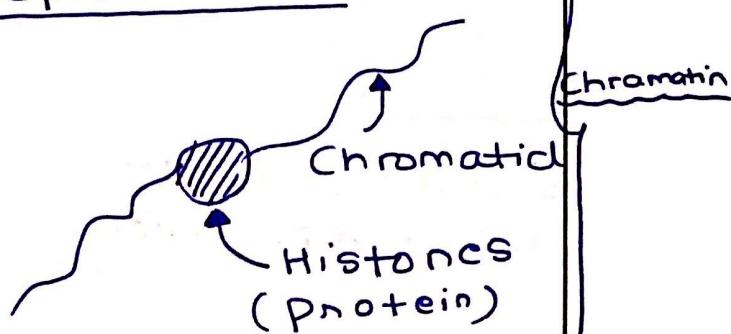


9.1  
- 9.4Genetics TerminologyLiving beings → Reproduction

Chromosomes  
 { 23 pairs }  
 Colored  
 Condensed



It comprises of Genes; present one after the other linked to each other.

Chromosomes [23P]

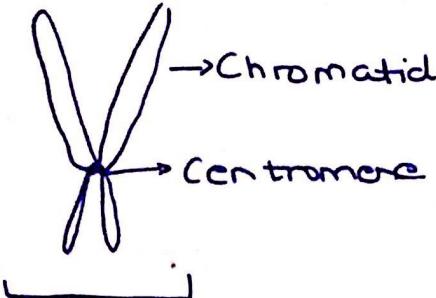
- 22P : Autosomes ; their genes are called as Autosomal.
- 1P determines sex so we call it Sex Chromosome. Its genes are called Sex-Linked.
  - [x ≈ 3y] ↳ In females; xx so 23<sup>rd</sup> pair is also homologous.

In 22P; the pairs of chromosomes are identical & genes are located at same place too. They are called as Homologous Pairs.

Length of chromosome (# of genes)

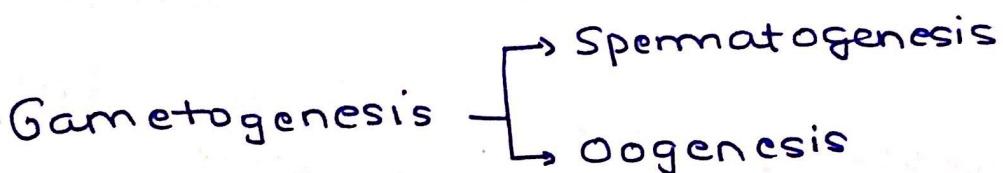
$\frac{1,2,3}{13,14,15} > \frac{4,5}{16,17,18} > \frac{X}{19,20} > \frac{21,22}{Y}$ ↳ Smallest
---

# U.P.S.C.



Sister-Chromatids  
during replication

Note: More together  
after recombination  
in Miosis.  
(reductive division)



Male/Female is almost 50/50 as  
weight of 'y' chromosome is less so  
it's probability is more.

Not  
genetic.

Non-Disjunction: Issues in separation.

- Single Gene issue → Disease      Chromosomal  
Abberation/  
Non- Disjunction
- Many Genes/Chromosome → Syndrome  
(Multiple feature change is there)

Gene: Location on chromosome that  
may affect a character.

The type of DNA sequence at  
Gene is called 'Allele'. There may  
be '2' alleles. But we always get  
2 alleles; one from father & one

- from mother. Further it is not necessary that 1 Gene controls 1 character.

Ex: Phenylthiocarbamide (PTC) Tasting

T → Taster  
t → Non-taster

Traits

→ 1 Gene & its 2 alleles completely determining the character [Tasting]

Ex: ABO → 1 Gene but Multi-allele  
(9<sup>th</sup> chromosome)  
 $I^A, I^B \& I^O \rightarrow 3$  alleles

Ex: Eye color → Multiple Genes control this character & god knows how many alleles in each gene.

Note: In simple cases; 2 alleles

determine the trait we get.

Ex:  $I^A I^B \rightarrow AB$  Trait of Blood Group (Character)  
(Allele)(Allele)

The combination of alleles → Genotype. \*

The expression of it is called → Phenotype. \*

If same allele present on the homologous chromosomes ⇒ Homozygous &  
if not ⇒ Heterozygous.

Ex:  $I^A I^A \Rightarrow AA$ ;  $I^A I^O \Rightarrow AO$

Again: Trait Inheritance determined by the alleles we get. The manner of inheritance of trait:

Position

① Autosomal & Sex-Linked

Type

② Dominant: When 2 alleles are present together one is expressed & other one does not. The one that expresses is Dominant allele.

Recessive: The allele that doesn't express itself in the presence of a dominant allele.

Genetics: Study of heredity (simple passing on).

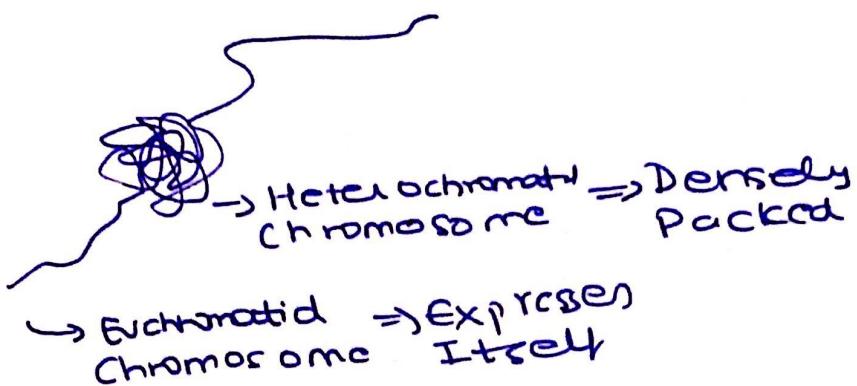
Species: Group of members who can potentially mate with each other to produce fertile offsprings.

Genetics coined by Bateson in 1906.

Sex-Chromosomes are also called as 'Autosomes'.

# U.P.S.C.

इस पाने में कुछ  
न लिखें  
(Don't write anything  
in this part)



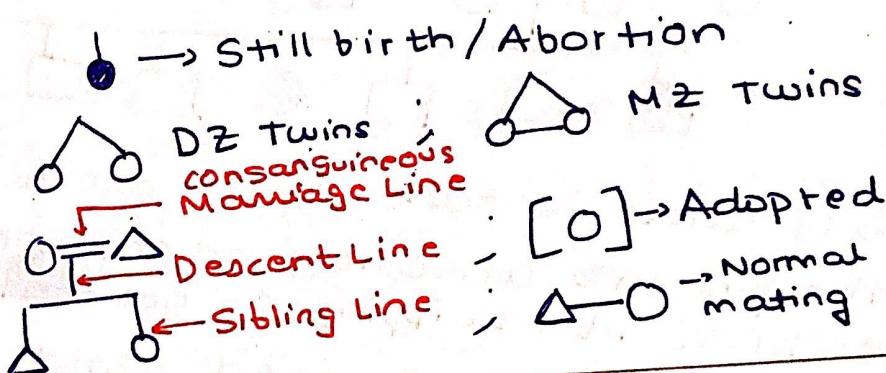
## Q Man - Family Studies

- (2) Biochemical
- (3) Immunological

The goal is to understand heredity & environmental impact. There are several methods in syllabus.

(1) Pedigree Analysis: Depicts family members & their relationships by means of standardised symbols.  
By Galton; a family tree generated.  
we study inheritance of traits.

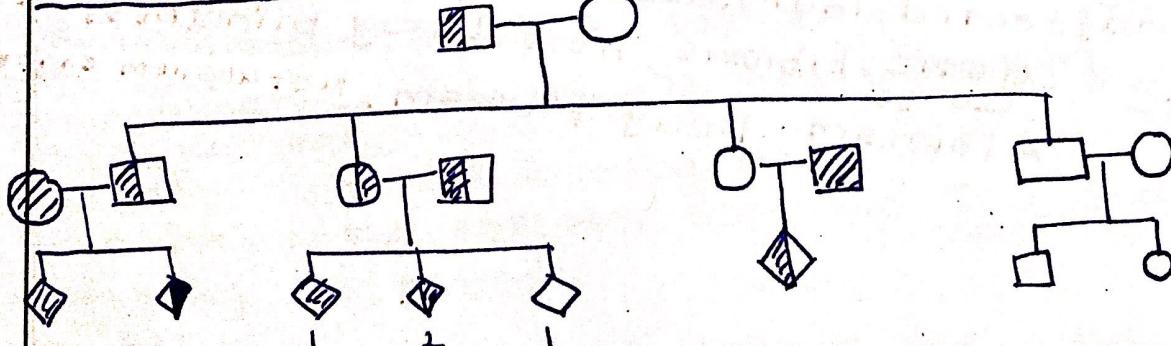
Legend:  $\Delta = \circ$  (consanguineous mating)



Proband / Prostista: Affected person under investigation

Traits: Autosomal / sex linked & Dominant & Recessive (type)  
(based on alleles) (Location)

### Autosomal Dominant Gene Inheritance Pedigree

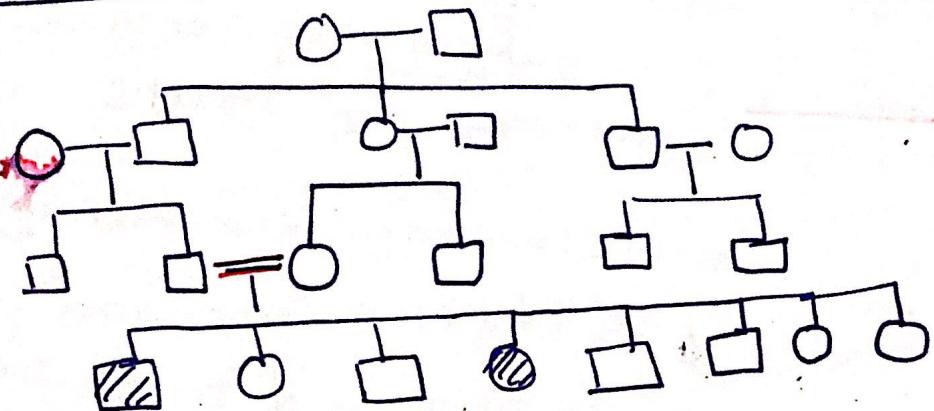


# U.P.S.C.

→ Each affected person has an affected parent to the ancestry where the mutant allele first arose.

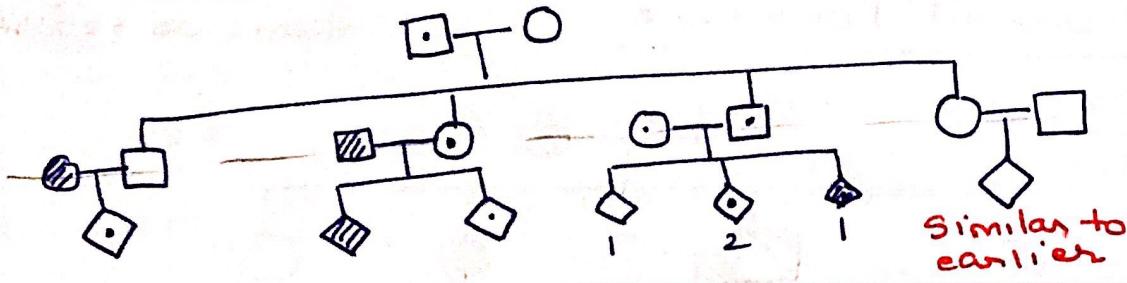
Ex: Huntington, Polydactyl, Cleft Palate, Lip, cold Urticaria, etc; Nail Patella too.

### Autosomal Recessive:

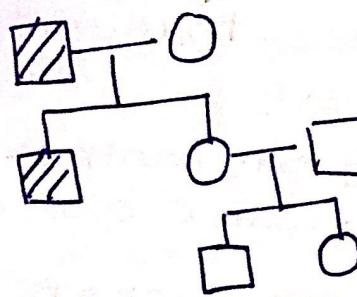


- If allele is rare; then almost never the parents, ancestry or collaterals express it. Skipping of generations.
- Siblings of affected child with normal parents have ( $\frac{1}{4}$ ) chance of being affected irrespective of sex.
- Parents of affected children are more likely to be related.
- Most cases are sporadic (i.e.) usually only 1 in family affected.
- Unaffected individual can be a carrier.
- Ex: Cystic Fibrosis, Hereditary blindness, (Lungs)  
Albinism, Deaf Mutism,

# U.P.S.C.



Y-linked: Author Recessive or Dominant  
it doesn't matter.  
**Holandric**

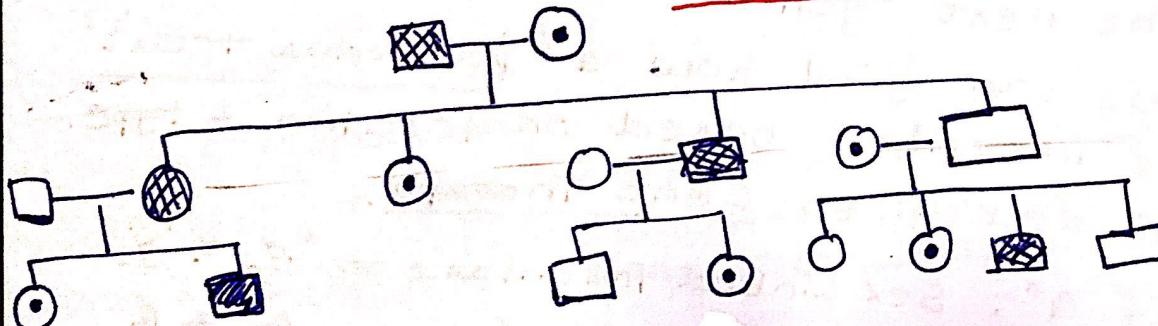


Here also males  
are hemizygous  
affected i.e.  
only 1 allele  
expresses itself.

- Only males affected; never females
  - All sons are affected & never daughters.
- Ex: webbed toes; Hypertrichosis of Pinna (hair)

X-Linked Recessive

Males are thus  
affected in  
hemizygous condition



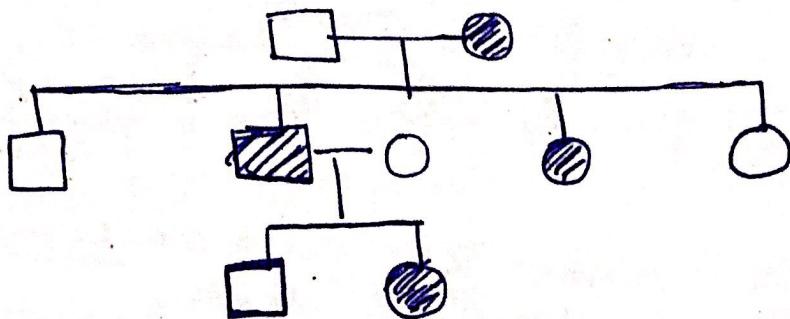
Ex: Haemophilia, G6PD deficiency,  
Red-Green blindness, Duchenne Muscular Dystrophy.  
(Deuteranopia)

- Mostly appears in Males whose mothers are heterozygotes. Her. Son has 50% chance of being affected.
- Affected males son's cannot get it from them & all daughters are atelectranier.

# U.P.S.C.

## X-Linked Dominance

same as before



- Affected female transmits to half of sons / daughter.
- Males only get from mother.
- Unaffected individual can be having dominant.
- Ex: Xg Blood Group, Rickets, Aicardi Syndrome.

Most people who refer genetics are normal ones or carriers  $\Rightarrow$  Genetic Counselling.

- Helps predict transmission of traits in the next-gen.
- We can find how a 'particular trait' is inherited based on location & type.
- Linked with Gene Therapy.
- If Q: Sex Linked Inheritance  $\Rightarrow$  X & Y  
Autosomal Inheritance  $\Rightarrow$  A & R.

# U.P.S.C.

## ② Twin Studies.

In 1874; Camille Dancste gave distinction between M<sub>z</sub> & D<sub>z</sub> twins. [Diagram very simple]

M<sub>z</sub> → Genetically identical & same sex.

(Identical Twins) If separation not full; then Siamese Twins (conjoined) occur. The differences later on are due to env only. No effect of mother's age.

D<sub>z</sub> → As good as siblings. can be of separate sex. Genes are also different. More common in older mothers.

	M <sub>z</sub>	D <sub>z</sub>	Sibling
Genes	100%	50%	50%
Env	100%	100%	100%

Twin's are offsprings produced by the same pregnancy. Env also impacts the twinning.

### Diagnosis of Twins:

- a) DNA fingerprinting
- b) Similarity Method: Blood Group, Serum Proteins, HLA, Genetic Markers, Ridge count, etc.
- c) Skin - Grafting
- d) Placental Method:

M<sub>z</sub> → Amnion Diff  
Chorion Same

D<sub>z</sub> → Amnion Diff  
Chorion Diff

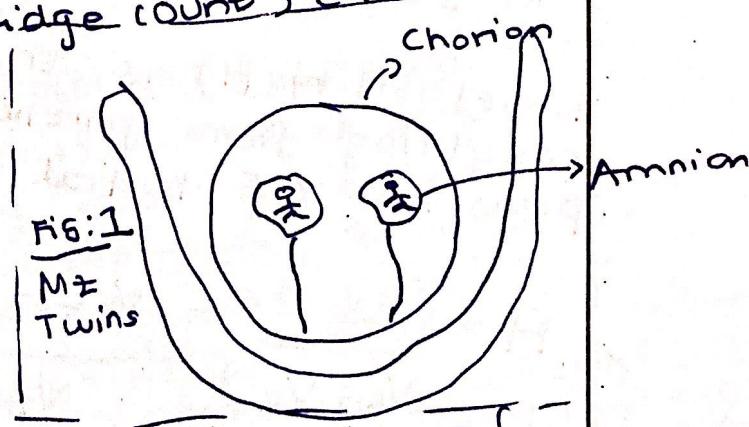


Fig:1  
M<sub>z</sub>  
Twins

Using Twins we can study role of Env & Heredity in dev of traits.

# U.P.S.C.

In Twin - Method; 2 types of twins ( $D_Z \& M_Z$ ) are studied at the same time. Concordance means how much both as % show trait & discordance is opposite.  
 (Both Yes  $\&$   
 Both No also)

**A]** Concordance - Discordance study to analyse discrete characters.

High concordance in  $M_Z$  &  $D_Z$   $\Rightarrow$  Environmental Determinism

High " in  $M_Z$  & Low in  $D_Z$   $\Rightarrow$  Genetic Determinism

Case Study: On Obesity by US Army (1979)

studied 4000 pairs of twins.

$M_Z \rightarrow 60\%$  concordance  $\rightarrow$  Genetic component in obesity too.

$D_Z \rightarrow 40\%$  concordance  $\rightarrow$  Genetic

Ex: Hair color : 99.6% 28%  $\rightarrow$  Genetic

Eye color : 88% 22%  $\rightarrow$  Genetic

**B]** Heritability Estimates / Rearing studies

It is more statistical in nature & analyses traits that are continuous like height, skin color, etc.

Heritability ( $H$ ) is the amount of variation resulting from genetic differences as a proportion of total variation.

$$H = \frac{VG}{(VG + VE)} = \frac{V_{DZ} - V_{MZ}}{V_{DZ}}$$

$\rightarrow \approx 1$ ; then trait genetic  
 $\rightarrow \approx 0$ ; then trait envt.

$V_{DZ} \rightarrow$  Variation between  $D_Z$  pairs & includes genes & env.

# U.P.S.C.

Concordance Rate (C') =  $\frac{C + 2C^*}{C + 2C^* + d}$  - C → concordant pairs  
 $C^*$  → No. of " " in which both members are independently ascertained  
d → No. of discordant pairs.

## Challenges of Twin Studies (IMP)

- ① ~~\*~~ Identical Twins may be treated more alike than actual siblings of different ages/Dz Twins.
- ② TS neither specifies the exact genetic env component
- ③ → Fails to tell us about the pattern of transmission.
- ④ ~~\*~~ Mz Twins may not be identical as the placental supply may vary.
- ⑤ ~~\*~~ Heritability estimates may not be applied to all aspects as some of them may have been significantly influenced by intra-uterine developments.
- ⑥ ~~OK~~ → Inter-pop<sup>n</sup> variations not considered in 'TS'.
- ⑦ ~~△~~ → Env of Twins may not be representative of env of pop<sup>n</sup> → Env creeps in; generalization of env of pop<sup>n</sup> → Env & Genes interaction is complex.
- ⑧ → Understanding traits involving complex interaction of Env & Genes is tough.  
Ex: IQ, Behaviour, etc.
- ⑨ ~~△~~ → Tends to underestimate env deviation as for behavioural traits it is difficult to accept that env diff betw<sup>n</sup> 2 members of a twin pair is representative of that betw<sup>n</sup> 2 random indiv. in the pop<sup>n</sup>.
  - Not exact treatment
  - △ → Env
  - ✓ → Not exact analysis
  - OK → Extra

Concordant $\Rightarrow$ Both affected / not affected	Discordant $\Rightarrow$ one affected.
---	--

# U.P.S.C.

Siemens (1924): commented on role of twins in genetic research:

1. Investigation of normal variability
2. Method of determination of zygosity.
3. Finding Genetic & Env contribution.

Eric Turkheimer (2003): Studied 'IQ'

Identical Twins Sets

- Affluent family: Genes play larger role
- Impoverished Family: 60% variance → Env

(Easy: Don't Panic)

Application

Collorary: Weinberg's Differential Method

to determine no. of M<sub>z</sub> & D<sub>z</sub> Twins in a Twin population. — Claude Bouchard

Unlike Sexed Twin → one 100% D<sub>z</sub>

M<sub>z</sub> Twin → same sex

D<sub>z</sub> Twin → same sex → 50%  
Diff sex → 50%

1<sup>o</sup> SR → Conception

2<sup>o</sup> SR → Birth

3<sup>o</sup> SR → Maturation

All : Male - all  
Male : female : female

1 : 2 : 1

∴ Total D<sub>z</sub> Twins ⇒ 2 × No of unlike-sexed Twins

Total M<sub>z</sub> Twins = Total Twins - Total D<sub>z</sub> Twins

(3) CO-Twin Method

Identical twin & its co-twin I  
 Fraternal twin & its co-twin are separately  
 studied. Then results are compared.

Note that this is diff from Twin-Method  
 wherein each 'pair' of twin is studied  
 as a combined unit & then comparisons  
 are made.

This pairwise analysis results in  
 double counting of trait. Thus rates  
 are higher in CO-Twin Method as having  
 trait concordance counted twice

So there is deviation in result of  
Twin & CO-Twin methods. [So Proband  
wise analysis is used in CO-Twin Method  
 to eliminate this error.]

Ex: Schizofrenia analysed.

→ Any twin can be registered & the  
 other twin traced.

Challenges

→ Same as Twin-Method.

NASA Study (2019)

of Scott & Mark Kelly,  
Michael Schneider

# U.P.S.C.

## ④ Foster Child / Adoption Studies

To understand nature v/s nurture debate or dev of traits [usually mental]. Here we find effect of Env!!

Children are selected at Random  $\Rightarrow$  so Genetic variation eliminated.

Placed in homes classified as Good, Average & Poor. Since assignment is random the distribution of genetic traits is uniform. Then few years later tested.

If mental traits affected by Env, then results should indicate so.

① Ex : Chicago study showed that IQ  $\propto$  to quality of home. It implies that Env has huge effect on IQ.

② Case study : Minnesota study ; found that both env & heredity affect IQ. Children whose biological parents had a high IQ also did well. As did children of foster parents of high IQ.

Osbome (1951) has highlighted the following challenges / Requirements for the use of this method:

- Early placement in foster home to be uninfluenced by env of their original home of biological parents.
- Random placement absolutely essential; though in reality tough.
- Adequate sample of adoptive home children at various  $S^2$  levels must be included in the survey.
- foster - children should be from one population to eliminate various ethnic sources of information.
- Minnesota Study needed info on biological parents which is tough to get.

Foster-child is key tool in behavioural genetics & often combined with Twin studies to make heritability estimates.

# U.P.S.C.

## ⑤ Cytogenetic Method

Branch of genetics concerned with study of chromosomes & how they relate to cell behaviour. To study chromosomes we must stop them at Metaphase when they are aligned & condensed. A staining agent may be used to clearly see the structure of the chromosomes.

→ Karyotyping

Methods → Analysis of G-banded chromosomes

→ Molecular Genetics <sup>cyto-</sup> a) Comparative genome hybridisation  
b) Fluorescent In-situ Hybridisation.

### Applications

- Map genes to chromosomes : Ex: Duffy blood group locus to Chromosome 1.
- Rel<sup>n</sup> betw<sup>n</sup> Chromosomal Abnormalities & diseases can be studied.  
Ex: Autosomal & sex-Linked.
- Study evolutionary pattern of primates by Karyotype comparison. [Karyosystematics]
  - ↳ Not all genetic changes can be visualised by Karyotyping as some are extremely small.
  - (Karyotype is a part of Cytogenetics)
- Helps us understand / diagnose diseases.
- Chromosomal Theory of Inheritance dev N1900's due to it.

**⑥ Karyotype Analysis (Karyology) / Chromosomal Analysis**

Laboratory Technique used for visualization of chromosomes under a microscope

Staining with fluorescent dyes  $\Rightarrow$  Light & dark bands called Banding Pattern.

The banding pattern of each chromosome is specific & consistent for a certain stain. Photography or drawings also utilized. They are a characteristic of the species. Then the structure & abnormalities are studied.

Cells  $\rightarrow$  Add Phyto-haema-Glutinin (PHA) which induces mitosis

Methanol / Ethanol (3)

+ Glacial  $\text{CH}_3\text{COOH}$  (1)

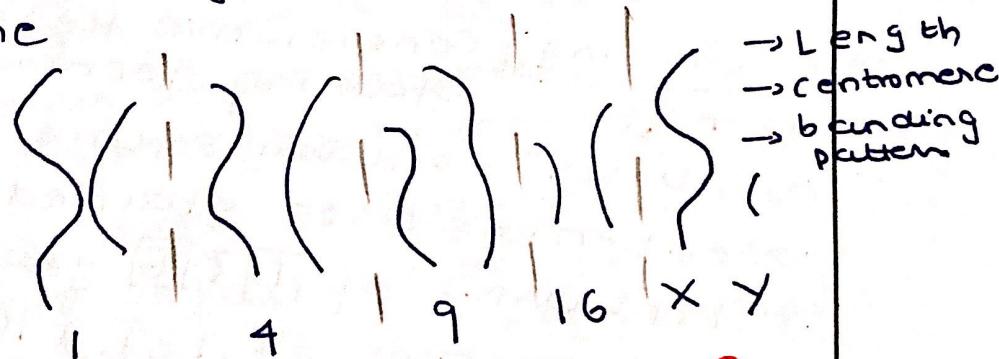
fixation & hardening of Chromosome

Colchicine arrest at Metaphase stage & promotes contraction of the chromosomes.

Sample :

Karyotypes

Draw size Table also



Types of Banding

Karyogram  $\oplus$   
Ordering based on size & position of centromere.

**① Q-Banding:** Quinacrine Mustard [fluorescent Alkylating agent] binds selectively to the guanine residues in the DNA. The following polymorphic regions are distinguished by it:

- 3 & 4 centromeric regions.
- 13-15 short arms & 21-22 satellites.
- distal long arm of Y.

# U.P.S.C.

It's limitations are:

- Needs fluorescent microscope
- Not permanent stain & rapid fading of fluorescence takes place.
- fluorescence of minor bands & sub-bands tough to differentiate.

② G-Banding: Post treatment with Protease  
(Trypsin) then Giemsa stain used. Very simple.

→ Enhances chromomere regions & the stain is permanent. Ex: Y, 1, 9, 1G.  
 ↓  
 2 small Densely stained  
 G-bands 2<sup>o</sup> constriction regions.

③ R-Banding: DNA is denatured by diff methods. The telomeric regions of chromosomes are stained. It is called as Reverse Banding & opposite to G gotten by heating it. Green color.

④ C-Banding [Consistutive Heterochromatin]  
Staining Technique

(G + Q)

Alkali SOI<sup>r</sup> → Warm saline → Giemsa

Centromeric area stained

→ Centromeric area stained

→ Short arms of D & G group are stained.

→ 2<sup>o</sup> constrictions of 1, 9 & 16

→ Distal Long arm of Y

⑤ T-Banding: Small structural changes involving telomeric regions. It represents the bands of R which are resistant to treatment with denaturing agents.

- ⑦ Family Method: Comprehensive family history essential
- Childs (1982): "to fail to take a good family history is bad medicine & someday will be a criminal negligence".
- Diagnosis → Info on natural history of disease & variation
  - Find if disorder is disease & variation genetic in origin. / in its expression.
  - Clarify pattern of inheritance; indicate & calculate risk to family members.

Need extensive data on many family members. Note infant death, still birth, abortions, etc. Also consanguinity, geographic & ethnic origin must be documented.

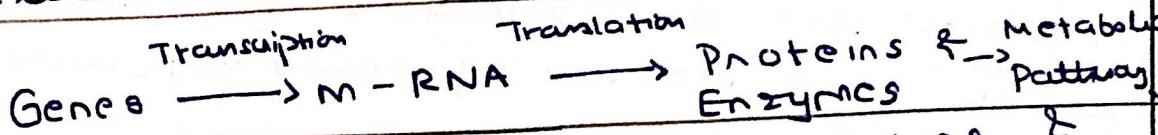
Useful to summarise as Pedigree for quick information.

Sample  
of  
error

# U.P.S.C.

## Biochemical Methods

They combine Genetics & Bio-chemistry to elucidate nature of metabolic pathways.



Phenotypic  
Expression

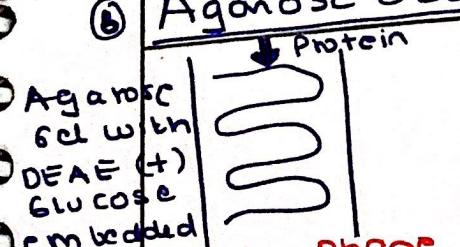
This is how genes express themselves & was demonstrated by Beadle & Tatum, 1941. The proteins control the chemical synthesis. AE Garrod is considered pioneer of this.

If error in metabolic pathway  $\rightarrow$  Disease.

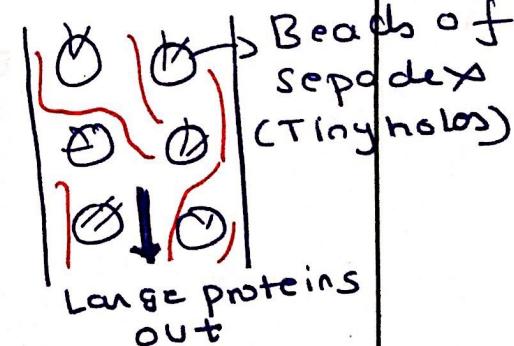
### ① Sep & Identification of Proteins:

② Gel filtration: Sep. proteins based on mwt; when they pass through Polysaccharide Sepadex G-25 which lets only high wt out.

### ③ Agarose Gel Electrophoresis



Speed  $\propto$  [Charge]  
[Weight]  
 $\rightarrow$  Polysaccharide gel.  
 $\rightarrow$  Stained by Ethidium Bromide



### ④ Ion-Exchange Chromatography

$\hookrightarrow$  So proteins with ' $-$ 've charge are attracted.  $\rightarrow$  Mixture washed down with buffer soln of diff pH & diff proteins are washed down at different rates.

After proteins are separated A.A can be analysed.

# U.P.S.C.

## ② DNA Sequencing:

→ Maxim Gilbert Method: Cuts DNA at 4 diff restriction places by Endonuclease enzyme. Segments are then analysed by electrophoresis (unequal length), & location of bases determined.

## ③ Northern Blotting → RNA:

✓ Southern Blotting → DNA;

Restriction → Electrophoresis → Blotted on "Nitro-cellulose" paper  
Hybridised with Radio-Agarose Gel Labelled Probe filter

To find if sample  
has our DNA sequence.

## ✓ Western Blotting → Protein:

Electrophoresis → Blotted on nitrocellulose paper → Treated with Antibody

Reacted &  
Labelled

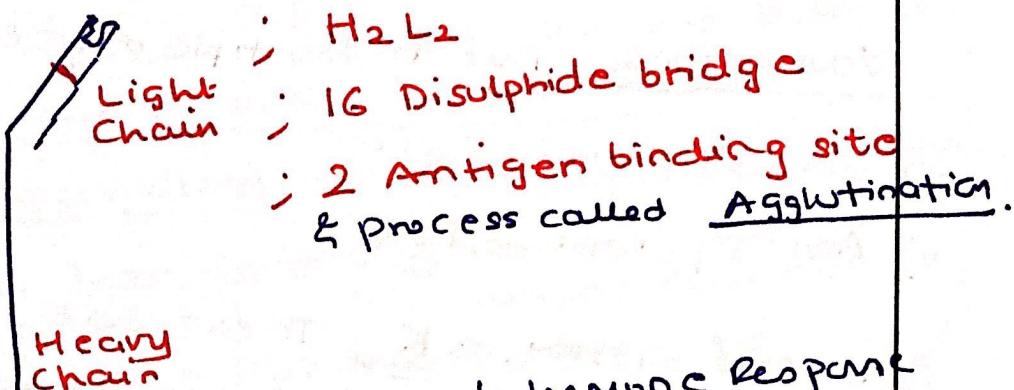
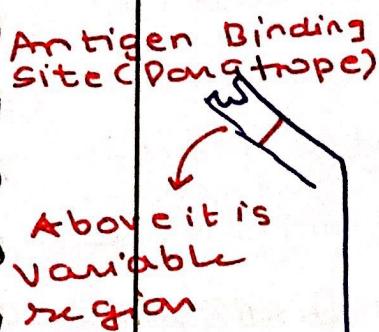
Antibody -  
Antigen Complex

These methods have been used to investigate diseases which are due to metabolic disorders caused by mutant genes.

Ex: 5 disorders associated with defective metabolism of phenylalanine have been thoroughly studied.

IMMUNOLOGICAL METHODS : 1980's

Based on Antigen-Antibody interaction to study Genetics. Antibodies are also called as IMMUNOGLOBULINS [Proteins]



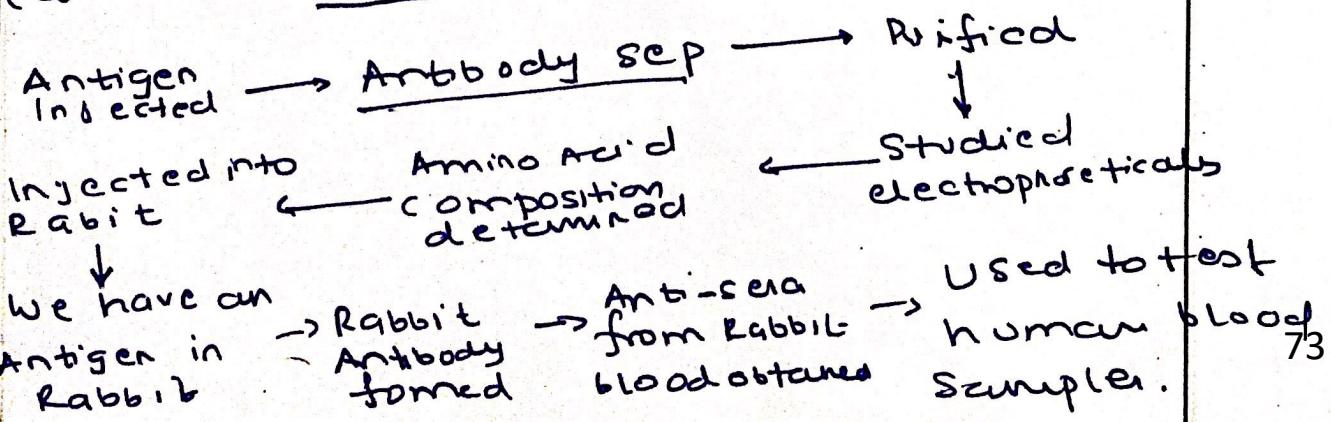
→ We study genetic basis of Immune Response.

There are 5 types of Antibodies: IgA, IgG, IgD, IgE, IgM etc.

Light chain → kappa ( $\kappa$ ) ; Lambda ( $\lambda$ ) ; either one present not both together.

Heavy chain →  $\gamma \rightarrow \text{IgG}$     $\mu \rightarrow \text{IgM}$   
 $\alpha \rightarrow \text{IgA}$   
 $\delta \rightarrow \text{IgD}$   
 $\epsilon \rightarrow \text{IgE}$

All 5 antibodies are present in humans but constant parts varies due to the genetic differences of this variation is called as Immunoglobulin's Allotypes.



# U.P.S.C.

The level of Antibodies is also a variation marker.

Variations : Due to multiple alleles

- a) GM System  $\rightarrow$  IgG
- b) Am System  $\rightarrow$  IgA
- c) Inverse System  $\rightarrow$  K; There are 3 inv factors: 1, 2, 3. Popn Survey with the Anti-Sera finds that  $1 \oplus 2 \rightarrow$  Venetulation includes (✓)  
European (✗)
- d) O, Z System  $\rightarrow$  L

# U.P.S.C.

## Applications

- Study structure, fn & cellular control of immunoglobulins.
- Related to IMMUNODEFICIENCY (SCID).
- Link with G.C. + Auto-immune Disorders.
- Detect Wiscot Aldrich syndrome, etc (HLA)
- Fusion incompatibility study & organ transplantation.
- ABO Blood Transfusions  $\Rightarrow$  Humoral Type of Immune reaction (due to WBC's)
- Crohn's Disease & Rheumatoid Arthritis.
- Due to Lymphocytes & Macrophages. ← Cell Mediated Immune Reaction.
- Evolution of primates studied.
- Stem-cell research.
- Immunogenetics of Ageing: Imp of genes in regulating immunological functions in maintaining human longevity.
- Gene Therapy targets.

## Mendelism

Mendelism

Gregor Mendel is the "Father of Genetics".  
He gave his theory in "Experiments in Plant Hybridisation (1866)". His main specimen was Garden Pea Plant [Pisum Sativum] which he studied for 8 years. He then gave the famous "Mendel's Laws of Heredity" which was lost & subsequently rediscovered by Hugo De Vries, Carl Correns & Erich von Tschermak in 1900.

Erich von Tschirch

→ Talk about extensive efforts required for research; to make F<sub>0</sub> pure  $\Rightarrow$  22 gen of inbreeding he did. & why pea plant? ✓  
monohybrid: 1 gene: LOD ① 7 u

## Experiments

Based on which  
he gave 3 Laws:

Based on which he gave 3 Laws:  
He had no idea about chromosomes, etc. He called them as factors & factors occur in pairs.  
He said this was basis of inheritance.

① Law of Dominance: ✓ ; there are plenty of exceptions ; Ex : ABO  $\Rightarrow$  co-dominance,  $\therefore$  Partial Dominance.

exception,  $\frac{HbA/HbS}{TT \times tt} \Rightarrow$  Partial Dominance  
Semi-Dominance  $\rightarrow$  Incomplete Dominance  
 $= Tt$  [All Tall]

∴ 1st Law is not universal.

∴ 1st Law is not universal  
What about multiple allele effects?  
" " Polygenic inheritance?

" " polygenic inheritance?

" " Epistasis?  
" " ~~influence~~

" " Epistasis! only if  
" " Hemizygous present still  
expresses.

Ex: Intermediate dominance  
G6PD<sup>d</sup>; % of proportions are maintained.  
 $0 \rightarrow 0\%$ . Shows 76%  $\rightarrow 50\%$ . traits.

# U.P.S.C.

## ② Law of Segregation (Purity of Gametes)

- No blending takes place. It is an universal Law; applicable to all species whose chromo-somes occur in pairs. [Not Prokaryotes]
- Segments occur in pairs.
  - Refuracing of trait in F<sub>2</sub>.
  - Non-disjunction is an anomaly.
- Called as Ultimate Discovery of Mendel, aka "Law of splitting of Hybrids".

## ③ Law of Independent Assortment:

- Only valid if 2 genes are very far apart or are located on diff chromosomes.
- Incorrect due to crossing over & Linkage group presence.

④ Crossing over occurs only in Prophase - I.

↳ Give Diagram

The 7 traits chosen by mendel were on 4 diff pairs of the

chromosomes [1 + 3<sup>2</sup>] with sufficient distance so he was safe.

TR	Tr	Ty	ty	tR	tr
TR	TTRR	TTry	TtRR	ttRR	ttrr
Tr	TTry	TTyy	TtRr	Ttrr	
tR	TtRR	TtRr	ttRR	ttRr	
tr	Ttrr	Ttry	ttRr	ttrr	

Dihybrid cross = 9 : 3 : 3 : 1

Ratio

TT : 2Tt : 2tT : RR : 2Rr : 2rr

Handy Weinberg Proportion

Note: Crossing over & Distance.

Infact chromosome has been divided into segments & these 2 segments have become independent of each other.

[2]

\* Most app<sup>n</sup> of Mendel  $\Rightarrow$  1st 2 Laws only

Chromosomal Theory of Inheritance: By Sutton,

~1906 Boveri, Thomas Hunt Morgan & Castle. Said genes on the same chromosome are inherited together.

This phenomena is called Linkage.

Truth is actually in between. ✓

UROP: Alfred Sturtevant also apply in Cytogenetics as a Sophomore.  
Short note.

### Criticism

- ① Extranuclear mt-DNA only from mother & thus does not follow Mendel pattern.
- ② Sex-Limited Characters: Here the express, completely dependent on sex. Ex: Milk Production.
- ③ Sex-Influenced characters: expression of gene depends on hormones & varies with sex.

	Men	Women
BB	✓	less
Bb	✓	✗
bb	✗	✗

Ex: Baldness

# U.P.S.C.

## Applications of Mendelism:

→ Led to Pop, Human, Immuno, Molecular, Bio-Chemical & Medical genetics.

### ① Medico-Legal + Paternity Disputes

via ABO system.  $\hookrightarrow$  Motherhood is an absolute certainty.  
(10-15% of cases)

Others need more adv: MNS, Rh, Duffy, Celano, Kidd, Kell, P, CcDEe, etc.

→ Cases of infidelity. Hb's, Serum proteins.

### ② Genetic Counselling

via Pedegree Analysis, (diagram)

### ③ Hybrid Varieties

GR & Operation flood; Animal breeding.

### ④ Medical Application: Study of modes of inheritance of various histocompatibility & metabolic disorders through Mendelism has led to dev of their cures.

Ex: Haemolytic Disease of New born (HDNB)

But Anti-Rh Bovine Injection to mother within 72 hours of each delivery destroys all Anti-Rh antibodies.  $\hookrightarrow$  85% of world popn  $\Rightarrow$  Rh+ [more]

[Diagram of Placenta & Foetus] Even Serological & Cytogenetic appn in reproductive biology are there.

Note : *Eugynthroblastis foetidus* is an exception to Hybrid Vigour.

Lethal Gene : Cuenot & Baur (1905)

The possession of a 'certain' genotype of Lethal Gene kills its possessor.

**Types**

- ① Dominant Lethal : kills in homozygous as well as heterozygous condition  
→ very rare; as can't be maintained in the popn.
- ② Recessive Lethal : kills in homozygos condition only. It can act as a carrier.  
bc TT/tt also. Most are like this. Ex: Achondroplastic Dwarfism.
- ③ Gametic Lethal
- ④ Conditional Lethal → only in certain env conditions.  
Ex: G6PD; Erythroblastosis foetalis, Albinism → Plants ✓ ? → Humans X

Note: A Lethal Gene may be phenotypically dominant but recessively Lethal. Also recessive means TT/tt & not tt only.

**Ex:** Mice coat color  $\Rightarrow$  Y → yellow (Dominant) phenotype  
y → grey

$Yy \times Yy$  | But 'YY' recessive lethal also.  
~~YY~~  $\frac{Yy}{Yy}$  | ∵ we get 2:1 phenotypic ratio contrary to mendel.  
 $Yy$   $\frac{Yy}{Yy}$

The frequency of Lethal Alleles found to be much higher than what one would expect from NS:

Dobzhansky

In Heterozygous condition the Lethal allele provides an advantage.

Ex: HbS/HbS  $\Rightarrow$  Lethal.  
HbA/HbS  $\Rightarrow$  Malaria resistance.

Mueller

→ Modern Medicine & oral practices counter NS leading to the preservation of such Lethals.

Only Lethal Gene

# U.P.S.C.

Ex : Dominant : ?

Recessive → Tay-Sach's Disease, where  
"some say individual young child dies as unable to  
produce enzymes needed for normal  
fat metabolism; the fat accumulation  
in nerve sheaths hampers transmission  
of nerve impulses leading to poor  
muscular control & mental deficiency."

B) Sub-Lethal: Kills in infancy,  $\geq 90\%$  don't  
reach adulthood  
→ Dominant: Epilepsy  
→ Recessive: Thalassemia; Sickle Cell Anemia

There role is linked to balanced & transient  
polymorphism (draw diagram); Explain B.P.

C) Semi-Lethal: After attaining reproductive age.  
→ Dominant: Huntington Disease. They do pass  
on genes to their offspring.  
→ Recessive: Haemophilia  
(Draw Pedigree)

# U.P.S.C.

Lethal gene  $\Rightarrow$  Fertility & fecundity = 0;  
Thereby it is like 'Negative Selection'

# U.P.S.C.

## Monogenic & Polygenic Inheritance

(Single factor)  
sort off

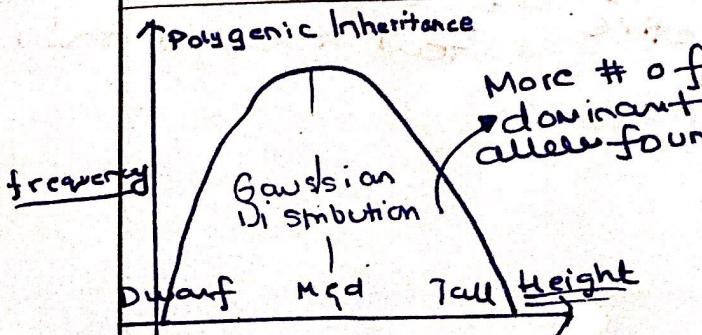
(1 locus)

- ① Result from 1 Gene; follow Mendel's Law of Segregation; usually the phenotype is discrete; Less impacted by the environment; 5 types: elaborate.
- Qualitative Inheritance; single dominant gene influences the trait.
- May have dominant phenotype; complete trait.
  - Accounts for limited phenotype Ex: (TT) = (Tt) = Taster ABO, Rh
  - Such genes called Monogenes.

⇒ Refers to sum-total of many genes.

- But there are several quantitative traits like skin & color that display continuous variations & cannot be explained by the simple Mendelian inheritance. To account for such traits RA Fischer proposed: Mutigene [Polygenic] Inheritance.

- Result from several Genes: Dominant alleles have a cumulative effect with each dominant allele expressing a part of the trait.
- Phenotype is continuous (gradual) More impacted by env Quantitative Inheritance;
- Explains why offspring of phenotypically diff parents mostly express an intermediate phenotype.  $TT + tt \Rightarrow$  Heterozygous medium tall Progeny.
  - The full trait is shown only when all the dominant alleles are present.
  - Each dominant allele controls only partial quantitative expression of the trait.



- Ex: Deavenport (1913) on Skin color; 3 genes  $\Rightarrow$  6 alleles.  $(1:6:15:20:15:6:1)$
- Ex: Troelich (1970): Japanese in Hawaii 3-4 inch taller due to better nutrition. 84

**U.P.S.C.**

→ Doesn't follow Mendel Law collectively but at each indiv loci it does.

$F_1 \rightarrow$  Intermediate }

$F_2 \rightarrow 1 : 4 : 6 : 4 : 1$  ]

→ In human's, polygenic inheritance accounts for majority of phenotypic variation.

Monogenic

$O \rightarrow O$

$O \rightarrow O$

$O \rightarrow O$

Polygenic

$O \rightarrow O$

$O \rightarrow O$

$O \rightarrow O$

Pleiotropy

$O \rightarrow O$

$O \rightarrow O$

$O \rightarrow O$

Ludwig Plate coined term Pleiotropy.

Ex : Phenylketonuria  $\rightarrow$  Increases AA called Phenylalanine in blood      } varied effects

(PKU)  
Chromosome 12

Ex : TYR Gene  $\rightarrow$  Albinism      } Hair  
    } Eyes  
    } Skin

Ex : Marfan Syndrome  $\rightarrow$  Affects connective tissue  $\rightarrow$  People are very tall & very thin

Gene Interaction: Interaction of the allelic & non-allelic factors on the phenotypic expression.

(A)

Intra-Genic  
Intra-Allelic

(B)

Inter-genic  
Non-Allelic

→ When  $\geq 2$  more alleles of a gene interact in such a way to produce a phenotype apart from the usual dominant recessive phenotype.

Ex: Co-Dominance

Incomplete Dominance (*canalization*)

Multiple Allele

Lethal Gene

Pleiotropic Gene [when gene controls  $> 1$  character]

Ex: Epistasis

Duplicate gene

Complementary/Supplementary Gene

Epistasis: It is masking or suppressing of expression of gene by another gene.

The gene which suppresses another gene is called "Epistatic Gene". The gene which is being suppressed by presence of another gene is termed as Hypostatic Gene. However it may be also that both genes are said to be mutually epistatic.

Types

- Dominant
- Recessive
- Dominant Recessive

# U.P.S.C.

## Multifactor Inheritance

- Many factors are involved including the environmental & genetic.  
Ex: Multiple Sclerosis, Diabetes, etc.
- It is a wider effect than Polygenic Inheritance.
- Genetic imprinting also plays a role as often one gender more frequently affected than the other.  
Ex: Hip Dysplasia is 9x more common in females.
- Sometimes very tough to find out what contribution the genes & env had. So need to do twin-studies, etc.

## Epi-Genetics

: How env affects gene expression  
They are reversible & don't change the gene sequence. It can even be transmitted to the next gen.

# U.P.S.C.

For Ques (1)  
Ques (2)

## Genetic Polymorphism

When a gene exists in form of  $\geq 2$  alleles with  $\geq 3$  genotypes resulting in  $\geq 2$  phenotypes then the situation is called as Genetic Polymorphism.

If the frequency of various alleles in the popn remains constant over generations then it is called as "Balanced Polymorphism" provided that:

SPL  
TYPE  
of  
G.P.

- ① Frequency of least common allele  $\geq 1\%$ .
- ② The frequencies are maintained by the nature & not due to recurrent mutation. This implies NS is operating on it to keep it constant.

Ex: PTC Taster & Non-Taster  $\Rightarrow$  Polymorphic  
Sex:  $x = 0.75$  &  $y = 0.25 \Rightarrow$  population permanently polymorphic.

### Features:

- ① GP  $>>$  PP as not all GP is expressed.
- ② Ultimate source of all polymorphism is Mutation which is non-directional. But since rate less it cannot maintain the Polymorphism. NS acting on the Phenotype maintains it. ✓
- ③ If gene  $\rightarrow$  1 allele  $\Rightarrow$  Popn genetically monomorphic.
- ④ If only 1 phenotype expressed  $\Rightarrow$  Popn is phenotypically monomorphic.  

$$(0.2)(0.17)(0.62)$$

Ex: A, B, O groups frequency can be quoted. It will fetch marks.

# U.P.S.C.

① cellular: Antigen Polymorphism as in ABO.

Types of Polymorphism

② Chromosomal: . . . . .

③ Protein: Structural differences ( $10, 20, 30, 40$ ) & even in enzymes.

④ Restrictive Fragment Length Polymorphism

Cellular → ⑤ Variable Number of Tandem Repeats

→ SNP: 1 BP 'Δ'. Ex: Sickle Cell & Cystic Fibrosis.

⑥ Indel: Add/Subtract BP. + + + many others.

DF Roberts: An Intro to Medical Genetics (1991)

Case Study: Sickle cell trait (HbS)

HbC } Thalassemia

HbE ]  
HbF ] Fetal & changes to HbA in Gm;  
after birth.

Hb A → Normal & all others are called Abnormal Hb's.

(HbA/HbA) → Most common.

HbS → RBC swelled → Less SA → O<sub>2</sub> capacity (↓).

Genotype	Sickling	O <sub>2</sub> (↓)	
HbA/HbA	—	—	frequent ⇒ Malaria weakens immunity so perish
HbA/HbS	8 - 15%	5 - 10%	⇒ Survives //
HbS/HbS	60 - 75%	75%	⇒ Die before maturity

SCT  
SCA  
So HbA/HbS → Africa & Mediterranean.  
↳ Partial Dominance shown.  
(not found in high altitude areas)

HbA = 0.5 }  
HbS = 0.5 }  
HbA/HbS ⇒ Many popn in world  
one like this (100%)

↳ Balanced Polymorphism ideal ex.

# U.P.S.C.

## Relevance of G.P

① Genetic variability & its pros & cons.

② Makes blood & organ donation more complicated.

Let us discuss issue ①:

Most GP is at DNA level which may not be final; so is GP actually useful?

→ Kimura: Says GP is selectively neutral.

→ Ewens & Johnson: say that even non-final GP is selective as it provides a reservoir from which the species can choose to adapt if & when there is change in the env. It also helps avoid build up of recessive lethal & sublethals. So it is good as per them.

However GP is only good upto a level as if we have too much it might ( $\downarrow$ ) avg fitness of popn compared to most optimum genotype. So such GP cause Genetic Load which leads to consequent thinning of the popn. [Crow]

∴ Consequent thinning of the popn. [Crow]

⇒ If G.P selective  $\Rightarrow$  B.P. ✓

Note: If G.P selective  $\Rightarrow$  B.P. ✓

Case Study: Heterozygotes need not always be favoured. Yet G.P occurs.

Ex: Rh factor  $\rightarrow$  RR V; SD / SD still rr V

As Pr(+) born to rr (-) mother are selected against by Erythroblastosis Foetalisis / Rh Hemolytic disease.

Selected Polymorphism

Relaxed / Transient G.P.: Due to ' $\Delta$ ' in env

- ① Industrial Melanism
- ② Height & Rh-factor the extremes are being selected & middle ones are being lessened.
- ③ Hb E in NE pop is (T).

Dobzhansky : "Reproductive community of sexual & cross fertilizing indiv def'n of M.P. who share a common gene pool"

→ Nowadays cl factors are more relv in maintaining isolation than geo factors.

## Population Genetics

The proper unit for evolutionary studies is the common gene pool of the entire population and evolution is the change in frequency of genes in the gene pool.

Mendelian Population: Group of people who share the same gene pool.

→ Distinct & closed genetic system i.e. a "breeding isolate": → Totally separated from other groups.

↓  
Members of group mate within the group only. → Reproductively unstratified so that all indv contribute/ share equally in the same gene pool

→ M.P. exist in a series of hierarchies depending on the extent to which they share the common gene pool. So each M.P. may contain several other smaller M.P. within it. The largest such popn is obviously the entire species.

↗ Mathew & Gregg: S-T group of conspecific interbreeding individuals.

→ Members capable of successful reproduction.

Gene Pool: Sum total of all allelic variations present in a group of individuals. It is thus the total genetic information possessed by the group.

→ Population aka Demes.

Gene frequencies: Sum total of allele frequencies. ↗ Contrast with allele frequencies. Which is always equal to 1.

# U.P.S.C.

## Hardy-Weinberg Law [Law of Genetic Equilibrium]

The Law of Godfrey Hardy & Wilhelm Weinberg given in 1908:

"Under certain conditions ; the proportion of genotypes in a pop<sup>n</sup> will remain constant gen<sup>n</sup> after gen<sup>n</sup>".

Conditions: If followed then the pop<sup>n</sup> will not evolve.

- All matings should be random & equally fertile i.e. no Inb or Hyb.
- NS not acting on alleles under study.
- the alleles under study don't mutate.
- The pop<sup>n</sup> is sufficiently large so that there are no sampling errors [G.O.] due to small pop<sup>n</sup> size.

These are ideal conditions & no population can satisfy all these conditions at the same time. Thus no pop<sup>n</sup> can stay in genetic equilibrium. Thus Pop<sup>n</sup> will have to evolve.

"A pop<sup>n</sup> will stay in G.E. provided that micro-evolutionary forces don't act on it."

Golden Pea Plant [Pisum sativum] Draw simple plant to show frequencies same over the generations.

### Significance:

- One can analyse ' $\Delta$ ' in gene frequencies of a pop<sup>n</sup> under study & find the cause.
- we can find direction of evolving ' $\Delta$ '.
- Genetic Structure & nature of pop<sup>n</sup> can also be determined.
- Immense scope & foundation of Pop<sup>n</sup> Genetics

Hardy Weingberg Law Equation: Proportion of genotypes of gene is represented as proportion of square of sum of the allele frequencies.

If gene has  $\Rightarrow p + q = 1$        $\downarrow \text{sum}$

2 alleles { $p, q$ }      Ratio of Genotypes :  $p.p + p.q + q.p + q.q$   
 $\downarrow$   
 $p^2 + 2pq + q^2$   
 $\downarrow =$   
 $(p + q)^2$

If gene has  $\Rightarrow p + q + r = 1$        $(p + q)^2$ ,  
3 alleles { $p, q, r$ }       $\downarrow \text{sum}$   
 $p^2 + q^2 + r^2 + 2pq + 2qr + 2rp$   
 $\downarrow (p + q + r)^2$

It is called as "Hardy Weinberg Proportion".  
In G.E. ;  $\rightarrow$  The proportion would be constant over gen's.

### Application in Popn Genetics:

#### ① Genetic Structure of Popn:

a) we know % of non-tasters ( $N$ )  $\Rightarrow q^2 = N$  ; PTC : Phenyl Thio Carbamide

They are recessive :  $q \cdot q$        $[q = \sqrt{N}]$

we know  $p + q = 1 \Rightarrow [p = 1 - \sqrt{N}]$

b) Similarly for ABO  $\Rightarrow q = \sqrt{\bar{O}}$       derived after simplification  
 $\bar{O} = \text{Percentile of people with } \underline{O} \text{ blood group.}$        $\uparrow \text{Change appropriately.}$

 $q = 1 - \sqrt{\bar{O}} + \bar{A}$ 
 $p = 1 - \sqrt{\bar{O}} + \bar{B}$

Principles of Human Genetics by Curt Stern (1949)

- ② we can find direction of 'evolution' in popn.
- Study twice at different periods of time.
  - Divide popn into diff age groups, then study variation in allele frequency across.

**U.P.S.C.**

the various ages. This represents the direction of evolutionary change.

③ we can find if a pop<sup>n</sup> is a M.P.:

$$\left. \begin{array}{l} A = [P^2 + 2Pr]n \\ B = [q^2 + 2qr]n \\ O = r^2 n \\ AB = 2Pq n \end{array} \right\} \rightarrow \text{The } \chi\text{-chi squared test [Test of Goodness of fit]}$$

$$\chi^2 = \frac{(O_{\text{obs}} - O_{\text{exp}})^2}{O_{\text{exp}}}$$

$$\Rightarrow \sum \chi^2_{A,B,AB} = \sum \frac{(O_{\text{obs}} - O_{\text{exp}})^2}{O_{\text{exp}}}$$

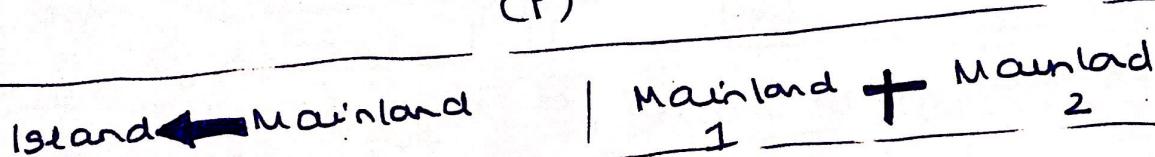
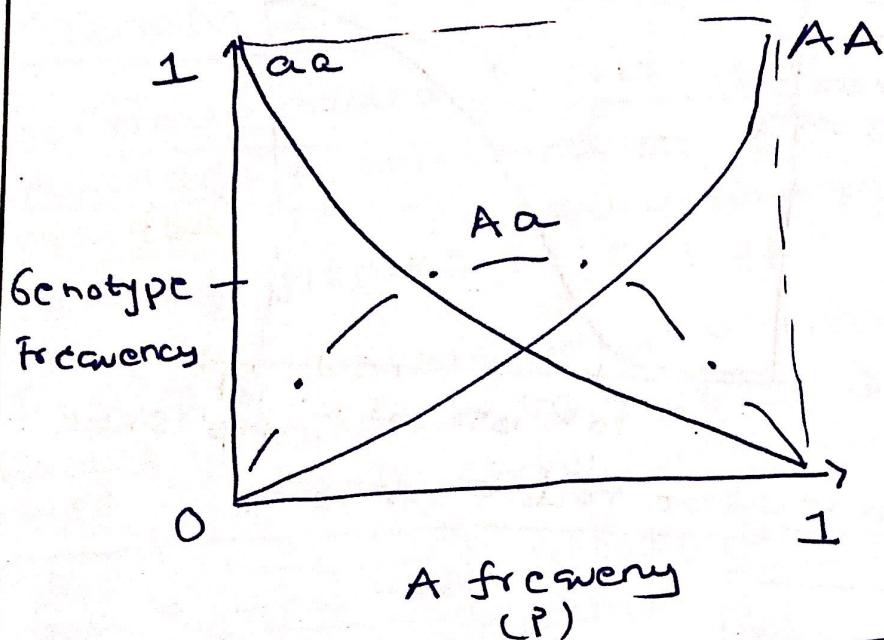
If  $\sum \chi^2 < 3.84$  [df = 1; P < 0.05], then we consider population to be a M.P..

④ we can test validity of sample drawn from previously known M.P.; If  $\sum \chi^2 < 3.84$ , then the sample is a true representation of M.P..

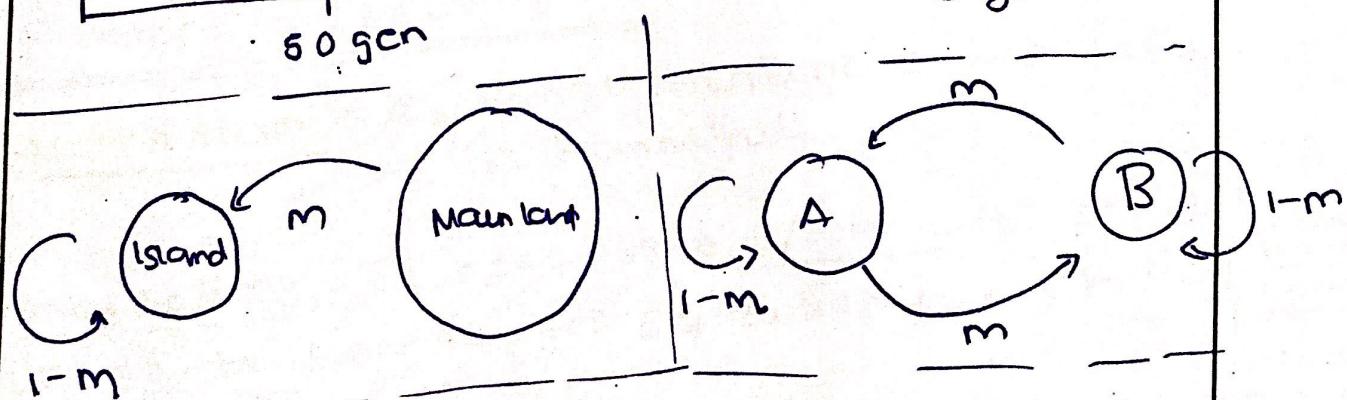
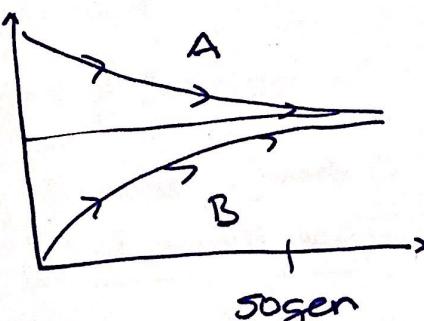
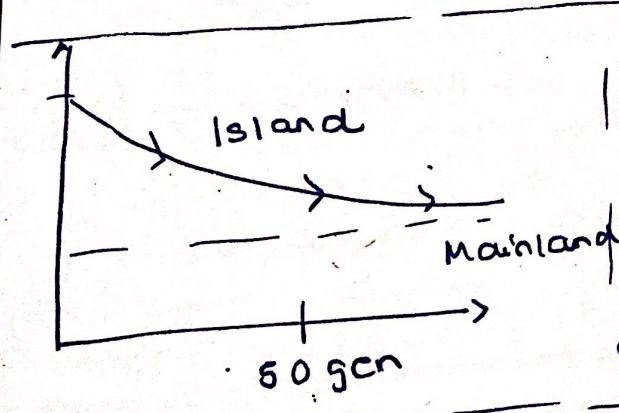
H.W.L is the 1<sup>st</sup> mathematical expression of combination of Pop<sup>n</sup> Genetics of Mendel & Mathematical Genetics which is responsible for growth & dev of Genetics today.

→ Myth of 'Genophagy' of dominant alleles eating up recessive ones was busted.

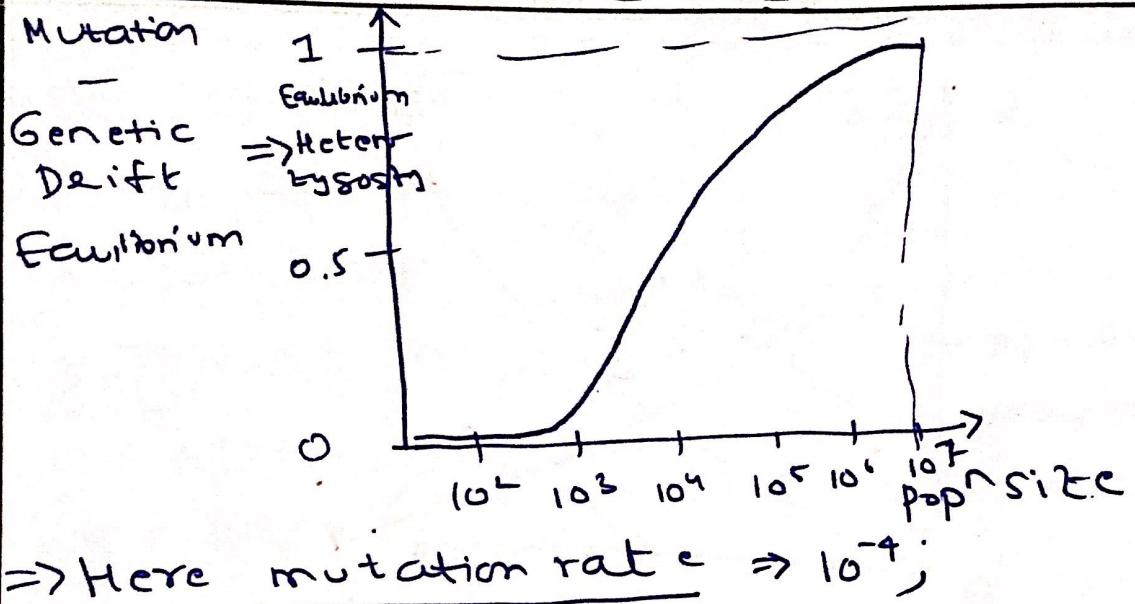
# U.P.S.C.



Mainland + Mainland



- Note : ① Mutation & NS balance  
 ② Mutation & Genetic Drift Balance  
 ③ Mutation & Gene-flow Balance



Genetic Load

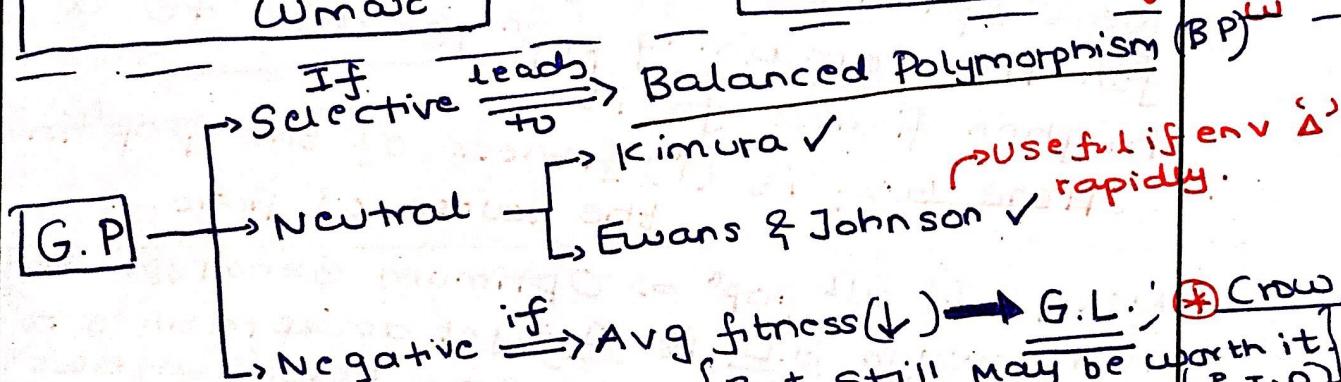
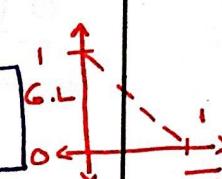
Initially called "costs of NS" by JBS (1937)  
Haldane & renamed as G.L. by Muller  
 in 1950. It is a quantity to measure  
 loss of fitness in a pop.

Def'n: Relative ( $\downarrow$ ) in avg fitness of the  
 population to that of the maximum  
 fitness shown by optimum genotype.  
 (Crow) 1958

$$G.L. = \frac{W_{max} - \bar{W}}{W_{max}}$$

Ideally  $\{W_{max} = 1\}$

then,  $G.L. = 1 - \bar{W}$

Factors affecting it:

① Mutation: As most mutations are said to be harmful.

② Inbreeding: If recessive L/Semi-L then it leads to homozygous condition which reduces  $\bar{W}$  & (T) G.L.

③ Hybridisation: Opposite effect of above.

④ Env: G.L. varies with it; as env determines the optimum genotype & which traits are adaptive.  
 Ex: HbA/HbS → Optimum in Malaria zone but G.L. in normal zones.

Segrega-  
tional  
Load

usually  
more  
impact  
than  
mutation

# U.P.S.C.

It measures the probability of selective death of individual in a given population.

However latest research shows some unique findings:

If  $\frac{\text{pop}^n}{\text{carrying capacity of env.}} > 1$   $\Rightarrow \frac{G.L(\uparrow)}{\omega(\downarrow)}$  Thinning of the pop<sup>n</sup>  
[As pop<sup>n</sup>]

Now optimization of resources occurs for the remaining pop<sup>n</sup> leading to a higher fitness for it.

Here G.L. is ( $\uparrow$ ) fitness of the pop<sup>n</sup> in the course of time.

Note: If all pop<sup>n</sup>  $\Rightarrow$  Optimum Genotype then even though G.L. is 0; yet adaptability to changing env would be very less. (Dangerous).

Calculation: Let rel fitness:  $\begin{cases} AA = 0.8 \\ Aa = 1 \\ aa = 0.6 \end{cases}$

and pop<sup>n</sup> freq =  $0.5 ; 0.5$  of alleles

$$L = 1 - \bar{\omega}; \quad \bar{\omega} = A^2 + 2Aa + a^2$$

$$L = 1 - \left[ \frac{1}{4} \times 0.8 + \frac{1}{2} \times 1 + \frac{1}{4} \times 0.6 \right]$$

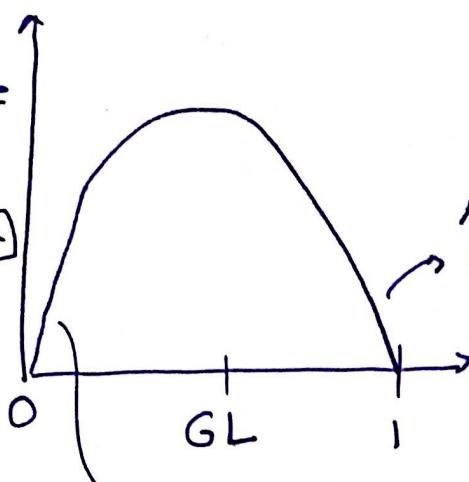
$$L = 1 - 0.85 = \boxed{0.15}$$

# U.P.S.C.

प्रश्न संख्या  
(Question No.)

इस पारा में कृत  
न लिखें  
(Don't write anything  
in this part)

Chance  
of  
fitness  
[Survival]  
\*



As all popn is not all  
healthy so bad.

If change in env occurs than  
population becomes doomed.

Moderate amount of G.L is thus  
considered as optimum soln.