Central obesity added
- Summarized the main characteristics of the syndrome as four component
  - Central obesity, IGT, hypertriglyceridaemia, HTN

Historical background

2001

Adult Treatment Panel III of the National Cholesterol Education Program

- **Proposes diagnostic criteria for metabolic syndrome**

a. Abdominal girth *b. Blood pressure*

c. S.Cholesetrol *d. S.Triglyceride* *e. Fasting Glucose*

Historical background

2005

International Diabetes Federation (IDF)

- **Defines Metabolic syndrome**
  - Central obesity (waist: 94 cm for European men & 80 cm for European women)

  PLUS

  - Two of four-
    - ***TG*** *> 150mg/dl*
    - ***HDL*** *< 40 mg/dl (m) ; < 50 mg/dl (f)*
    - ***HTN*** *>130/80 mm of Hg or under treatment*
    - ***Fasting glucose*** *> 100 gm/dl or previously diagnosed as DM type-II*

WHO Diagnostic Criteria of Metabolic Syndrome

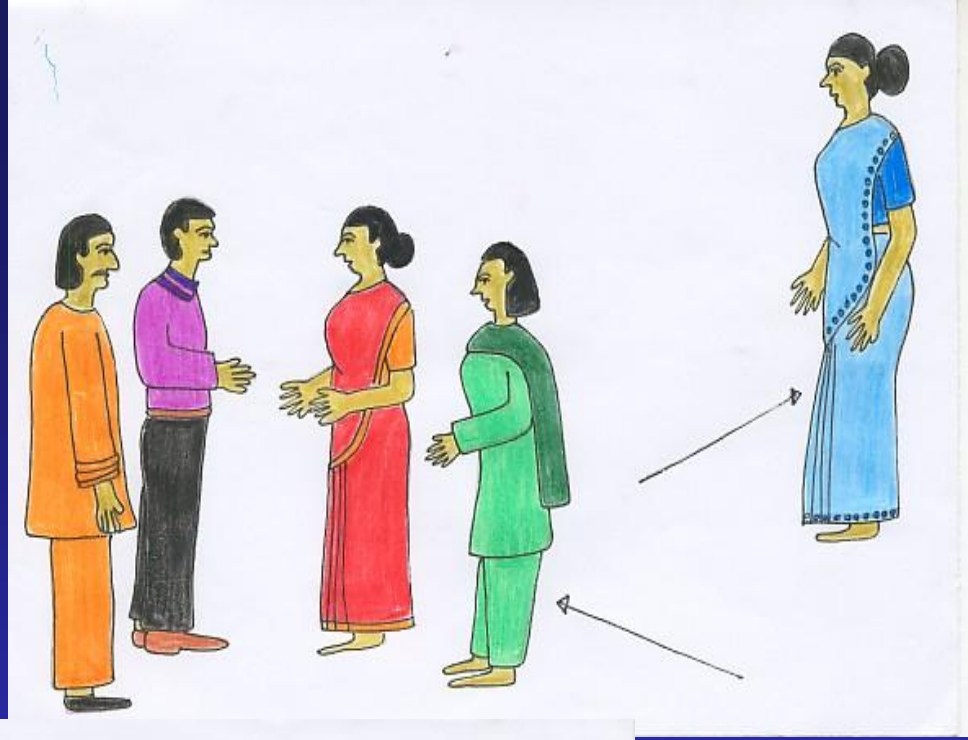
Glucose intolerance / DM / Insulin resistance

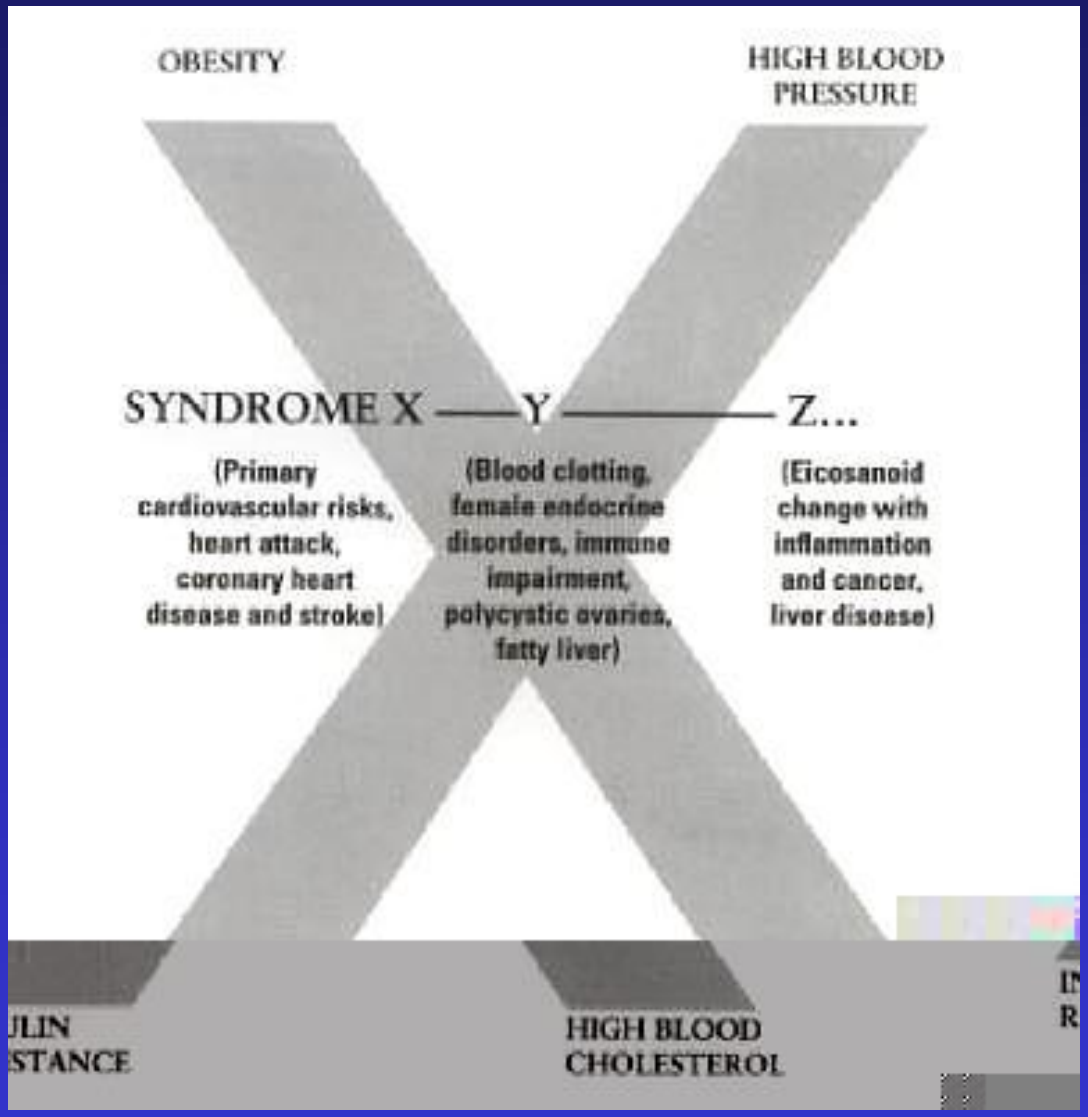
PLUS

Two of the followings-

- HTN
- ↑ TG
- Obesity
- Microalbuminuria

Variation of diagnostic criteria in different times by different scientists




OBESITY
HIGH BLOOD PRESSURE
SYNDROME X — Y — Z...
(Primary cardiovascular risks, heart attack, coronary heart disease and stroke)
(Blood clotting, female endocrine disorders, immune impairment, polycystic ovaries, fatty liver)
(Eicosanoid change with inflammation and cancer, liver disease)
HIGH BLOOD CHOLESTEROL

Some Contradictory Comments against Metabolic Syndrome

- In polycystic ovary syndrome
  - obesity, insulin resistance, increased risk of cardiovascular disease
- ***Is it a metabolic syndrome ???***

Hypertension is not a metabolic disease !!!!

- In glucocorticoid excess
  - Diabetes mellitus, hypertension, obesity, insulin resistance

- ***Is it a metabolic syndrome???***

High uric acid level is associated with hypertension, diabetes & obesity.

Why hyperurecaemia is not included in metabolic syndrome???

Insulin resistance without obesity possible!!

Other components without obesity ---- metabolic syndrome ???

- No uniform genetic background of metabolic syndrome / components
- Variations of diagnostic criteria in different times from history
- Many conditions mimic metabolic syndrome which are not considered or included in metabolic syndrome

So ... ...

All aspects of metabolic syndrome (definition, pathogenesis etc) are not yet clear

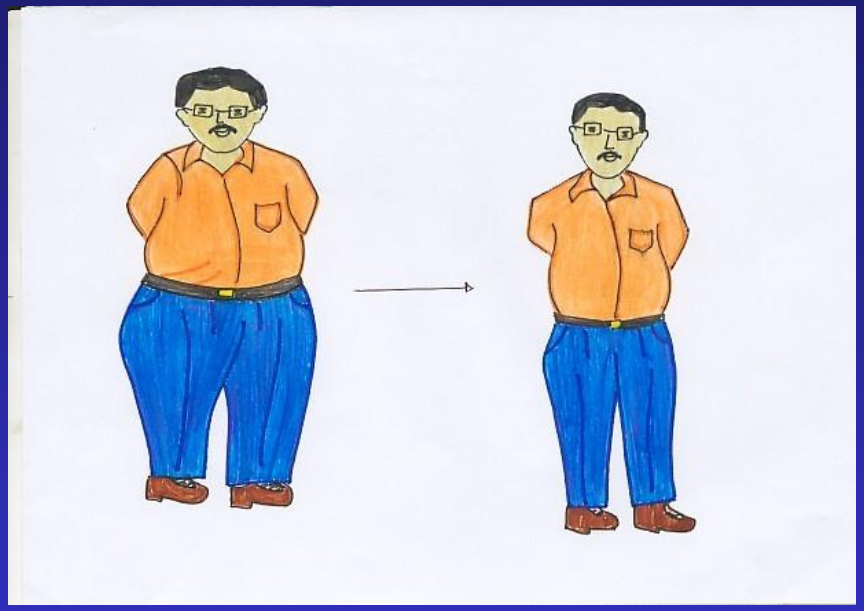
Similarities of Components of Metabolic Syndrome

Same consequences

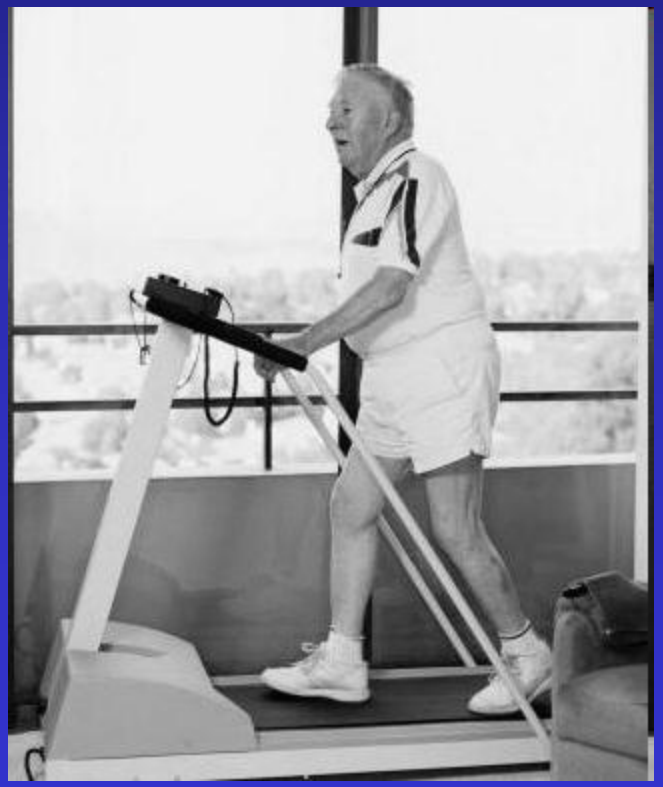
CVS risk factors

Diabetes mellitus

Same Treatment Strategy



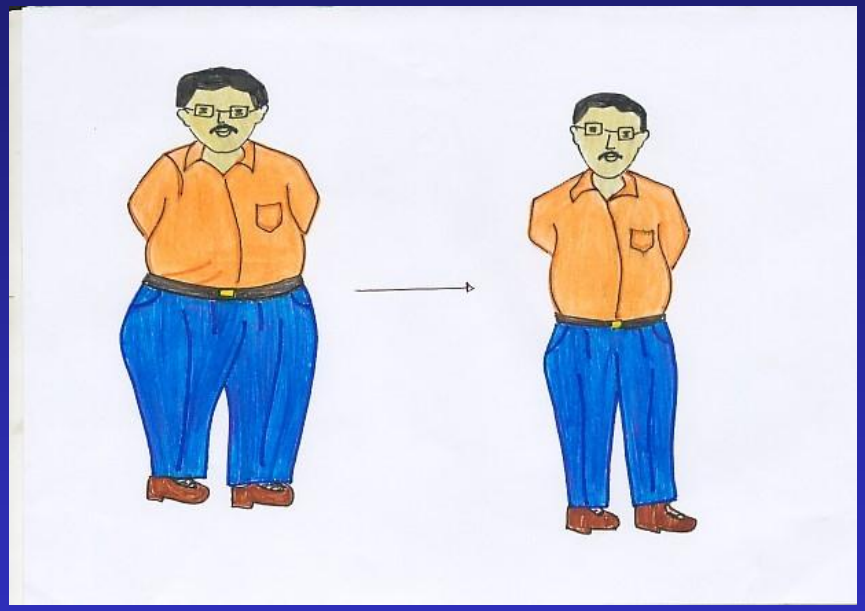
Weight loss (BMI < 25 kg/m^2)



Exercise regularly
30 min/day
5 days/ week

Diet Pyramid

Same Treatment Strategy for all Components



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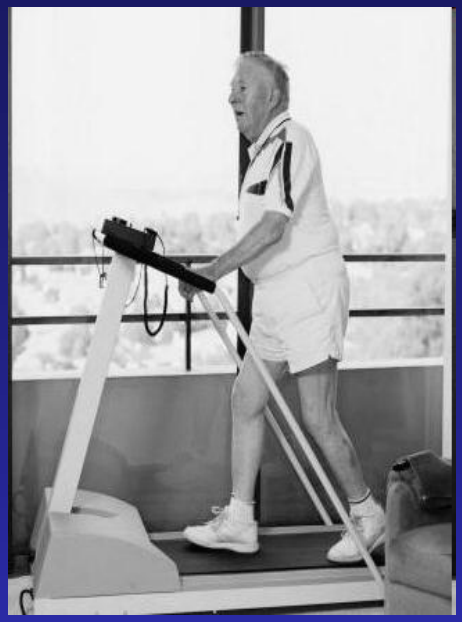

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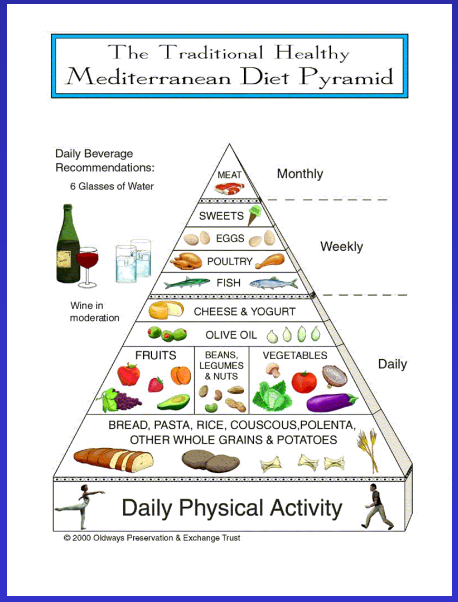
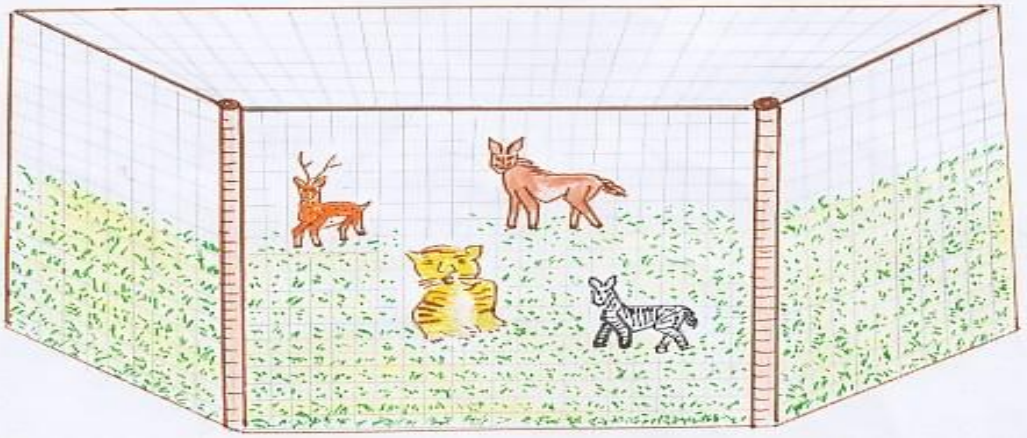
Diet



Weight loss + Exercise

- Blood glucose stabilizes to a normal level
  - ↑ HDL & ↓ total cholesterol
    - ↑ muscle mass & ↓ fat
      - ↓ Blood pressure



Considering Same Consequences & Treatment Strategy

Metabolic syndrome

↓

Can be taken as syndrome till today

But-

To get an uniform consensus in the unsettled issues of metabolic syndrome----


Long way to go……

THANK YOU