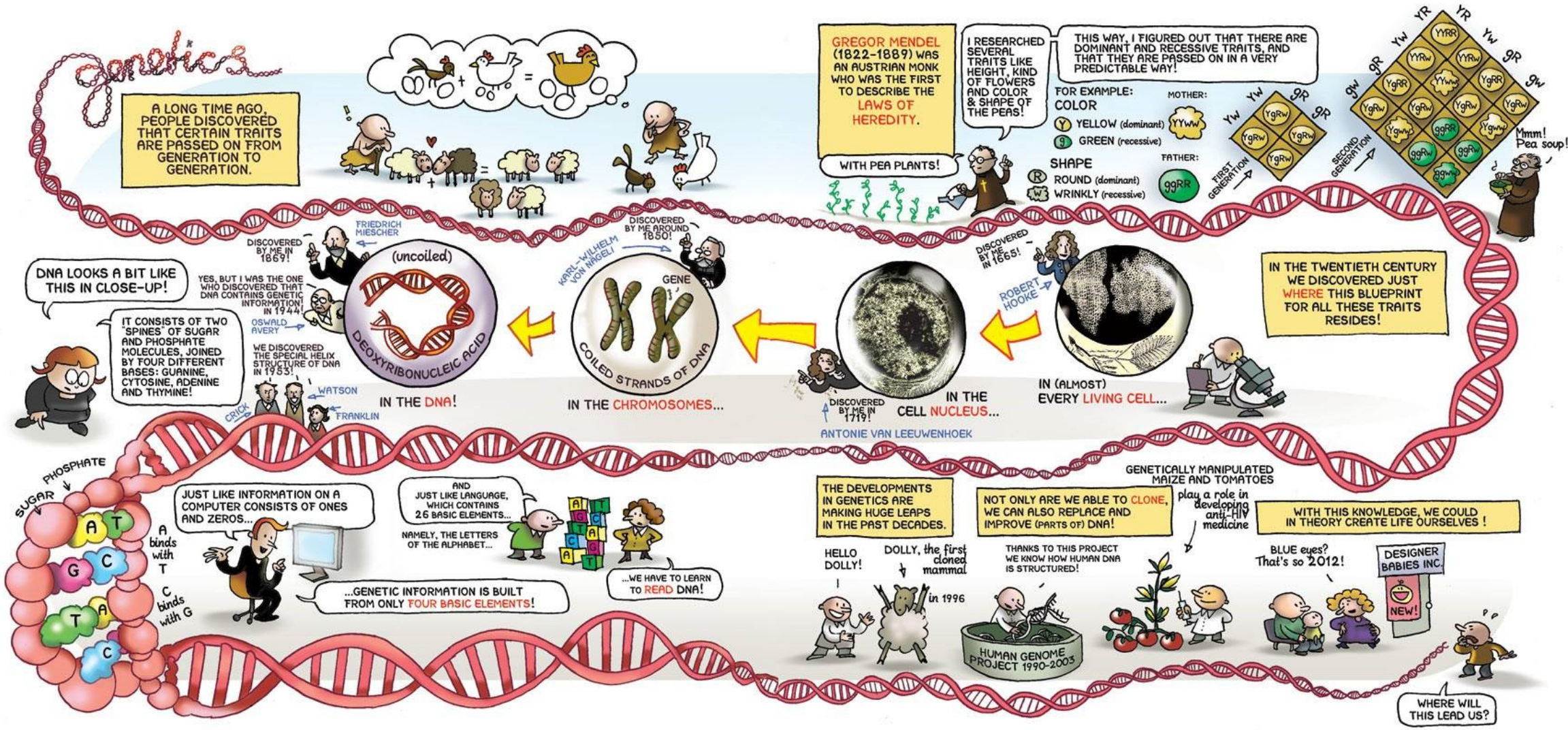
Lecture 1

The Basics of Heredity

History of genetics



History of genetics „pre-mendelian era“

- The effects of heredity are observed by human kinds form its down
  - Children resembles of their parents
  - Domestication of animals and plants, selective breeding for better traits
  - People of Mesopotamia used hybrids of domesticated and wild donkeys to pull their war chariots about 4,500 years ago (Y-chromosomal and mitochondrial DNA)
  - Sumerians horse breeding records

SCIENCE ADVANCES | RESEARCH ARTICLE

GENETICS

The genetic identity of the earliest human-made hybrid animals, the kungas of Syro-Mesopotamia

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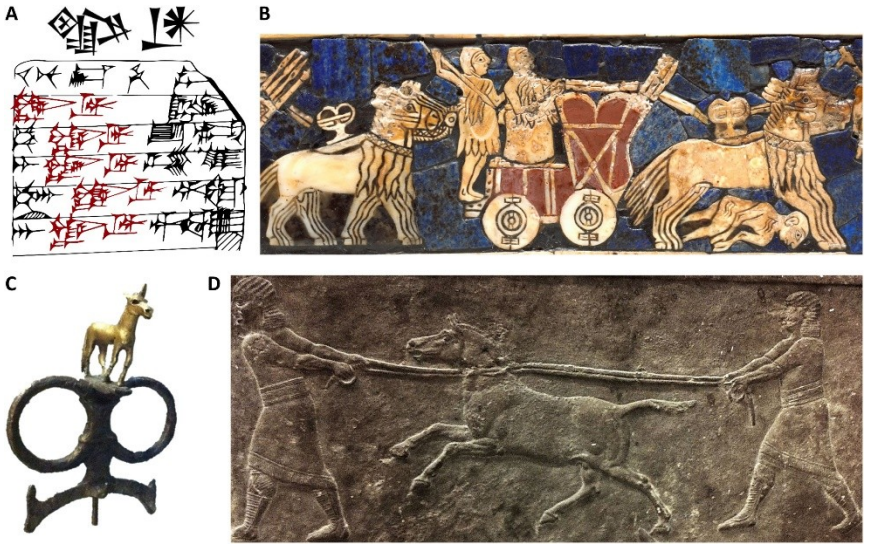
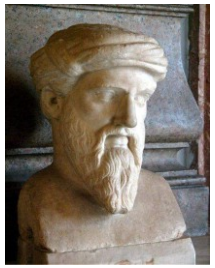
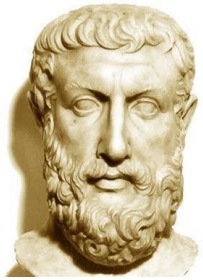


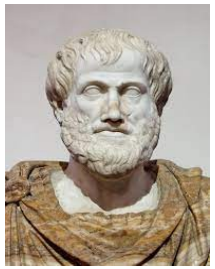
History of genetics: early Greek philosophers



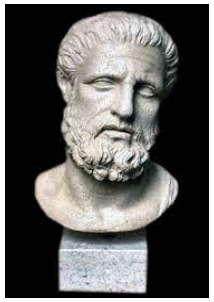
- **Vapour theory** *(Pythagoras*)
  - man body – embryo – uterus of female)



- **Fluid theory** (*Empedocles*)
  - fluid from all parts of each parent create embryo



- **Spontaneous generation** (*Aristotle*)
  - Origin of live from decaying matter
  - Reproductive Blood Theory- embryo is produced due to the mixing of reproductive blood of the two parents



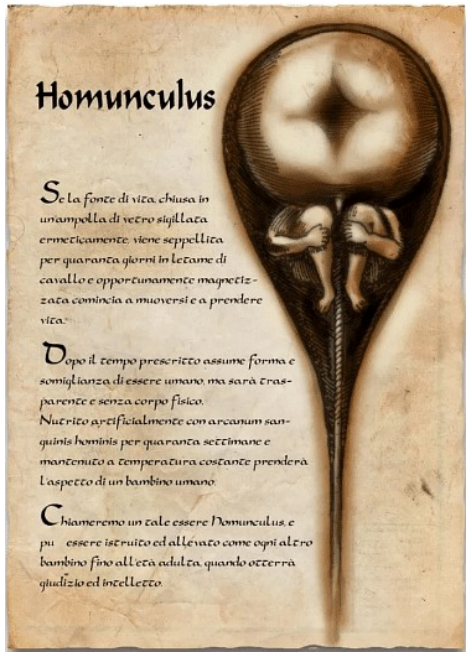
- **Pangenesis** (*Hypocrates*)
  - invisible “seeds ,” from organs of parents are like miniaturized building components and are transmitted during sexual intercourse, reassembling themselves in the mother’s womb to form a baby

History of genetics: Middle age theories

1) Preformation theory (*Malphigi, Swammerdan, Bonnet*)

- miniature individual of extremely small size is present in sperm or egg, grows into a new individual after it receives nourishment in the womb of a female
- Spermists vs ovists – which cells bear key components for gender development?

  - *Da Vinci* – proposed equal contribution of parent´s traits to of spring
  - *Van Leeuwenhoek* - **animacules** (aka sperms of mammals nad frog) are associated with eggs
  - *Malphigi, Swammerdan, Bonnet* miniature individual of extremely small size is present in sperm or egg (**hommunculus)**



History of genetics: Middle age theories

2) Particluate theories – 18 - 19th century

- **Theory of Acquired Characters** *(Lamarck)*
  - ➢ new character once acquired by an individual shall pass on to its progeny (neck of giraffes x Wiesmann – progeny of mices with cut tails had long tails…)

- **Theory of Pangenesis** *(Darwin)*
  - ➢ **gemmules** or **pangene partilces** (of given, oragn, tissue etc) are carried by the blood to the reproductive organ and are deposited in the sex cells, which again carry them to the next generation.
- **Theory of Germplasm** *(Wiesmann)*
  - ➢ Organisms with sexual reproduction carry two types of cells
    - somatic cells make up body (*somatoplasm)*
    - reproductive cells make up sperms and ovas (germplasm)

Gregor Johann Mendel (1822-1884)

- *** 20th July 1822 Hynčice, North Moravia,**
- 1840 – 1843 Philosophy at Olomouc University
- 1843 – join the Augustinian Abbey in Brno
- 1849 – 1851 - teacher at high school in Znojmo (Greek, Latin and German language, mathematics)
- **1851 – 1853** University of Vienna (math, – Doppler, deep understanding of statistics, Dawrin´s work (but Darwin did not known Mendel cause wrote in German language)
- 1854 – 1868 – teacher at Realschule at Brno (physics, biology)
- 1854 – 1863 first experiments with pea in abbey garden
- 1865 – series of lessons about his experiments in conference of biologists in brno (2nd and 3th of March)
- **1866** – publication „Versuche über pflanzen-hybriden“ (Experiments on Plant Hybridization)
- 1868 - abbot of St. Thomas' Abbey in Brünn
- 1881 – director of Moravian bank in Brno
- **6.1. 1884** – Mendel died from chronic nephritis, buried at Central Cemetery of Brno, Leoš Janáček played the organ at his funeral

Mendel´s education – Natural science at university of Vienna (1851-1853)

Experimental physics

(prof. Doppler)

Combinatorics, probability theories, mathematical description of results…

Plant physiology (prof. F. Unger)

„continuity of cells and cell lineage is necessary for birth to other organisms“

- Knowledge of basic principles of plant physiology, hybridization and plant selection combined with methodology of „hard data“ collection bring Mendel to idea of existence of **discreet particles**, which are located inside cells and responsible for expression of different traits
- During his studies, he developed a **theoretical model of transfer** of the traits from one generation to another with the use of those particles
- He returned to Brno with this „project“

Prof. Franz Unger: Botanische Briefe (1852)

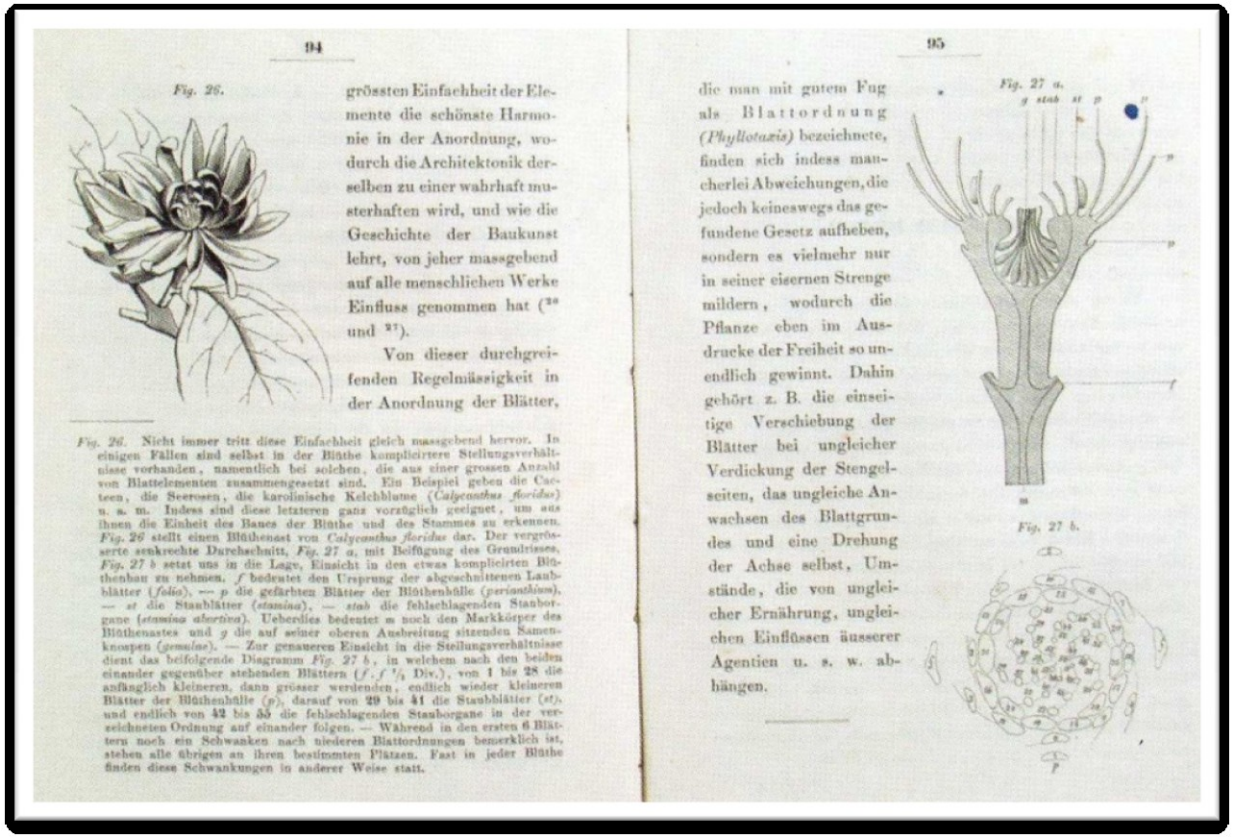


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Fig. 26.

grössten Einfachheit der Elemente die schönste Harmonie in der Anordnung, wodurch die Architektonik derselben zu einer wahrhaft musterhaften wird, und wie die Geschichte der Baukunst lehrt, von jeher massgebend auf alle menschlichen Werke Einfluss genommen hat (26 und 27).

Von dieser durchgreifenden Regelmässigkeit in der Anordnung der Blätter,

Fig. 26. Nicht immer tritt diese Einfachheit gleich massgebend hervor. In einigen Fällen sind selbst in der Blüthe kompliciertere Stellungsverhältnisse vorhanden, namentlich bei solchen, die aus einer grossen Anzahl von Blattelementen zusammengesetzt sind. Ein Beispiel geben die Cacteen, die Seerosen, die karolinische Kelchblume (*Calycanthus floridus*) u. s. m. Indess sind diese letzteren ganz vorzüglich geeignet, um aus ihnen die Einheit des Baues der Blüthe und des Stammes zu erkennen. *Fig. 26* stellt einen Blüthenast von *Calycanthus floridus* dar. Der vergrösserte senkrechte Durchschnitt, *Fig. 27 a*, mit Beifügung des Grundrisses, *Fig. 27 b* setzt uns in die Lage, Einsicht in den etwas komplicirten Blüthenbau zu nehmen. *f* bedeutet den Ursprung der abgeschnittenen Laubblätter (*folia*), — *p* die gefärbten Blätter der Blüthenhülle (*perianthium*), — *st* die Staubblätter (*stamina*), — *stab* die fehlschlagenden Stauborgane (*stamina abortiva*). Ueberdies bedeutet *m* noch den Markkörper des Blüthenastes und *g* die auf seiner oberen Ausbreitung sitzenden Samenknospen (*gemmae*). — Zur genaueren Einsicht in die Stellungsverhältnisse dient das beifolgende Diagramm *Fig. 27 b*, in welchem nach den beiden einander gegenüber stehenden Blättern (*f, f* ½ Div.), von 1 bis 28 die anfänglich kleineren, dann grösser werdenden, endlich wieder kleineren Blätter der Blüthenhülle (*p*), darauf von 29 bis 41 die Staubblätter (*st*), und endlich von 42 bis 55 die fehlschlagenden Stauborgane in der verzeichneten Ordnung auf einander folgen. — Während in den ersten 6 Blättern noch ein Schwanken nach niederen Blattordnungen bemerklich ist, stehen alle übrigen an ihren bestimmten Plätzen. Fast in jeder Blüthe finden diese Schwankungen in anderer Weise statt.

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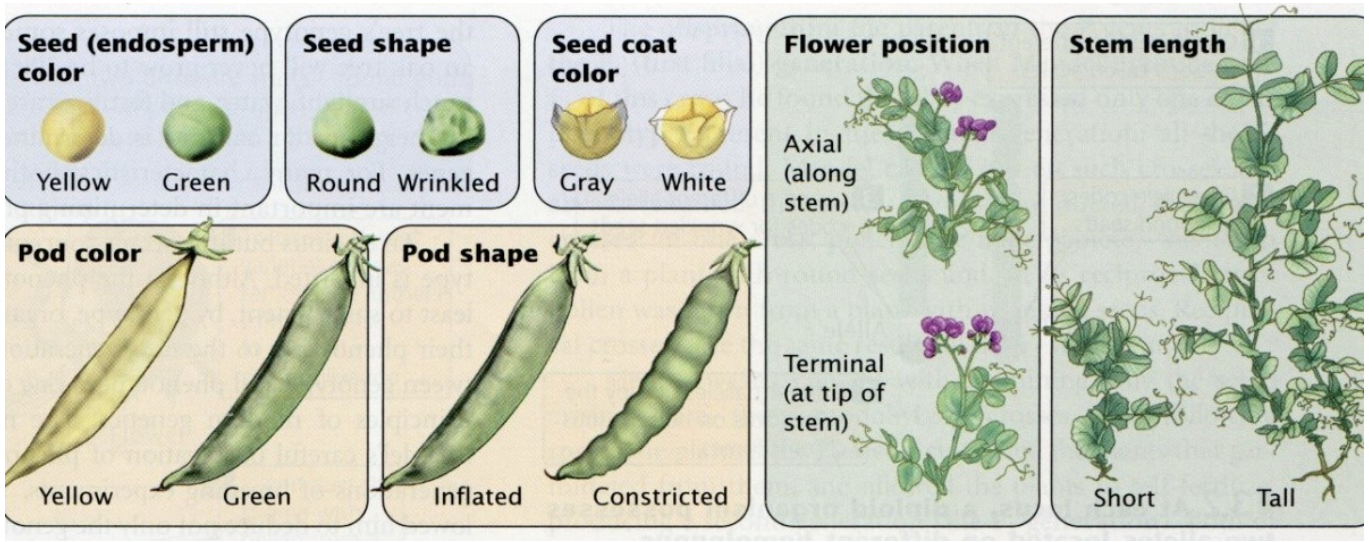
die man mit gutem Fug als Blattordnung (*Phyllotaxis*) bezeichnete, finden sich indess mancherlei Abweichungen, die jedoch keineswegs das gefundene Gesetz aufheben, sondern es vielmehr nur in seiner eisernen Strenge mildern, wodurch die Pflanze eben im Ausdrucke der Freiheit so unendlich gewinnt. Dahin gehört z. B. die einseitige Verschiebung der Blätter bei ungleicher Verdickung der Stengelseiten, das ungleiche Anwachsen des Blattgrundes und eine Drehung der Achse selbst, Umstände, die von ungleicher Ernährung, ungleichen Einflüssen äusserer Agentien u. s. w. abhängen.

Fig. 27 a.

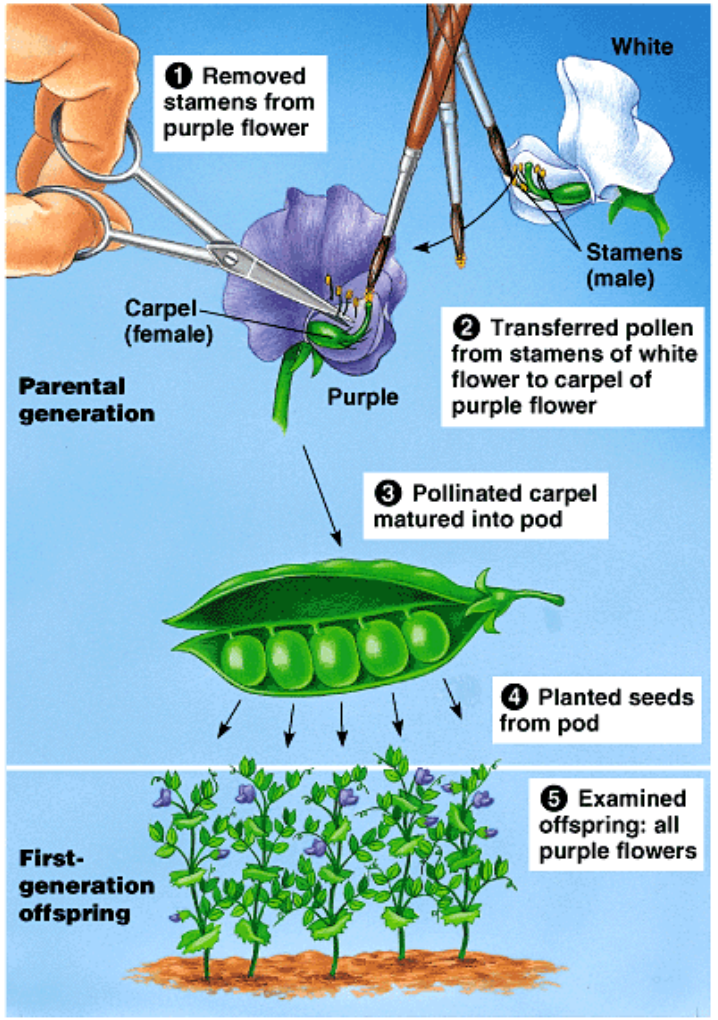
Fig. 27 b.

Wild pea (Pisum sativum) *- model object of Mendel´s experiments*

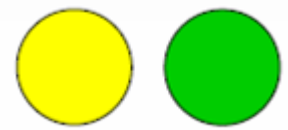
- True - breeding, self - pollinating plant with big blooms
- large number of varieties
- easy to grow, regular and steady yield
- possible control of plant fertilization
- 7 pairs of chromosomes *(2n = 14)*



Breeding



Mendels´ s experiments - character of trai



7 traits* – *stand alone, binar („yes or no“)

- *34* varieties – *2 years of observing* - ***22 varieties*** *with steady difference of traits*

***Parental varieties* = *homozygotes (AA, aa) - differences*:**

1.	***Seed shape:***	**round / wrinkled (chromosome 7)**
2.	***Seed color:***	**white / bright yellow or green (chromosome 1)**
3.	***Bloom color:***	**white / purple (chromosome 1)**
4.	***Pod shape:***	**inflated / constricted (chromosome 4)**
5.	***Pod color:***	**green / yellow (chromosome 5)**
6.	***Flower position:***	**axial / terminal (chromosome 4)**
7.	***Stem length:***	**1,9 – 2,2 m / 0,24 – 0,46m (chromosome 4)**

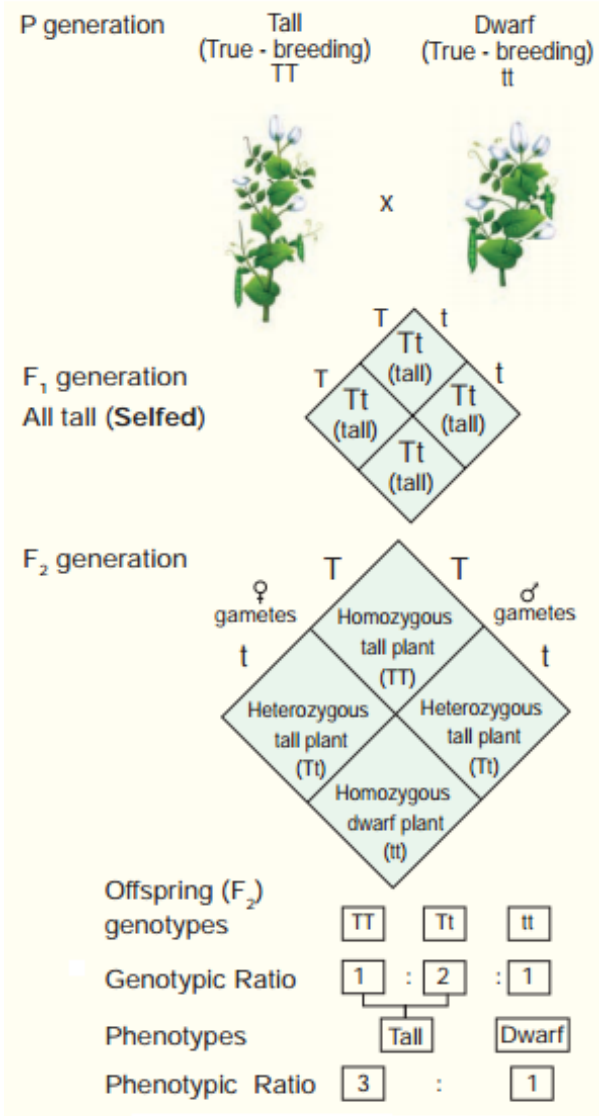
Example of monohybrid crossing: height of the pea plants (tall / dwarf)

1 pair of trait observed in parental (P) generation
offspring - 1st (F_1) and second (F_2) generation

DOMINANT **trait overcome in F_1**

RECESIVE **trait,**

which shows itself in generation F_2

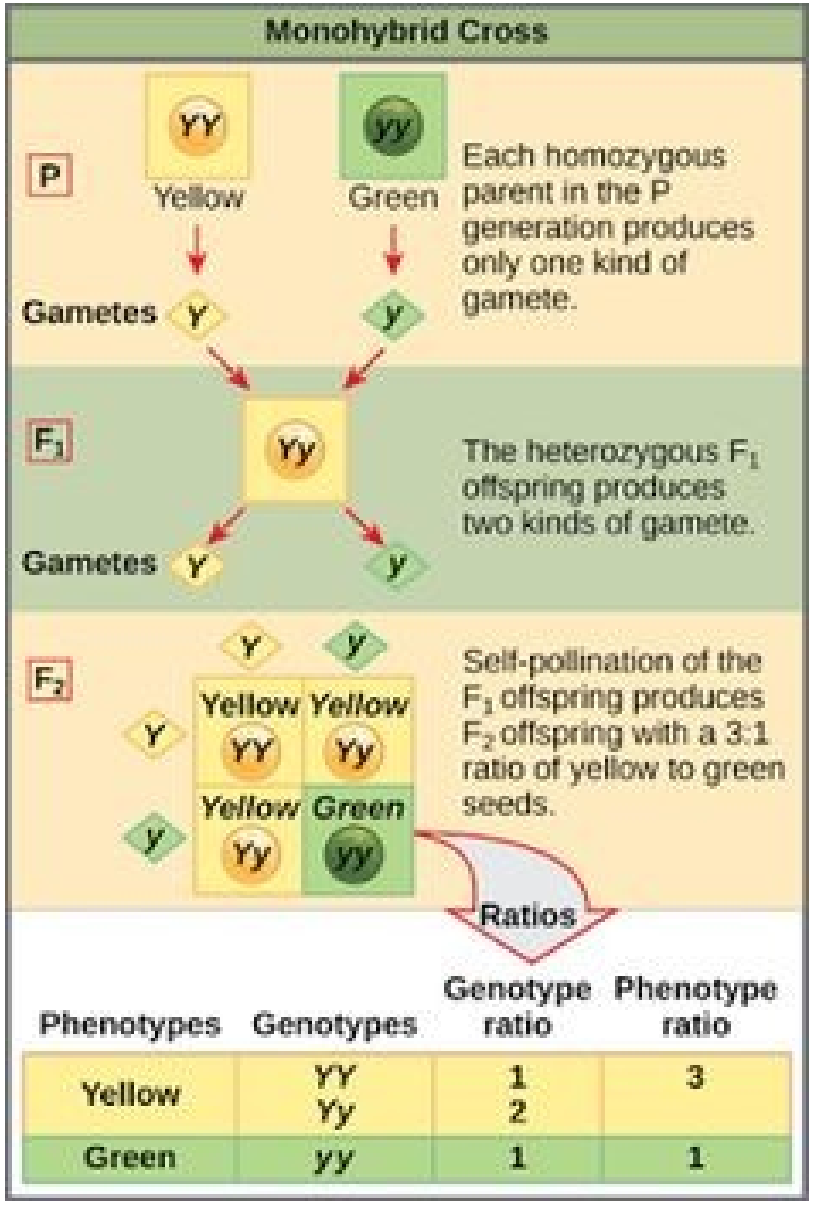


Monohybrid Cross

▶ **Tab. 3.1**

Výsledky Mendelových monohybridních křížení

rodičovské variety	potomstvo F_2	poměr
vysoké rostliny × nízké rostliny	787 vysoké, 277 nízké	2,84 : 1
kulatá semena × hranatá semena	5474 kulatá, 1850 hranatá	2,96 : 1
žlutá semena × zelená semena	6022 žlutá, 2001 zelená	3,01 : 1
fialové květy × bílé květy	705 fialové, 224 bílé	3,15 : 1
klenuté lusky × zaškrcované lusky	882 klenuté, 299 zaškrcované	2,95 : 1
zelené lusky × žluté lusky	428 zelené, 152 žluté	2,82 : 1
úžlabní květy × vrcholové květy	651 úžlabní, 207 vrcholové	3,14 : 1



2 identical copies of gene (alleles) segregate into gametes

F_1 monohybrid (heterozygote) carry 2 different unique alleles in given proportion 50% (0,5)

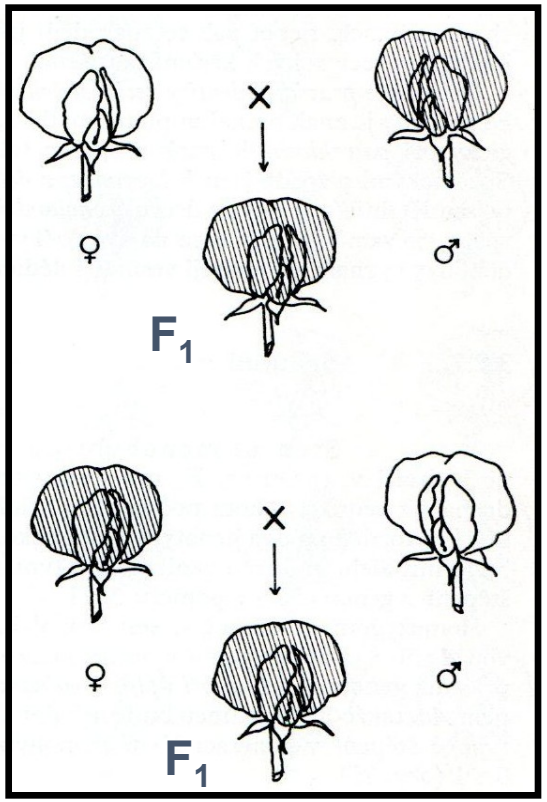
gametes are joining randomly YY (0,25), Yy (0,25)*2, yy (0,25)

Identity of reciprocal crossing

There is no difference if trait comes from mother or father!

A cross, with the phenotype of each sex reversed as compared with the original cross, to test the role of parental sex on inheritance pattern

→ **identical results in F_1**



74. Výsledek reciprokého křížení v generaci F_1 u hrachu setého (*Pisum sativum*) při úplné dominanci.

dominant homozygote x recessive homozygote

P: AA x aa

	gametes	
	Aa	Aa
	Aa	Aa

heterozygote x heterozygote

P: Aa x Aa

	AA	Aa
	Aa	aa

recessive homozygote x heterozygote

P: aa x Aa

	Aa	Aa
	aa	aa

dominant homozygote x heterozygotee

P: AA x Aa

	AA	Aa
	AA	Aa


A
Gametes of a monohybrid - Aa
Mendel identified that heterozygote parents create gametes with one of their two allele with same exact probability … but how can prove this?
50 % A, 50 % a
a
a
A
A

Backcrossing - what kind of gametes and in what ratio are present in hybrids?

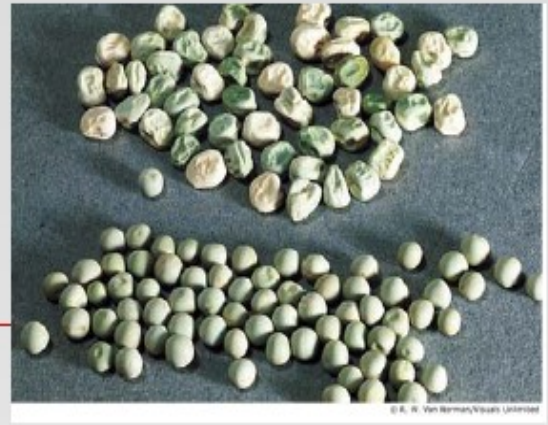
- **B_1 z – backcrossing of F_1 hybrid with parent with recessive alleles for given trait (Aa x aa)**

B_1 Aa x aa

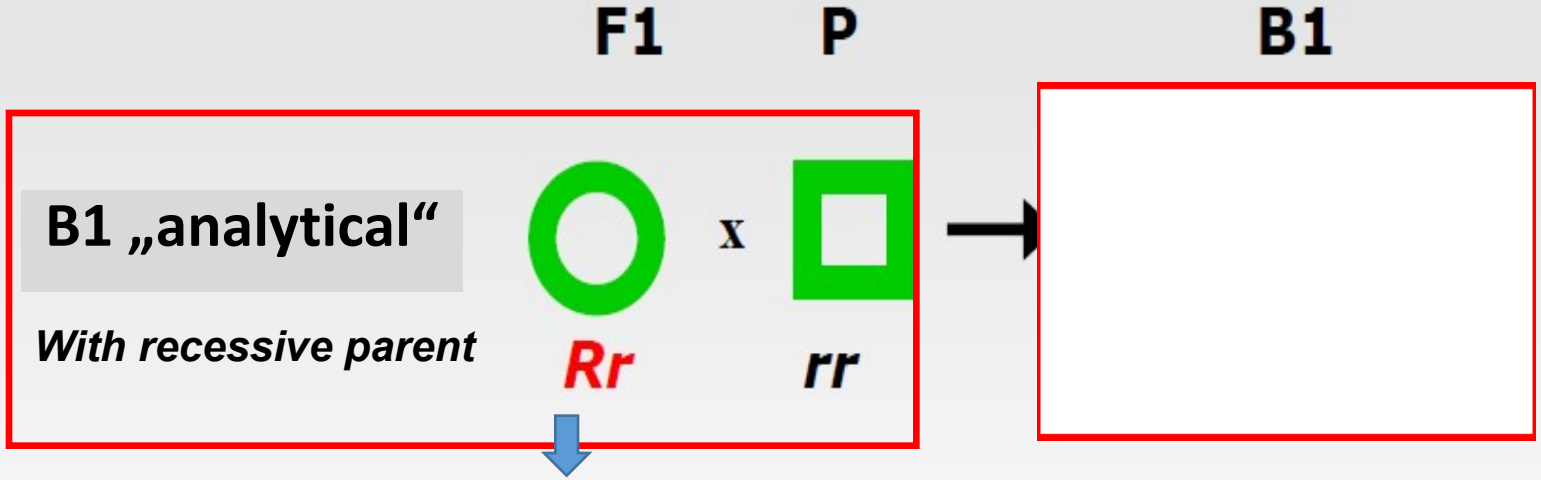
Gametes of hybrid will join with gametes of a parent carrying recessive alleles = highlighting the combination of alleles in gametes of the offspring!

$P:\ RR \times rr \rightarrow F_1 \rightarrow Rr$

Round Wrinkled Round

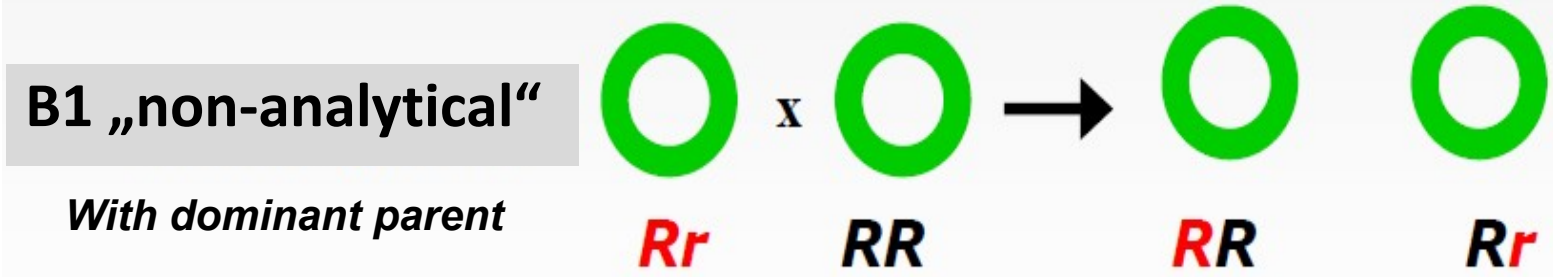


Backcrossing B1 (F1 x P)



2 types of gametes R, r ; ratio 1 : 1

B1 – 2 phenotypes; ratio 1 : 1



Only 1 type of phenotype

Mendel´s conclusions from the monohybrid crossing

- Each trait (f.e. shape of the seed –round/wrinkled) is controlled by a some form of **inheritance factor or determiner** (now known as genes)
- Every parent has a **pair of genes** in for every trait in all cells of the organism
- **Genes** are transferred to the next generation by **sex cells**
- F1 generation from two true-breeded varieties has one allele **dominant** over another, which is **recessive**. Those tow together create **allelic pair**
- F1 offsprings show only one parental trait - **dominant**
- The results of reciprocal crossing **were all the same** no matter whether which parent transferred dominant or recessive allele

Mendel´s conclusions from the monohybrid crossing

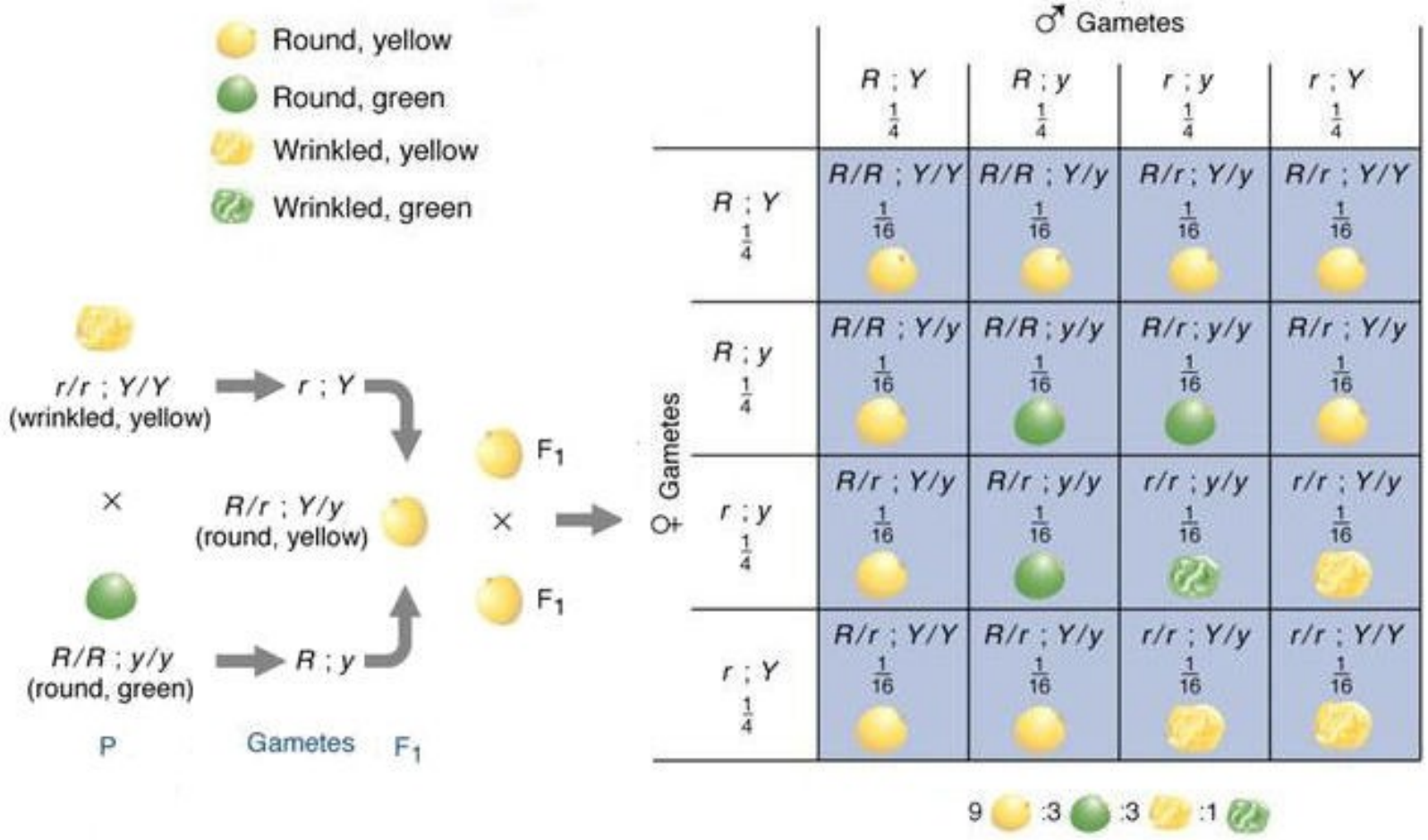
- **only one** of the two gene **copies** present in an organism is distributed to **each gamete** (egg or sperm cell) that it makes, and the allocation of the gene copies is random.

LAW of SEGREGATION

- Gametes fuse randomly and without regard to other associated gene pairs
- Trait not shown in F_1 generation reappeared in **F_2 generation in** 25 % offsprigns and the most importantly
- **Traits had qualities same in offsprings, did not blended and behaved as distinct units!**

Dihybrid Cross – 2 traits, are they inherited independently?

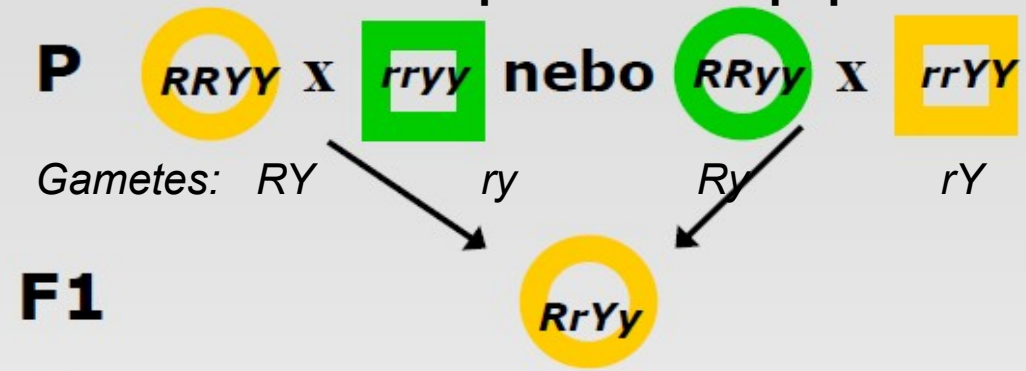
- Connection of two dominant and two recessive traits
- Each parent is homozygous for 2 genes = 2 allelic pairs
- Gametes – one allele from each pair
- Alleles of both pairs segregates INDEPEDENTLY =
- Dihybrid RrYy creates 4 types of gametes



Dihybrid cross

Two possibilities pf parental crossing !!!

Punett square



F2

gamety	RY	Ry	rY	ry
RY	RRYY	RRYy	RrYY	RrYy
Ry	RRYy	RRyy	RrYy	Rryy
rY	RrYY	RrYy	rrYY	rrYy
ry	RrYy	Rryy	rrYy	rryy

Phenotype ratio

9 *R-Y-* Round yellow

3 *R- yy* Round green

3 *rr Y* - wrinkled yellow

1 *rr yy* – wrinkled green

- **Diagonals of heterozygotes and homozygotes**
- **Breed novelties**
  novel homozygous combinations different from parents

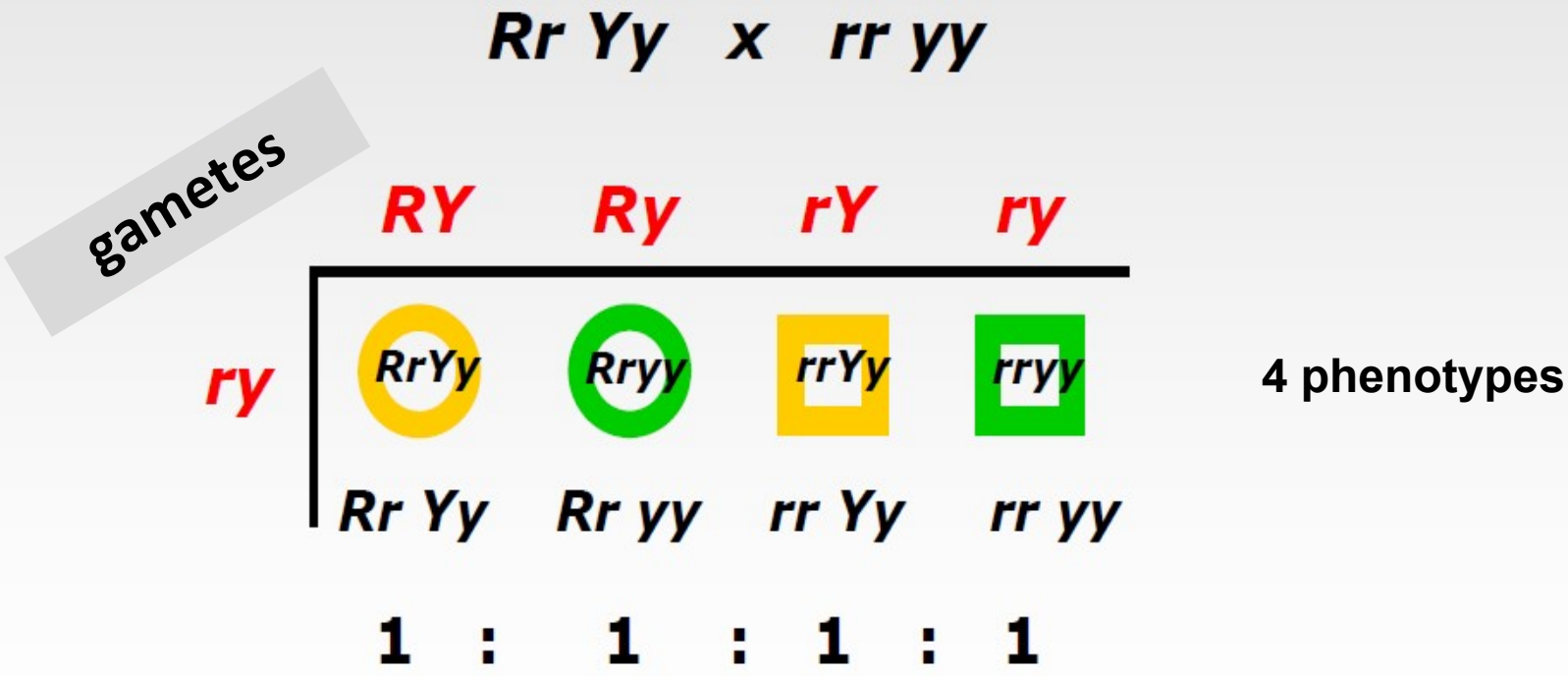
Genotype ratio

1 : 2 : 1 : 2 : 4 : 2 : 1 : 2 : 1

RRYY RRYy RRyy RrYY RrYy Rryy rrYY rrYy rryy

Dihybrid cross

- Backcrossing



4 phenotypes

Generalization for n-hybridism

	n=1	n=2	General
Nr. of gametes of hybrid	$2 = 2^1$	$4 = 2^2$	2^n
Nr. of different zygotes	$3 = 3^1$	$9 = 3^2$	3^n →
*Nr. of different homozygotes **	$2 = 2^1$	$4 = 2^2$	2^n
Nr. of raising novelties	$0=2^1-2$	$2=2^2-2$	2^n-2
Genotype ratio of F2 generation	$(1:2:1)^1$	$(1:2:1)^2$	$(1:2:1)^n$
*Phenotype ratio of F2 generation***	$(3:1)^1$	$(3:1)^2$	$(3:1)^n$

Number of different genotypes

* In all given allelic pairs

** In case of complete dominance in all allelic pairs

n- level of hybridism

Aa – n=1

AaBb – n=2

AaBbCc – n=3

Mendel's conclusions from dihybrid crossing

- F_1 hybrids express **only one variant from both parental traits – always dominant.**
- F_2 generation present **novel variants** completely **different from parents** (in our example yellow-wrinkled and round-green seeds). The exist because of **new combinations** of parental genetic material = **recombinants**

Recombination of hereditary factors (genes) is made according to **laws of probability**. Alleles of given genes are in each generation **chosen randomly** **(alleles of different genes are combined independently)**

LAW OF INDEPENDENT ASSORTMENT

- Hybrid F_2 generation showed **all combinations of parental traits** in specific ratio **9:3:3:1** **(full dominance)**

Mendel´s discoveries: overview

- **Traits are inherited as discreet pieces (elements)**

- **Units of heredity (genes)**
  1) are **material** in nature
  2) come **in pair** (inherited from mother and father)
  3) they are twofold: **dominant** or **recessive (hidden)**
  4) they are transmitted to the next generation via **sex cells**
  5) they are inherited **separately -** they are not **blended in nature**

- F_1 offsprings show only **one parental trait (dominant one)**

- Heterozygous alleles **segregate** into gametes in **random fashion**

- Alleles of different genes **segregate** (combine itself**) independently** of each other

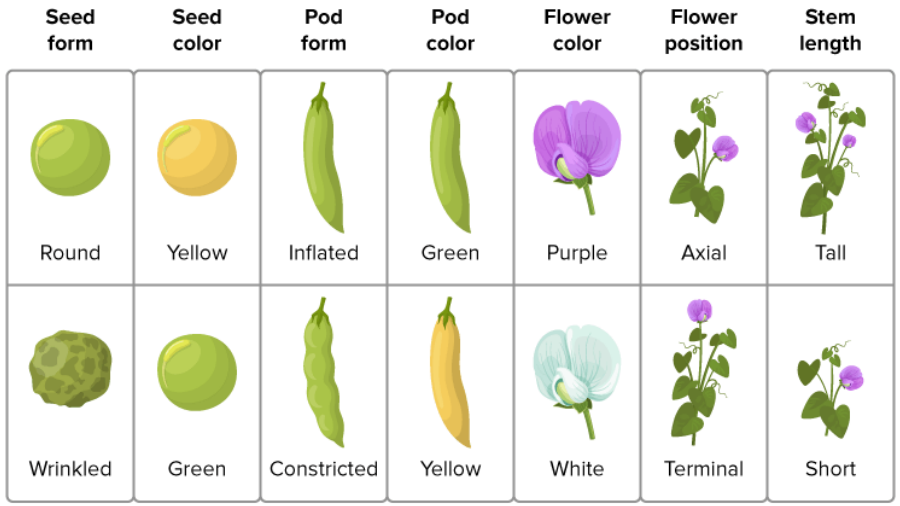
Mendel´s sweet pea traits… nowadays

Dominant alelle

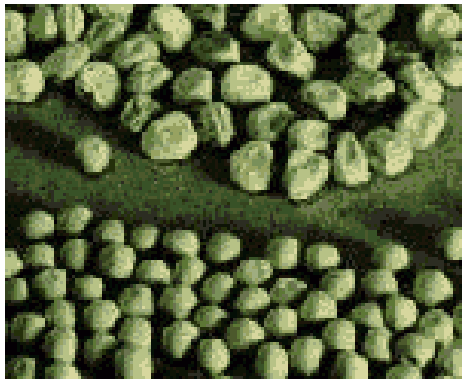
…ATCGGGAATCGGACCCGATG…

…ATCGGGAATCGTGACCGATG…

Recessive alelle - mutant



Mutation in pea genes create new allele!



Seed shape – round x wrinkled

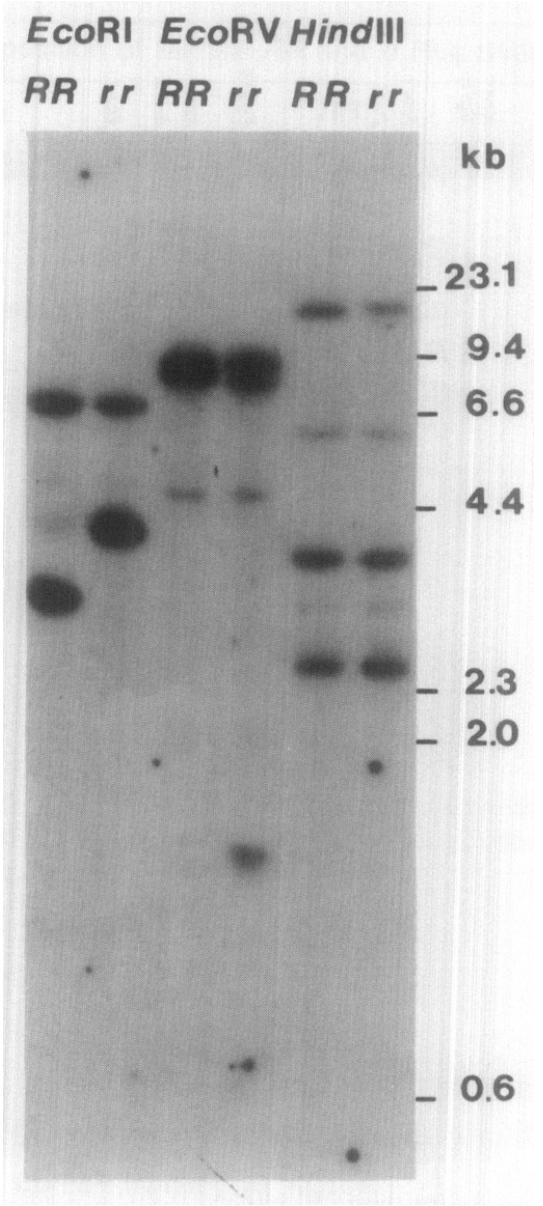
RR x rr

Cause of creation of *r* allele (wrinkled):

Mutation (transposone insertion) in gene which encode enzyme participating on creation of starch in seeds (SBEI) – development of inactive version of the enzyme

Result:

Accumulation of sacharose in seeds – change of osmotic pressure – wrinkled shape of the seeds after drying

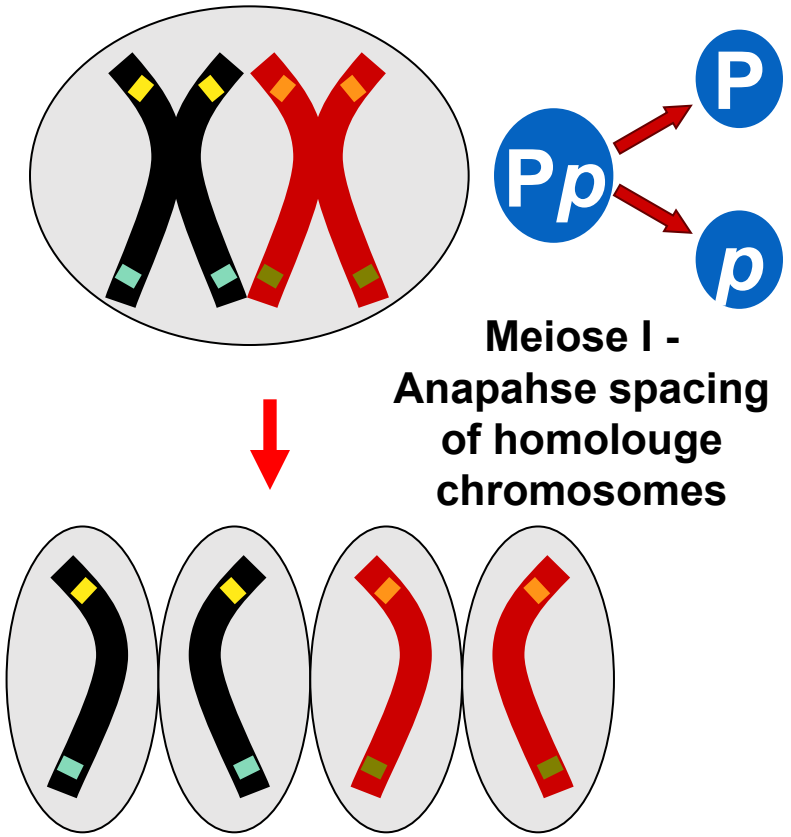


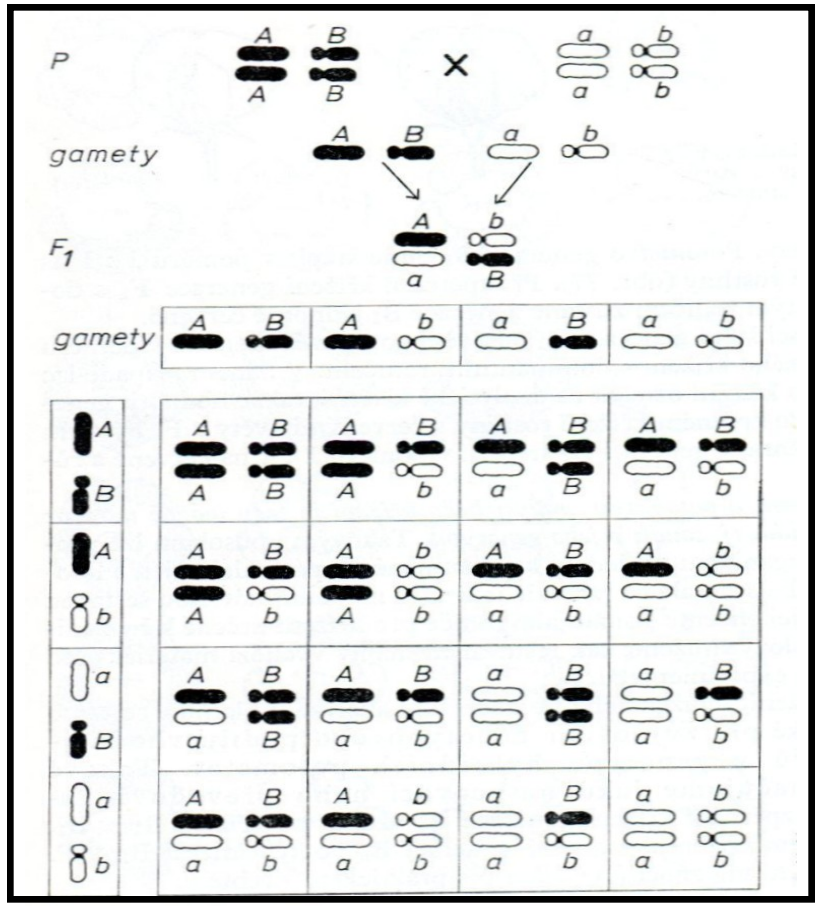
Bhattacharyya et al. (1993)

Mendel´s principles and chromosomes

a) **The reason for segregation and combination of alleles is the behavior of chromosomes during meiosis I (spacing of chromosomes during anaphase I of first meiotic division)**

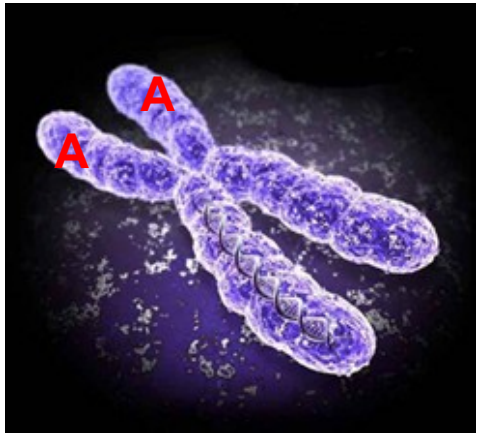
b) **The principle of combination apply for genes located on different chromosomes**





Description of genes and alleles on metaphase chromosomes

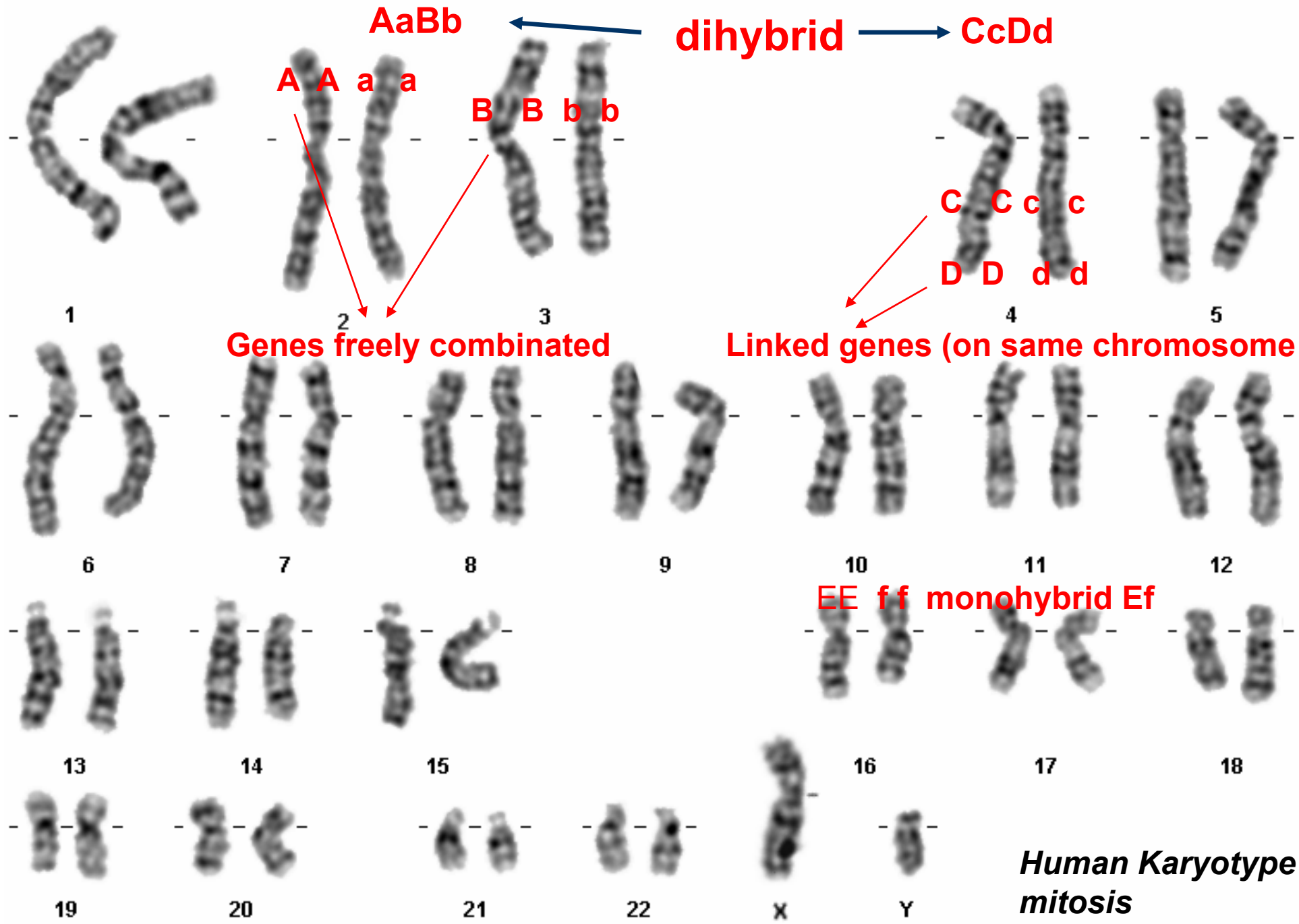
Gene A



Genotype AA

Genotype Aa ?

Metaphase chromosome = 2 identical chromatids!



Human Karyotype - mitosis

Exceptions from Mendel s ratios

- Incomplete dominance
- Codominance
- Multiple allelism
- Lethal alleles

→ **Effect of alelles of one gene**

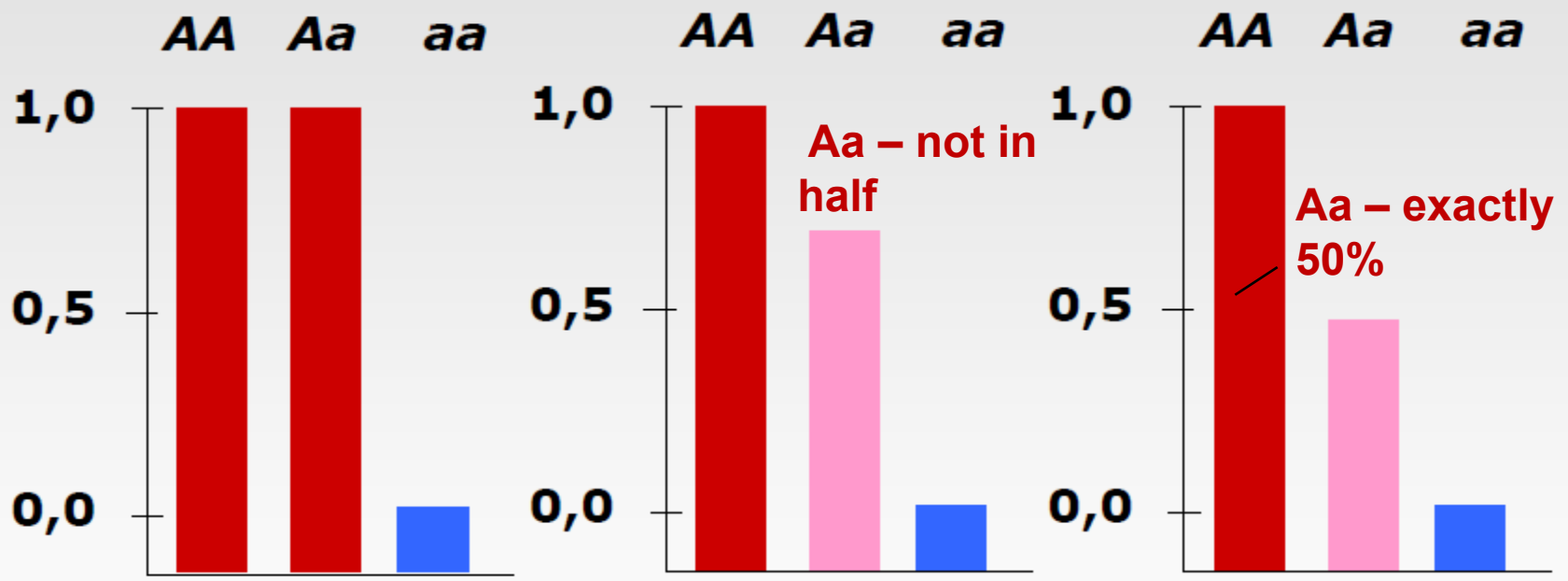
- Penetrance
- Expressivity

→ **Gene interactions**

- Pleiothropy
- Phenocopy

→ **Gene linkage**

Phenotype effects of dominance exceptions



Full dominance

Incomplete dominance

Codominance

Incomplete dominance – *Antirrhinum majus*

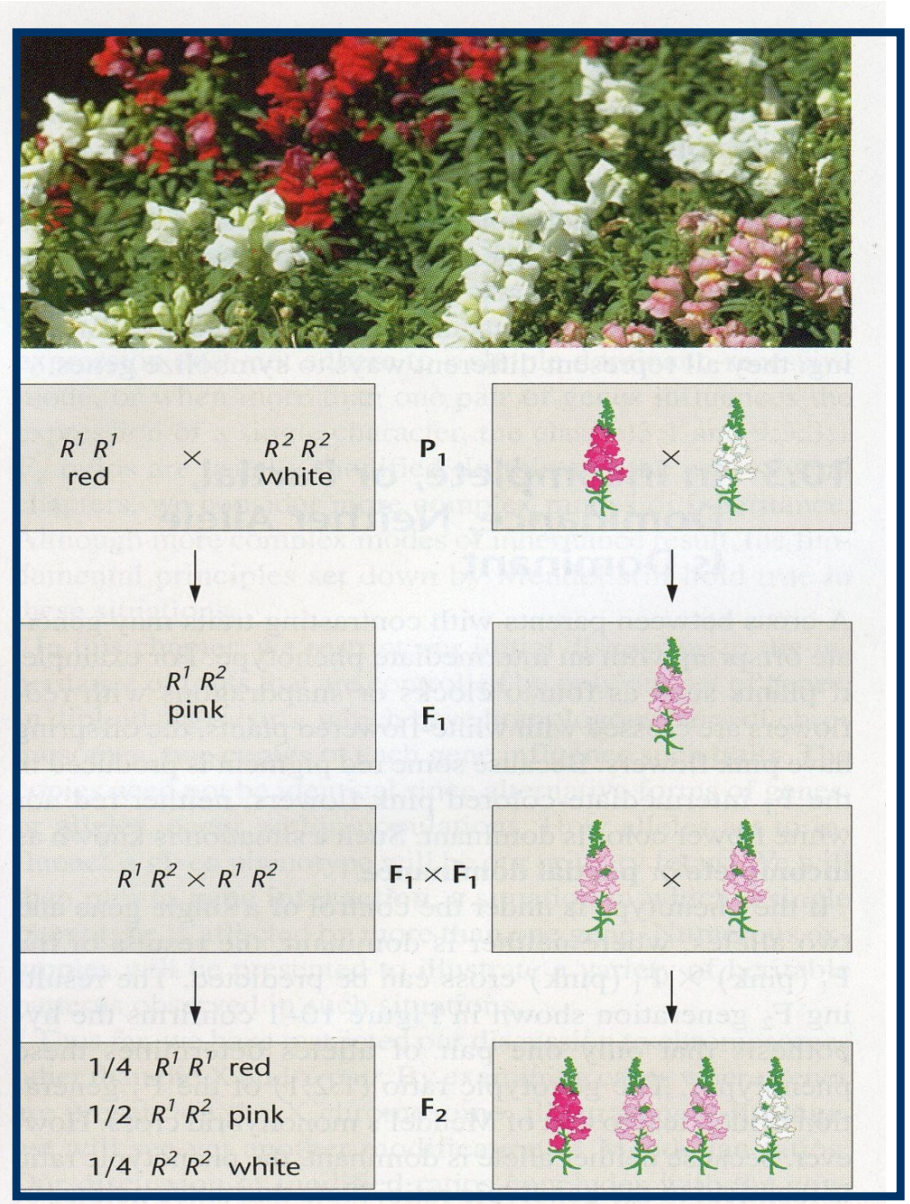
Explanation

Color of bloom depends on **amount of product**

Allele R^1 - color production

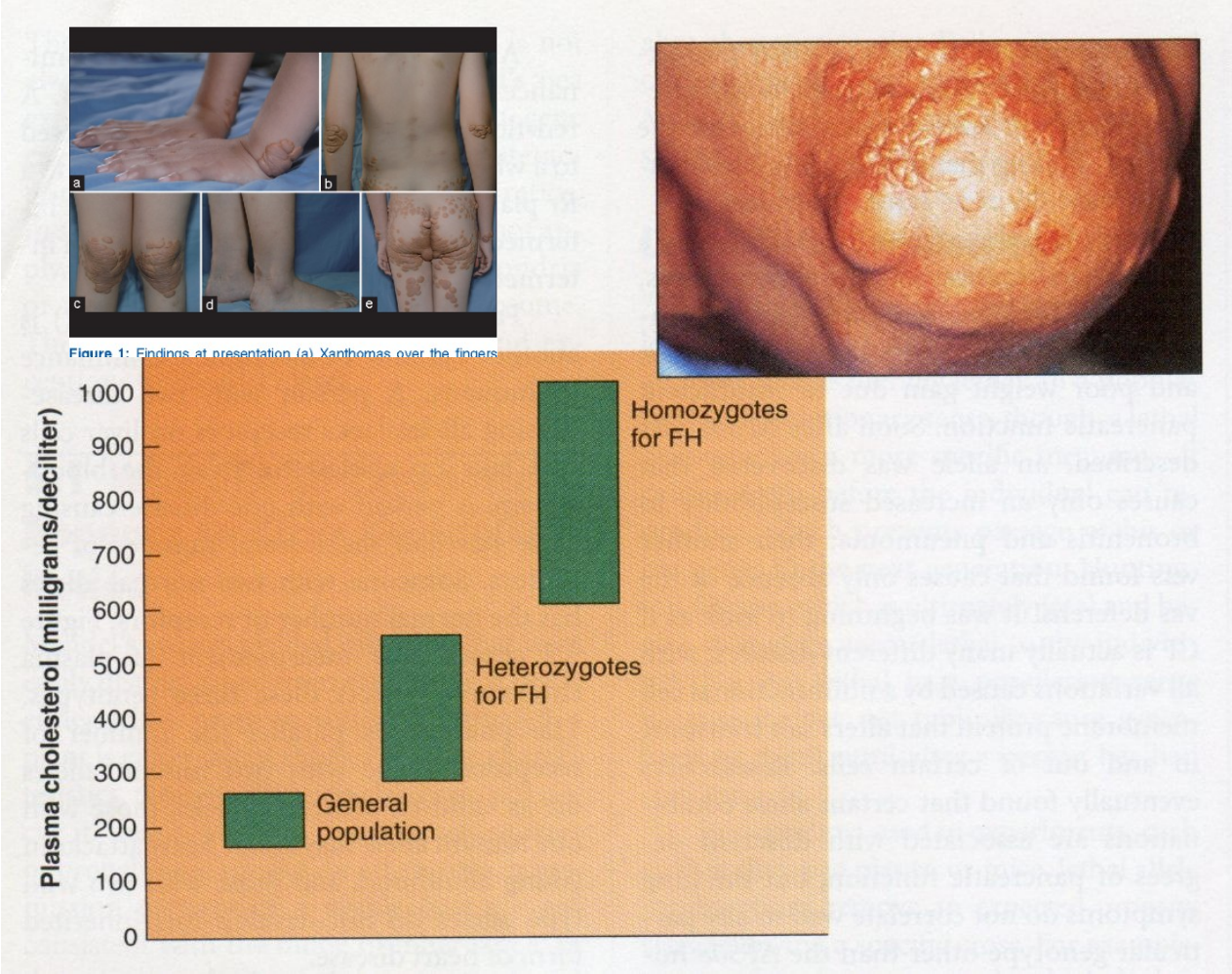
Heterozygote R^1R^2 – approx.. half amount of color production compared to R^1R^1

R^2R^2 - no color



Incomplete dominance – human familial hypercholesterolemia

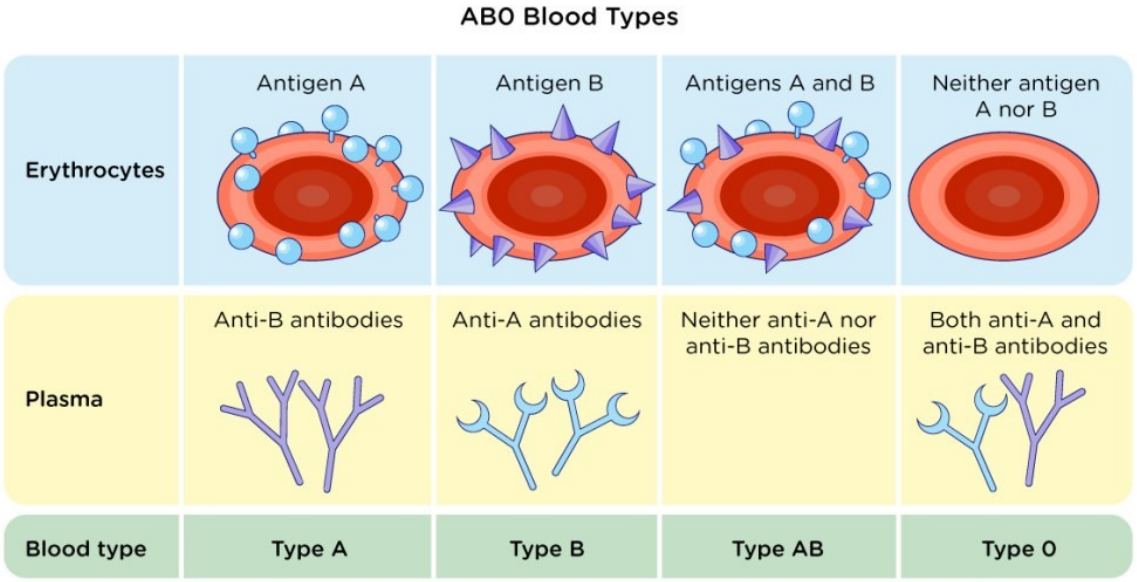
xanthomas

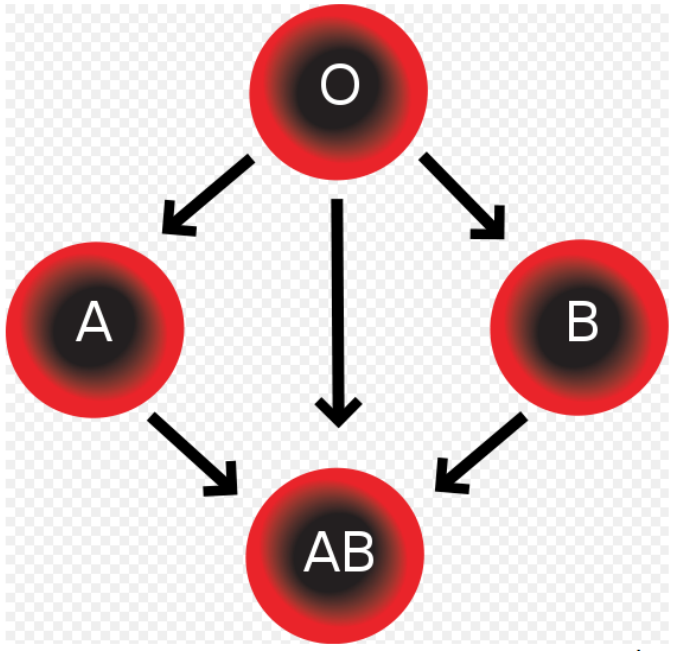


Brain and heart attacks risk at age 20 years

- Hereditary disease, incidence **1/250** in CR, cca 500 mutations described
- Caused by **high levels of LDL** (low density lipoprotein) cholesterol
- ***FH* gene** heterozygotes have approx.. only **half amount** of *LDL* receptors responsible for cholesterol
- Homozygotes in *FH gene* have no receptors – very rare

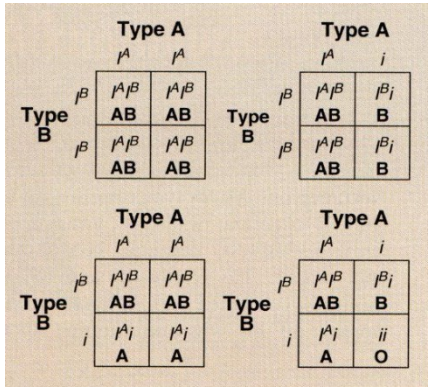
Codominance – human blood groups





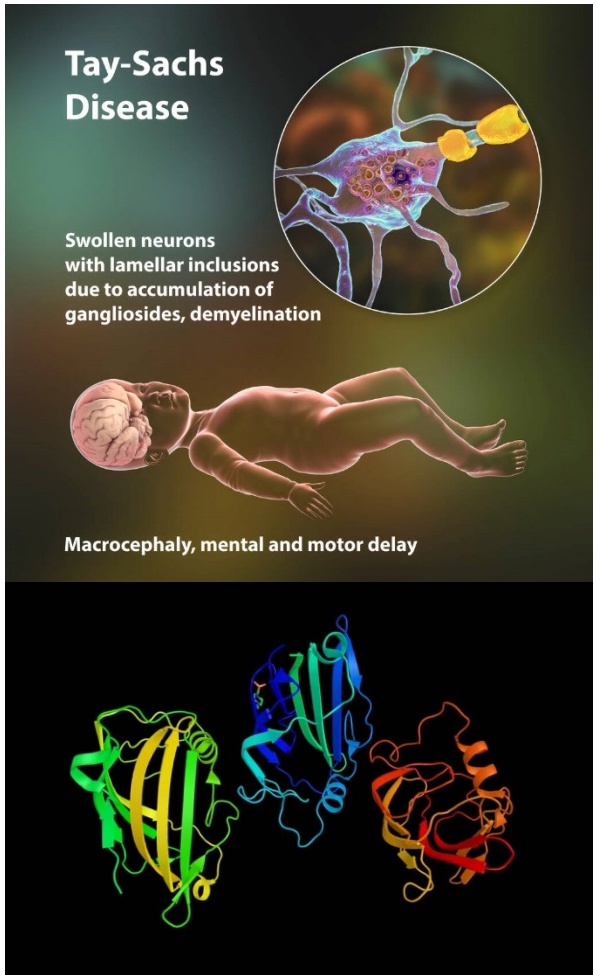
Blood Type	Genotype	
A	$i^A i$ $i^A i^A$	AA AO
B	$i^B i$ $i^B i^B$	BB BO
AB	$i^A i^B$	AB
O	$i\ i$	OO

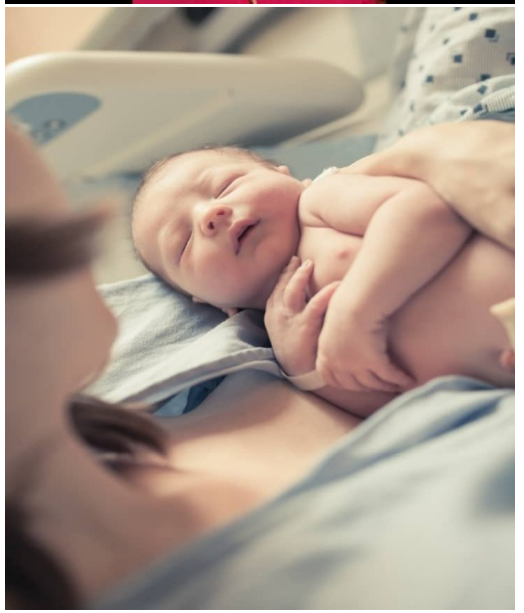
- **Gene *I*** – chromosome 9, **3 alleles I^A, I^B, I**
- Total of ***6 genotypes***
- Heterozygotes ***AB*** express **both antigens** (both alleles active)
- **Codominant** alleles ***A*** and ***B***, both **recessive** to ***i***
- Importance – blood transfuses, paternity testing, ..



Recessive lethal allele in humans – Tay Sachs disease

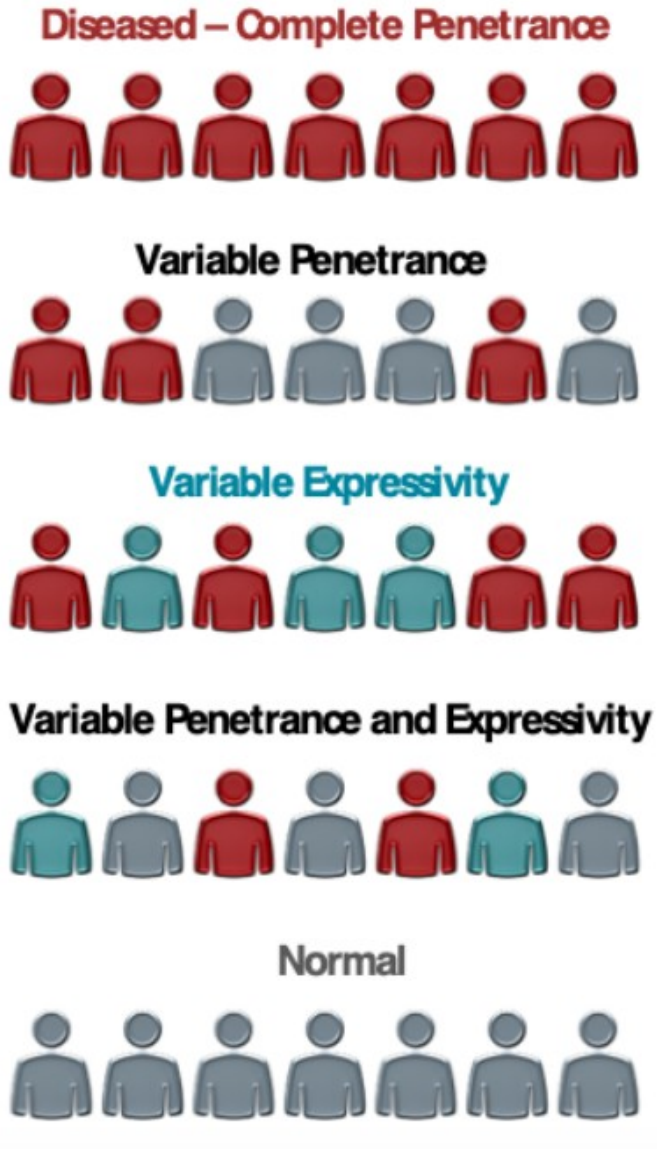
- **Mutation genu *HEXA* (enzyme hexozaminidase A absent)**
- Abnormal accumulation of lipid complex G_{M2} ganglioside on the surface of neurons (function: protection of cells) due to absence of degradation process of G_{M2}
- Newborns are normal
- **After 6 moths of age –** neurological degradation, mental retardation, deafness, blindness, at 2 years unable to move**, death usually 3-4 years**
- **Ashkenazi Jews - heterozygotes Aa 1 :** 30 (incidence 1:3600)





Penetrance and expresivity

- **Incomplete penetrance** – individuals do not show given trait, even though they have given genotype
- **Variable expressivity -** the of expression of gene differs in individuals carrying same trait (different phenotype
- Reason – effect of environment, genetic background…1



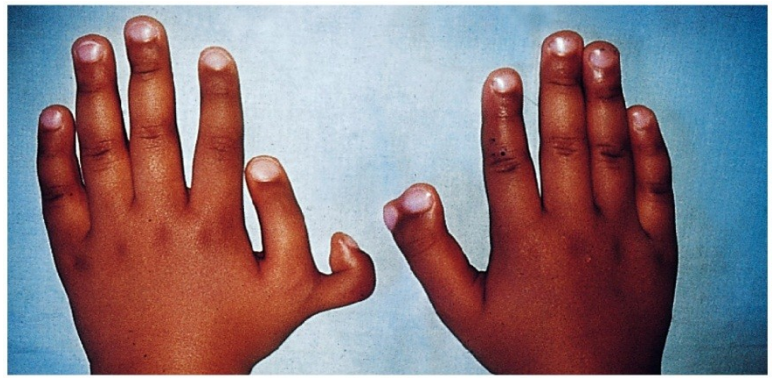
Penetrance vs Expressivity

More Information Online

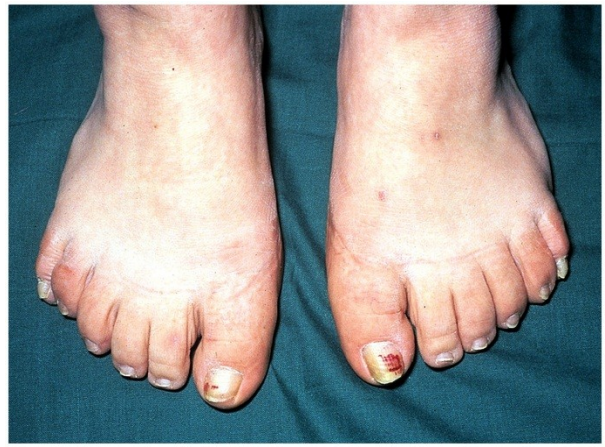
WWW.DIFFERENCEBETWEEN.COM

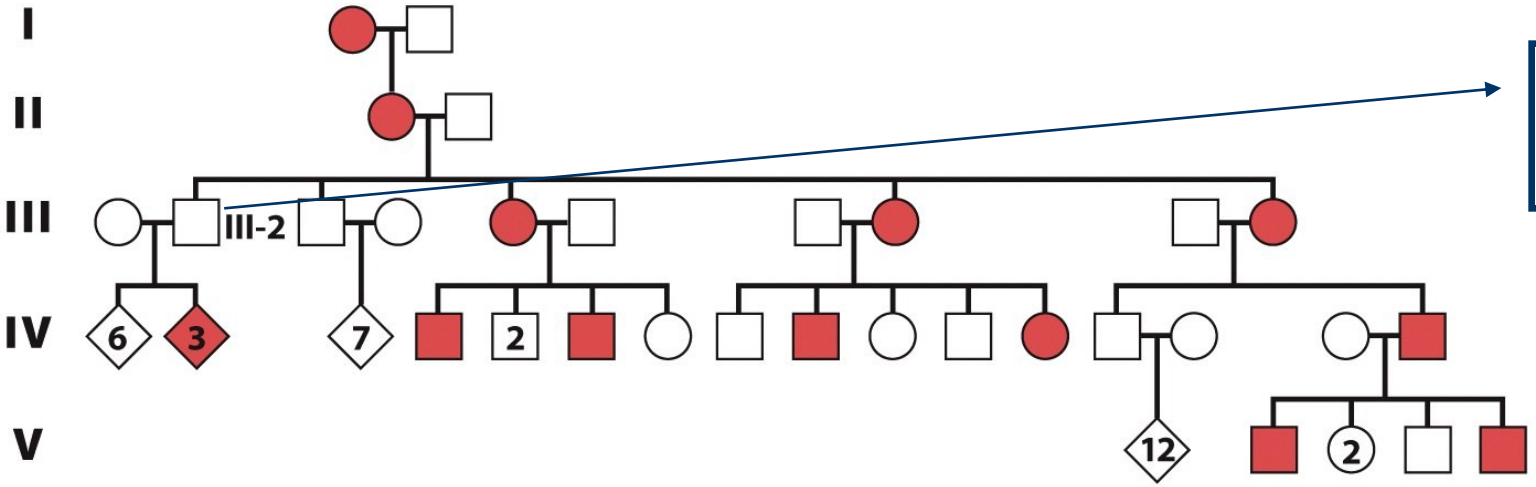
	Penetrance	Expressivity
DEFINITION	Percentage of individuals with a given genotype who exhibit the associated phenotype with that genotype.	The intensity of the phenotype in an individual.
MEASUREMENTS TAKEN IN	A population	A single individual
VARIABILITY	Statistical variability among a population of genotypes.	Individual variability.

Incomplete penetrance: polydactyly



- The trait is conditioned by a dominant mutant allele P
- Its expression is showed in just a few individuals expresses
- Influenced by genetic background

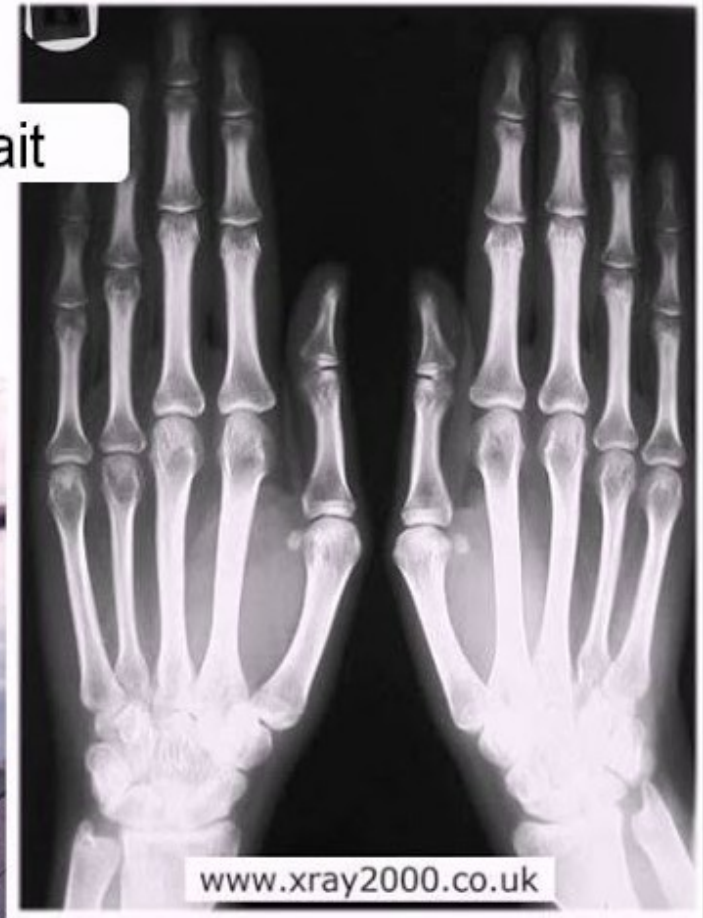




Mutation effect not expressed – healthy individuals

Pleiotropy

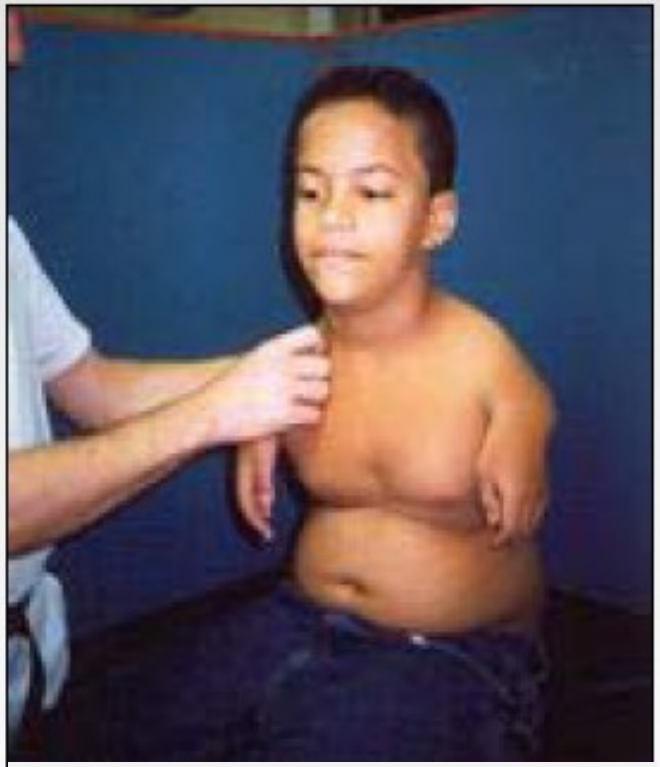
- Most genes are pleiotropic
  - one gene affects more than one phenotypic character
    - 1 gene affects more than 1 trait
    - dwarfism (achondroplasia)
- gigantism (acromegaly)



https://www.youtube.com/watch?v=OxehHPwTFtk&ab_channel=Shomu%27sBiology

Phenocopy

traits induced by environmental effects are identical to phenotypes caused by genotypes



Phocomelia –
inherited malformations of human arms and legs

Teratogenic **effec**t of **thalidomide** taken during early pregnancy

Gene interactions

- Traits are based on cooperation of more genes (pathways)
- **Gene interactions** – quantitative traits arise from cooperation of two and more allelic pairs from different genes
- If two genes interact with each others, same rules as in dihybridism applies (same for n – hybridism)
- Differences are detectable in phenotypes – in cases gene interactions there is lower number of phenotype classes

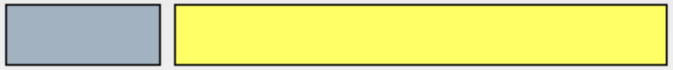
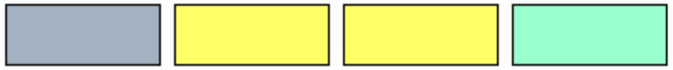
Gene interactions

- **Epistasis dominant / recessive**
  - in dominant epistasis, the dominant allele of one gene masks the expression of all alleles of another gene, while in recessive epistasis (*Dahlia variablis* bloom colors)
  - the recessive alleles of one gene mask the expression of all alleles of another gene.
  - Typical example – color of dogs coat
- **Complementarity -**
  - both dominant alleles are necessary for creation a product (*L. odoratus*)
- **Inhibition**
  - inhibitive allele has not another effect on phenotype than ability to suppress an effect of dominant allele (Feathers color of domestic fow)
- **Multiplicity**
  - bilateral relation of alleles of interactive genes, but in comparison with complementarity, each single dominant allele of any of these genes, even in itself, is sufficient for expression of a corresponding trait.

    a) non-cumulative (Siliqua shape of shepherd's purse) - phenotype is determined any dominant allele

    b) cumulative: (number Caryopsis color of wheat) - expression of phenotype is based on number of dominant / active alleles

Interaction of two genes changes in F2 ratios

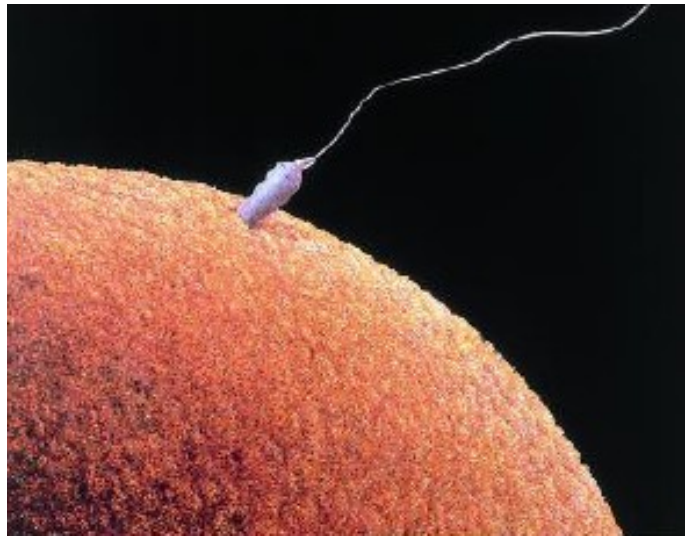
Dihybrid crossing		9:3:3:1
Inhibition		13:3
Complementarity		9:7
Recessive epistasis		9:3:4
Dominant epistasis		12:3:1
Duplicity non-cumulative		15:1
Duplicity cumulative (dominant)		9:6:1

Heredity of sexuality and sex-linked traits

- **Evolution** – asexual to sexual and haploid to diploid organisms
- Reason = to **maximize** to genotype **variability**
- Sexual organisms – change of haploid / diploid stage, reduction of diploid number of chromosomes (**meiosis**)
- Some organisms can reproduce asexually or can change periods of sexual /asexual reproduction
- The most of the **eukaryotic** organisms use **sexual** reproduction

Heredity of sexuality and sex-linked traits

- Basic **features** of sexuality are the **same in all eukaryotes** – there are two types of sex (sexual organs with production of **male or female gametes**) and new generation arise from connection of both gametes
- **Anisogamy** - difference in **size** of male / female gametes
- Evolution of separate sex leads to creation of haploid gametes - meiosis



Man 10^{12} sperms per life
Woman 2,5 millions of oocytes only 400 will mature

Heredity of sexuality and sex-linked traits

Sexual differentiation

- **Primary differentiation**
  - Include creation of reproduction organs (gonads)
- **Secondary differentiation**
  - Include differentiation of other organs (mammary glands, genitalia, etc.)

- **Organisms can carry**

A) just one type of gonads (male / female) dioecious (plants) , gonochorism (animals, higher mammals)

- The sex in gonochorism is determined by genetic traits (GSD) or by environmental factors (ESD)

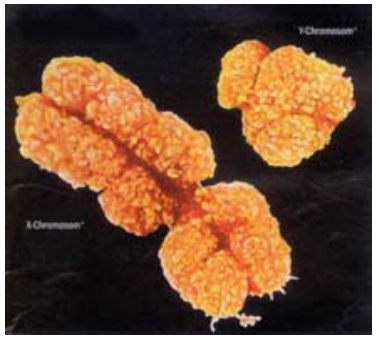
B) both male and female gonads at same time - monoecious, hermaphrodites

Discovery of sex chromosomes

- **1891**: H. Henking – „additional“ chromosome in *Pyrrhocoris* males
- **1902**: McClung - two types of sperm in several kinds of insect

- **1905**: N. Stevens - discovery of sex chromosomes in *Tenebrio*
  - small one (Y) is responsible for male sex determination
- **1906: E.B. Wilson –** XY designation of sex chromosomes
  - *Protenor* AAXX – females, AAXY males
- **1913: Seiler:** butterflies AAXY – females, AAXX males

Chromosomal determination of sex

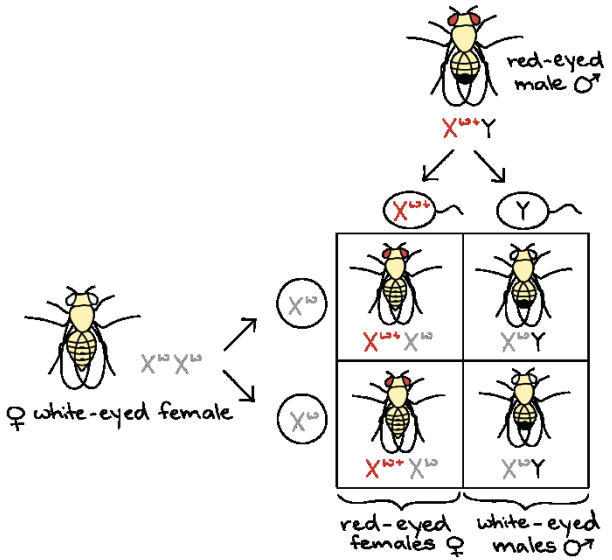


- Autosomes (somatic) x gonosomes (sex chromosomes)
- Humans 22 pairs of autosomes + 1 pair of gonosomes
- Designation of sex chromosomes: X and Y (or Z and W)
- XX: homogametic sex (one type of gametes)
- XY: heterogametic sex (two types of gametes)
- AA: two batches of autosomes

- ***There are 3 basic systems of chromosomal determination of sex***
- mammal type – (*Drosophila)*
- bird type – (*Abraxas)*
- type *Protenor*

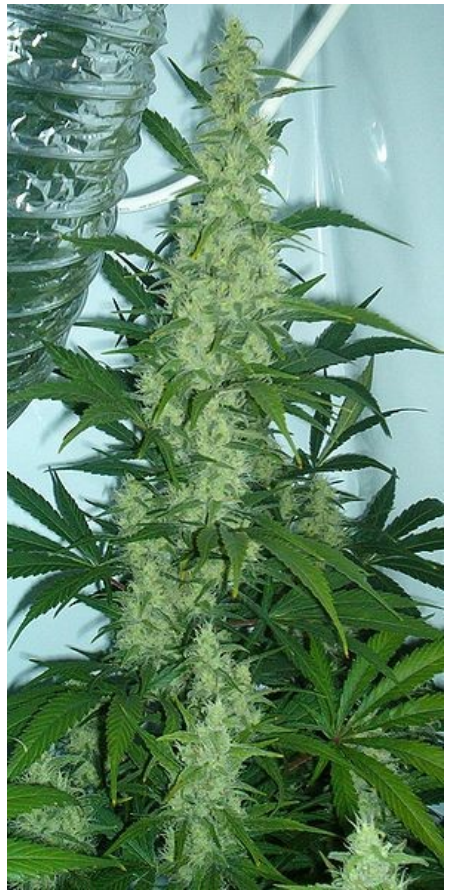
Chromosomal determination of sex: Mammal type

- Female sex: **AA XX** - homogametic
- Male sex: **AA XY** – heterogametic
- Each pair produce 50% of sons and 50% of daughters = **sex ratio 1:1**
- **Carriers** of the sex traits **are males**
- **Two types** of sperms are produced with **same** probability
- **Eggs** are always of same genotype (X)
- Mammals, insect, reptiles, several plants



	♀		♂
P:	**XX**	vs	**XY**
GP:	X, X		X, Y
F_1:	XX		XY
	1		1
	50%		50%

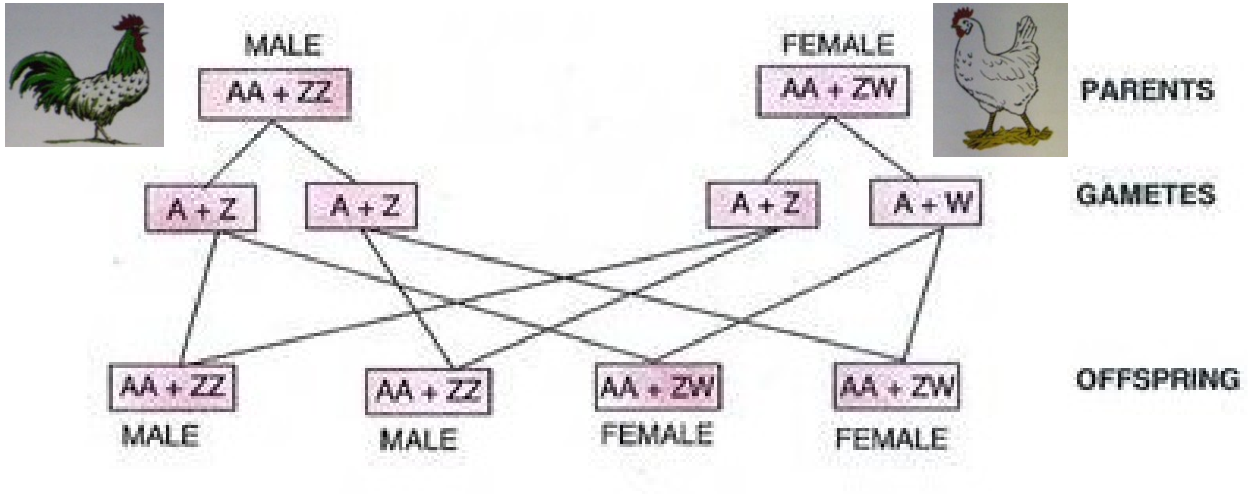
Mammal type of sex determination in plants – dioecious type of plants

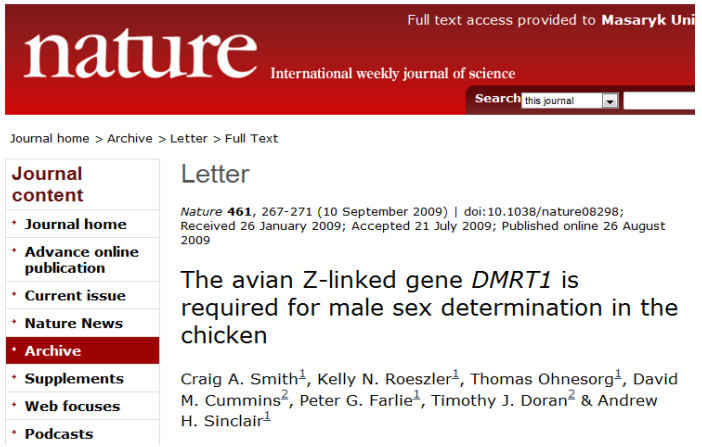


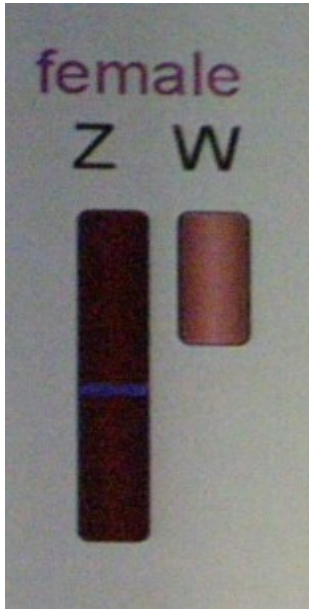
XX female and XY male plants

Chromosomal determination of sex – bird type

- Designation of genotypes **ZW - females, ZZ males**
- **Carriers** of sex traits – **females** (**2 types of eggs – Z,W**
- Males produce only one type of sperm (Z)
- Chromosome Z **–** locus of ***DMRT1 gene* –** development of male gonads **require 2 copies**
- **If one copy is disabled – females**



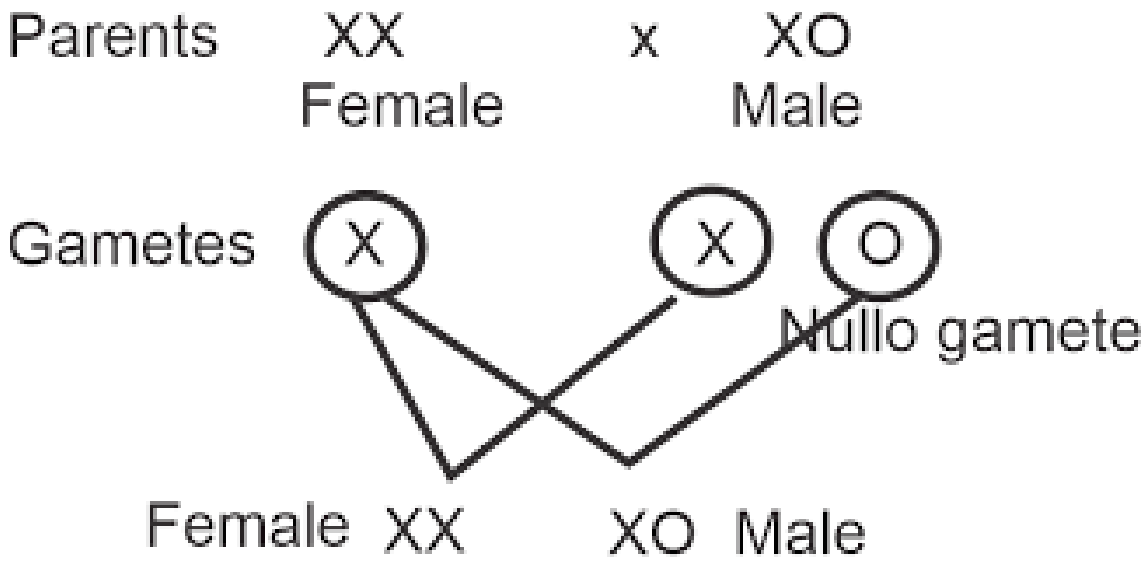




Chromosomal determination of sex – type Protenor

- Protenor (Lygaeus kalmii)
- Female sex: AA XX - homogametic; Male sex: AA X - heterogametic
- Mostly insect species

Protenor (*Lygaeus kalmii*)



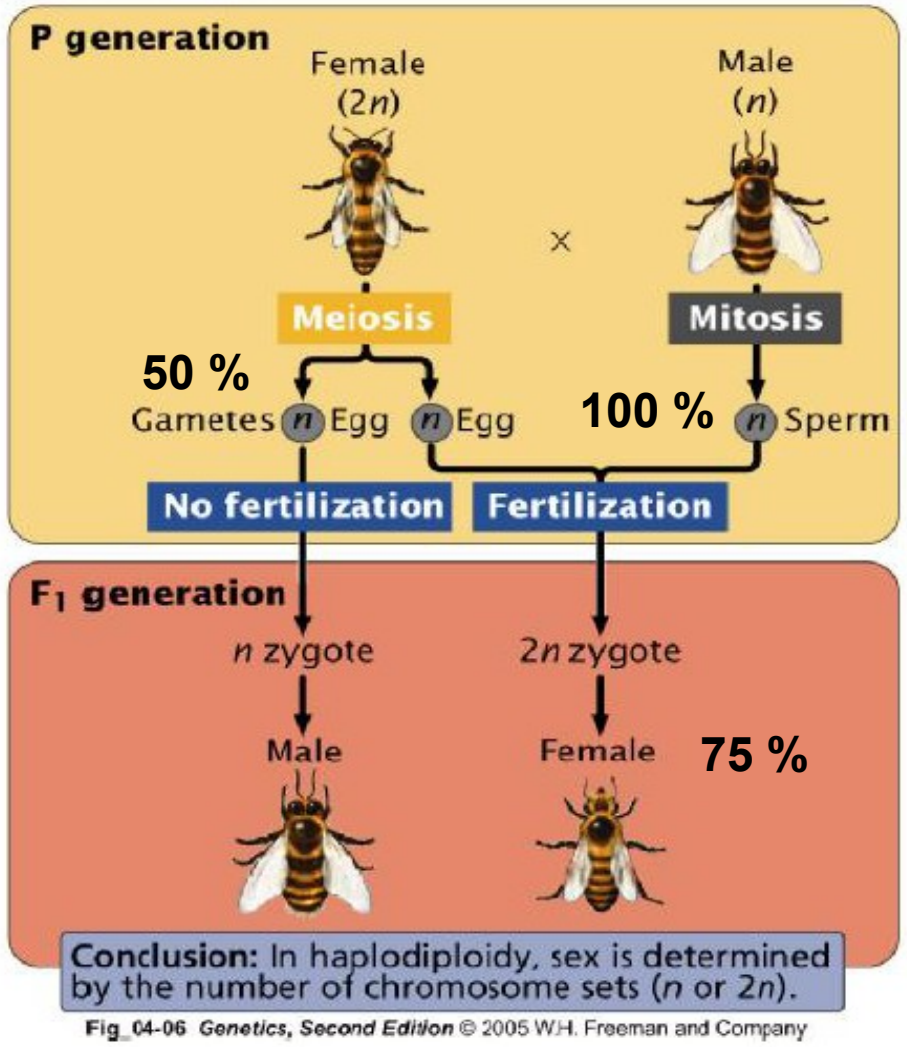
Sex ratio **1 : 1**

Females – 14 chromosomes

Males – 13 chromosomes

Chromosomal determination of sex: haplo - diplpoidy

- Females: **AA - diploid**
- Males: **A - haploid**
- Order *Hymenoptera* (bees, ants, wasps)
- **Bees**
  - **no sex chromosomes**
  - sex is determined by total number of chromosomes
  - Fertilized eggs **(2n)** produce **females**
  - Un-fertilized eggs (1n) - **parthenogenesis** = males
  - **Females** have on average **75 %** of common **genes** – higher **genetic affinity** – high level of social cooperation

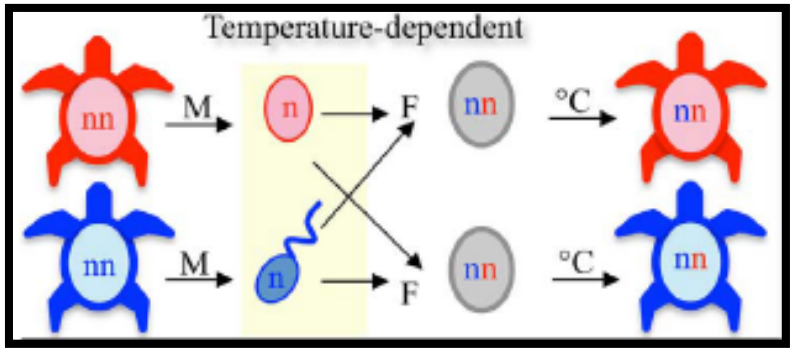


n=16, 2n=32

Environmental sex determination (ESD)

- Sex is determined by external factors f. e.

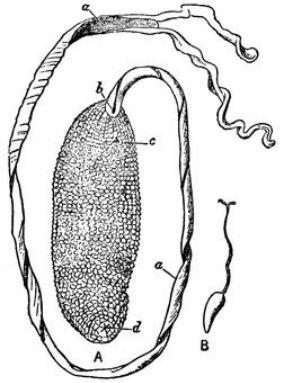
  a) Temperature (reptiles) - genetics (XX/XY or ZZ/ZW)+TSD (temperature dependent sex determination)



M. Crighton - **Jurassic park** (Spielberg movie 1993)

b) Social factors - *Bonellia viridis*

- If egg develops in **isolation** = **females**
- If **egg** migrates into the **tract** of female = **males**
- Males 1000x smaller than females



Genetic determination in humans

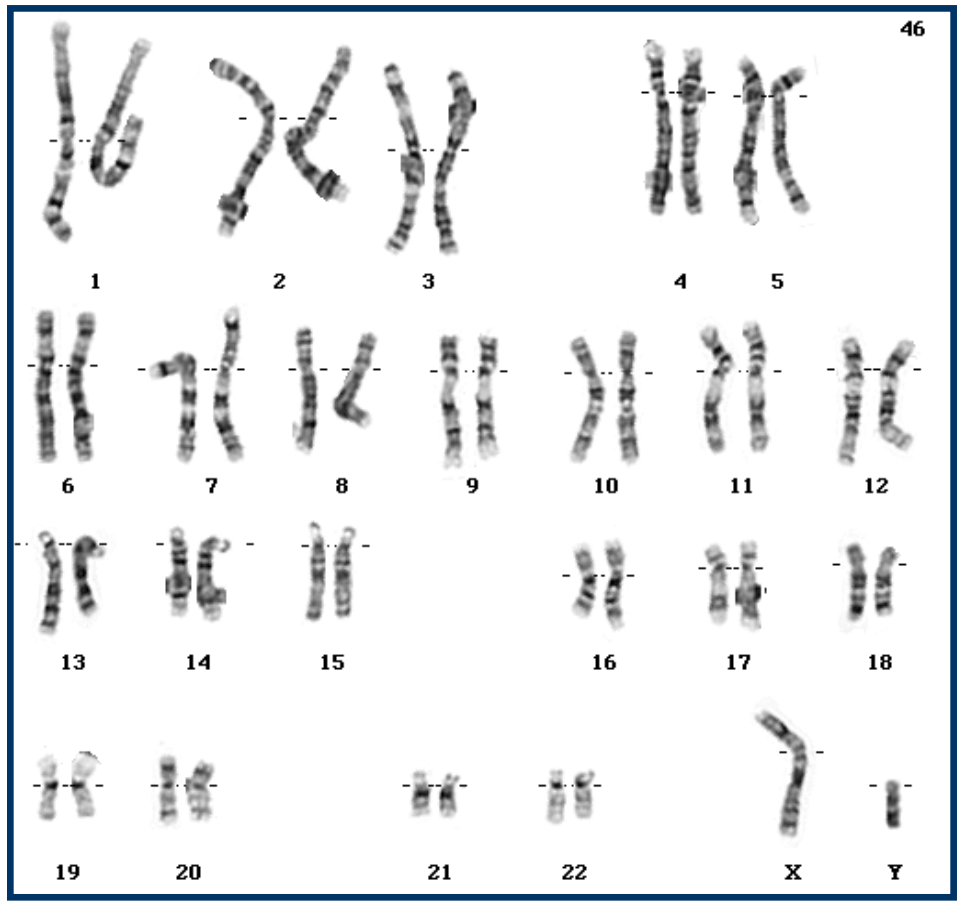
- **Presence** of different sex chromosomes and **product** of one specific gene ***SRY*** (sex-related region Y) determine the **phenotype** (sex) of the individual

- Expression of *SRY* activate the **cascade** of events leading to **development** of female or male **gonads (*master-switch sex determining gene*)**

Determination of sex in humans – significance of chromosome Y

Karyotype:

Male 46,XY Female 46,XX



X - 1669 genes

Y – 200 genes

(50-60 genes protein-coding)

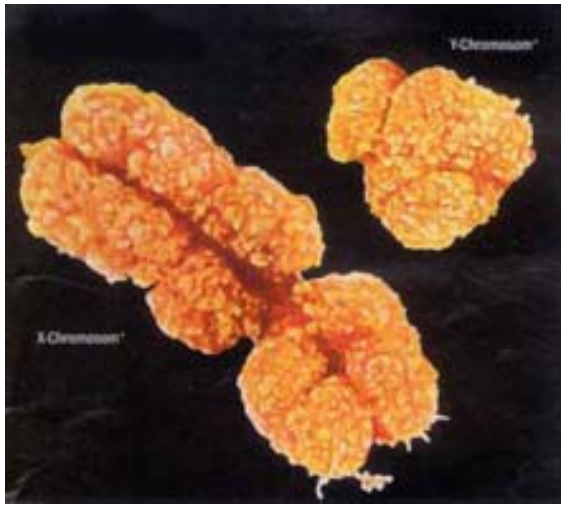
45,X – females

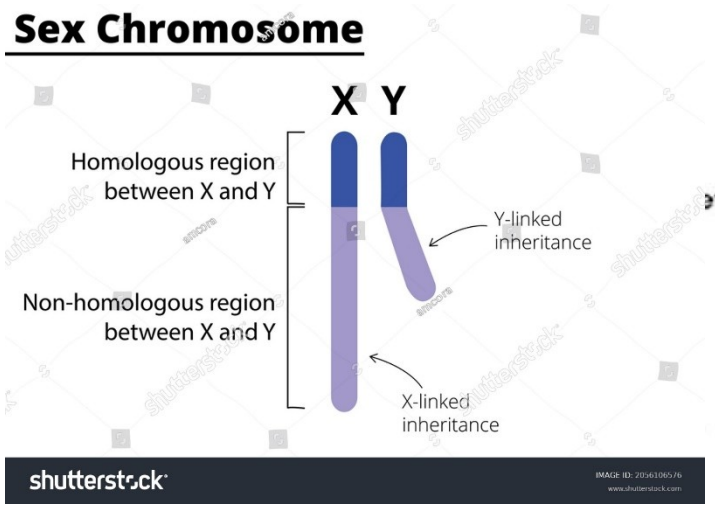
47,XXY- males

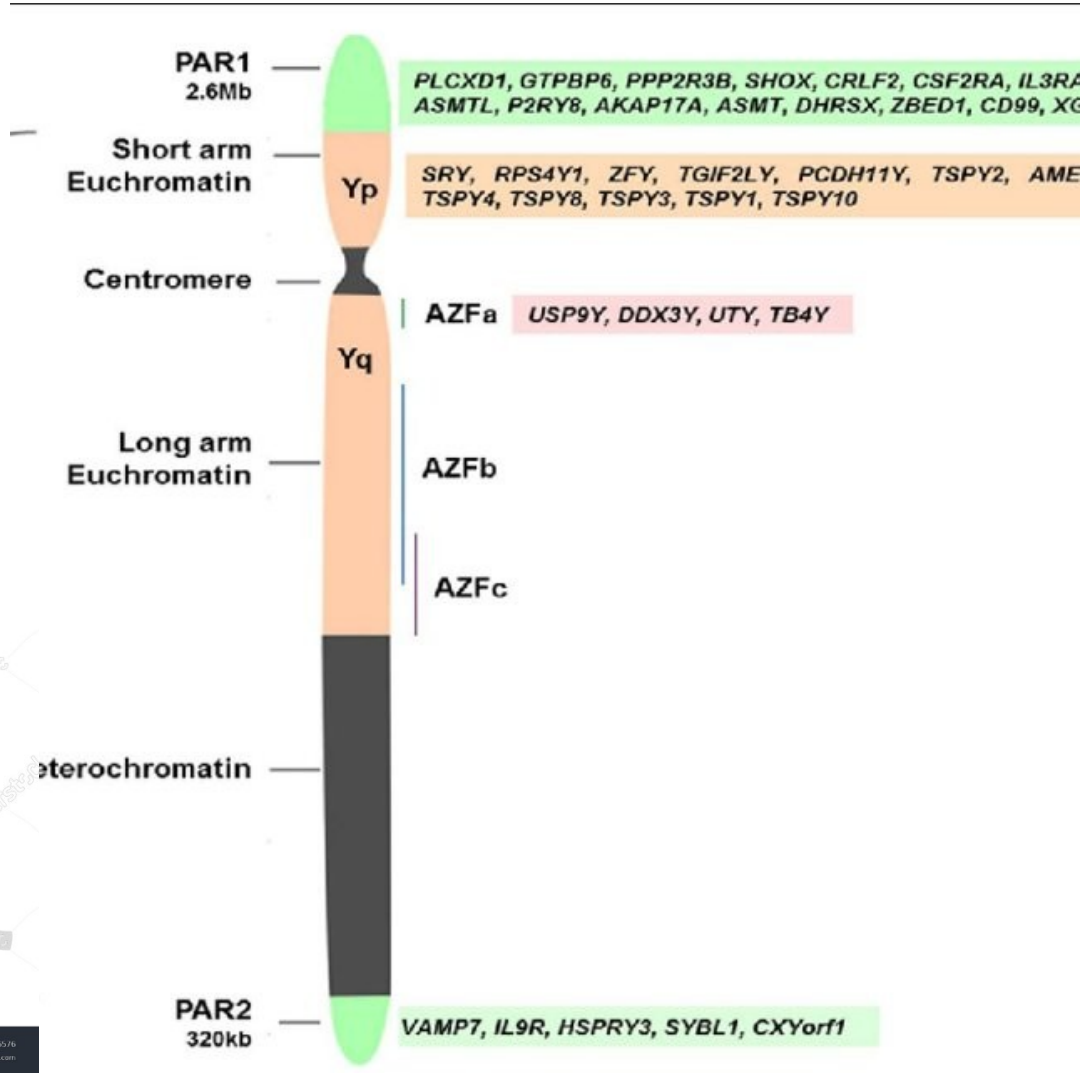
→ **Proof of chromosome Y is responsible for sex determination**

Genes located on chromosome Y

- Sex differentiation, sperm production
- 10-15% sequences comes from chromosome X
- Cca 60 millions of base pairs
- Spermatogenesis - genes encode 9 protein families in 2-35x copies







Development of sex in humans

- long-term process – start at 1st trimester
- activation of 37 proteins + sex hormones
- Ended after individual sexual maturation

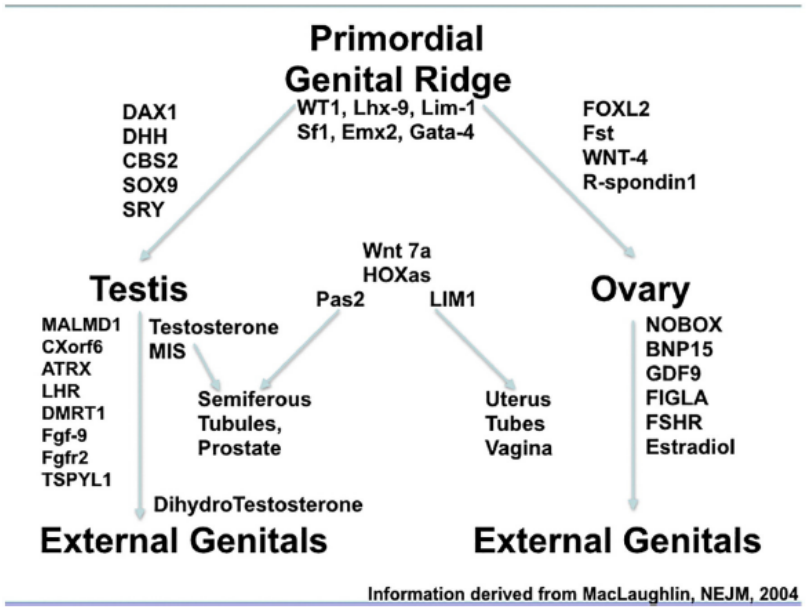
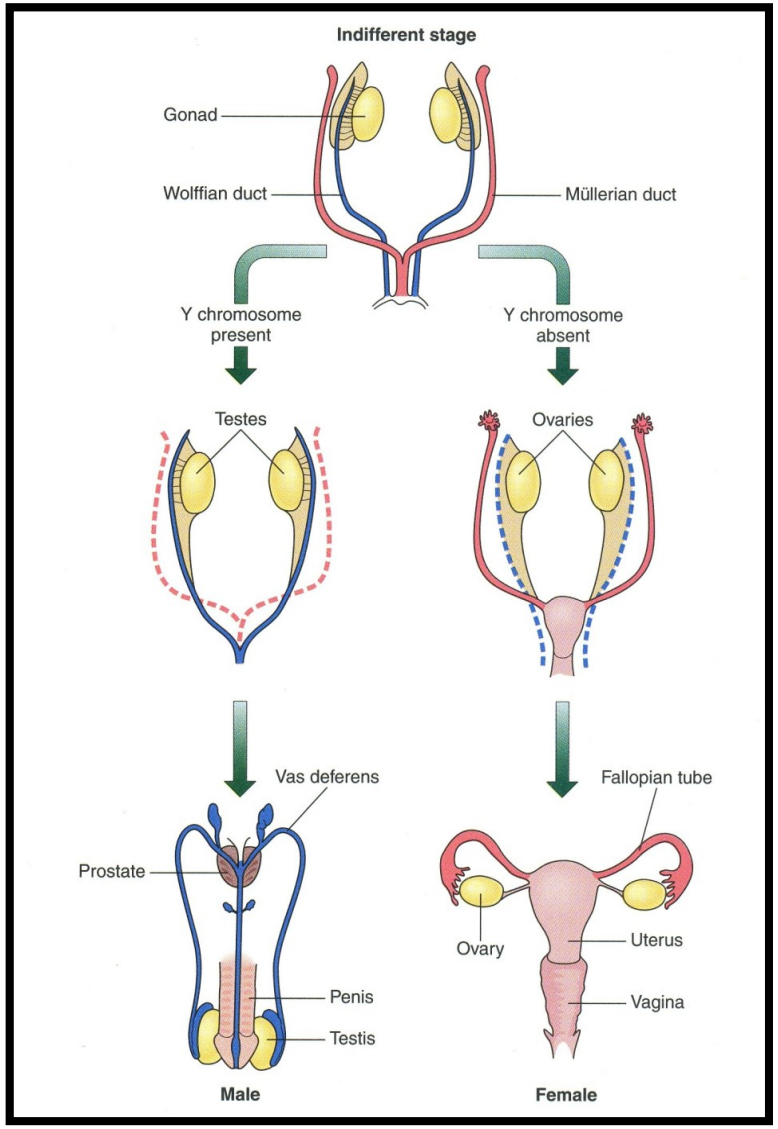
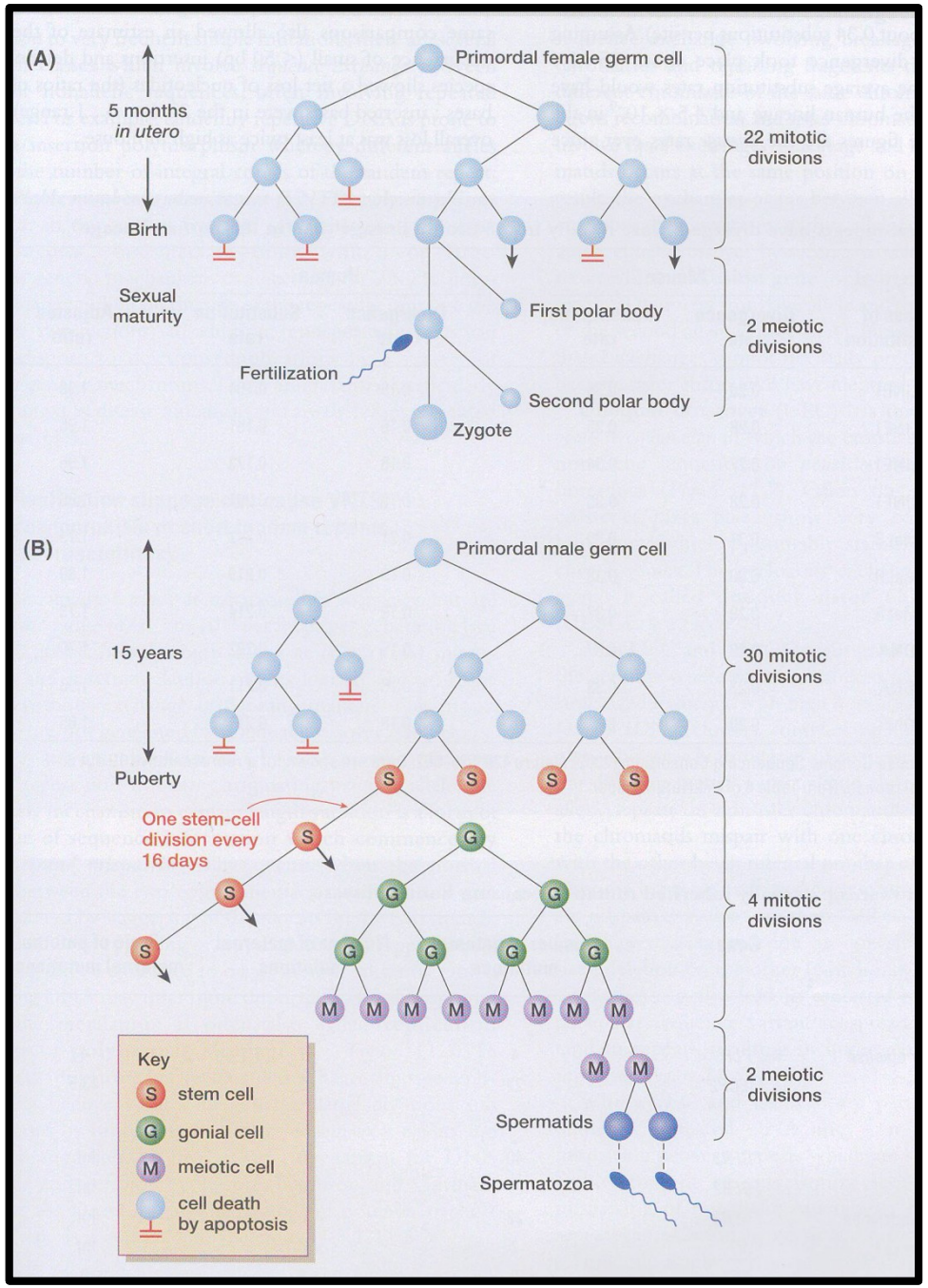


Fig. 1. Sex determination and gonadal differentiation require many proteins and endocrine stimulants to engender a fetus.[1] [1]MacLaughlin DT, Donahoe PK. Sex determination and differentiation. *N Engl J Med.* 2004;350 [4]:367–378.





Differences in development of gametes in humans

Women – 24 cell divisions

Men – 25 years

sperms – 265 divisions

Men - 50 years

sperms - 840 divisions !!!

Spermatogenesis - 64 days

DNA replication – *errors in the process - mutations in older men*

TABLE 8.1 Different classifications of biological sexual characteristics

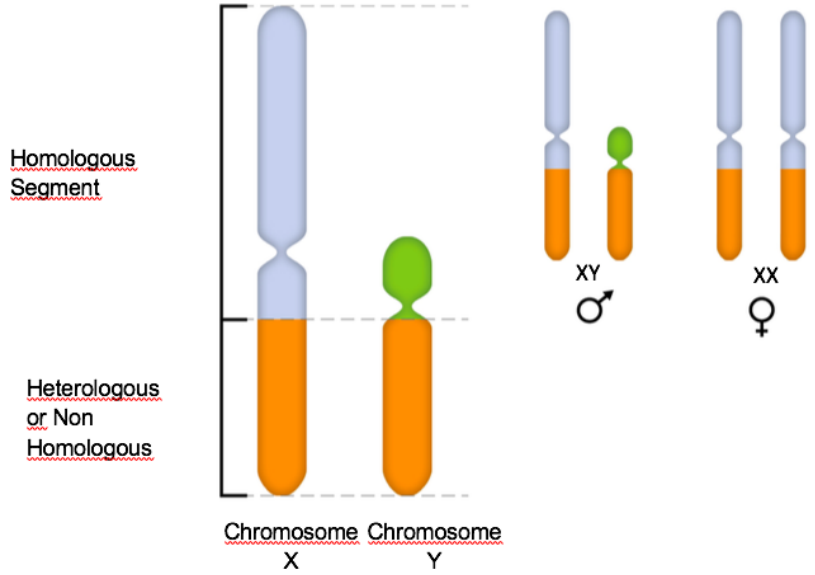
	Conventionally male	Conventionally female
GENETIC		
Karyotypic	XY	XX
Genotypic	SRY positive	SRY negative
GONADAL		
Gonadal	Testes	Ovaries
SOMATIC		
Primary somatic	Penis, scrotum	Vagina, cervix, uterus, fallopian tubes, clítoris
Secondary somatic	Face and body hair Narrower hip structure Greater upper body strength Ability to rapidly gain muscle mass	Breasts Little face and body hair Broader hip structure Less upper body strength Less ability to add muscle mass Increased body fat Menstrual cycle

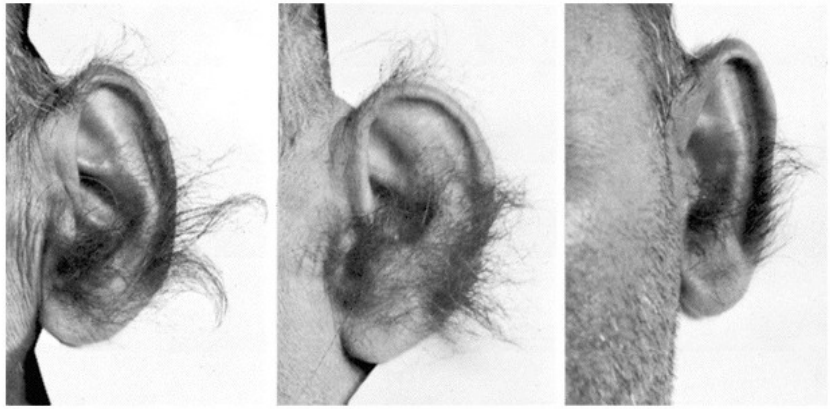
Heredity of sex-linked genes

Gonosomes (X,Y) are consisted of two regions carrying genes – **heterologous and homologous**

- **Non-homologous regions** - determine genes with full sex-linked inheritance
- **Homologous regions** **-** determine genes with incomplete sex-linked inheritance (= Mendel s laws)

  – Genes with loci of Y non-homologous regions determine **holandric traits** (father to son – Y-linked inheritance)
  – Genes with loci in non-homologous regions of X chromosome - **X-linked inheritance**

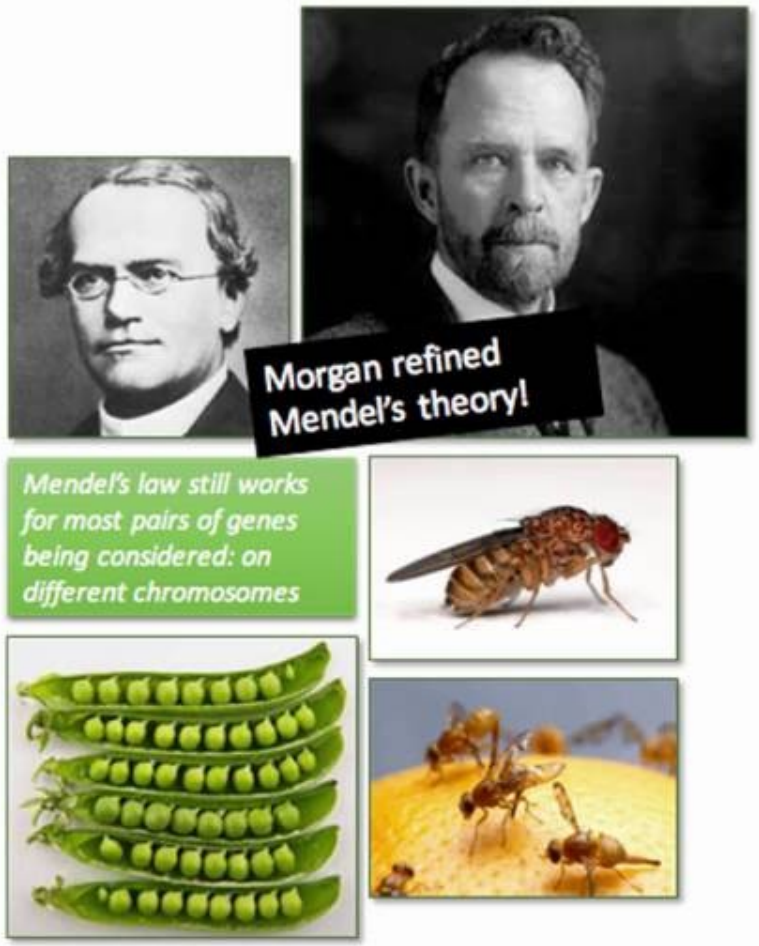




XY
↓
XY

Morgan's discovery of non-Mendelian ratios in *Drosophila*

- **Mendel** was the ***pea guy***
- Developed a theory to explain all his results → **law of independent assortment**
- New results from 20th century didn't fit his model
- Thomas Hunt Morgan developed the idea of *linked genes* to explain the anomalies investigating *Drosophila* flies
- Male and female flies showed different inheritance patterns → **sex linkage**



T.H. Morgan 1910

"Certain factors follow the distribution of the X chromosome and are therefore supposed to be **contained in them**."

Genes lie on chromosomes !!!

SEX LIMITED INHERITANCE IN DROSOPHILA

T. H. MORGAN

Woods Hole, Massachusetts

Sex-linkage heredity

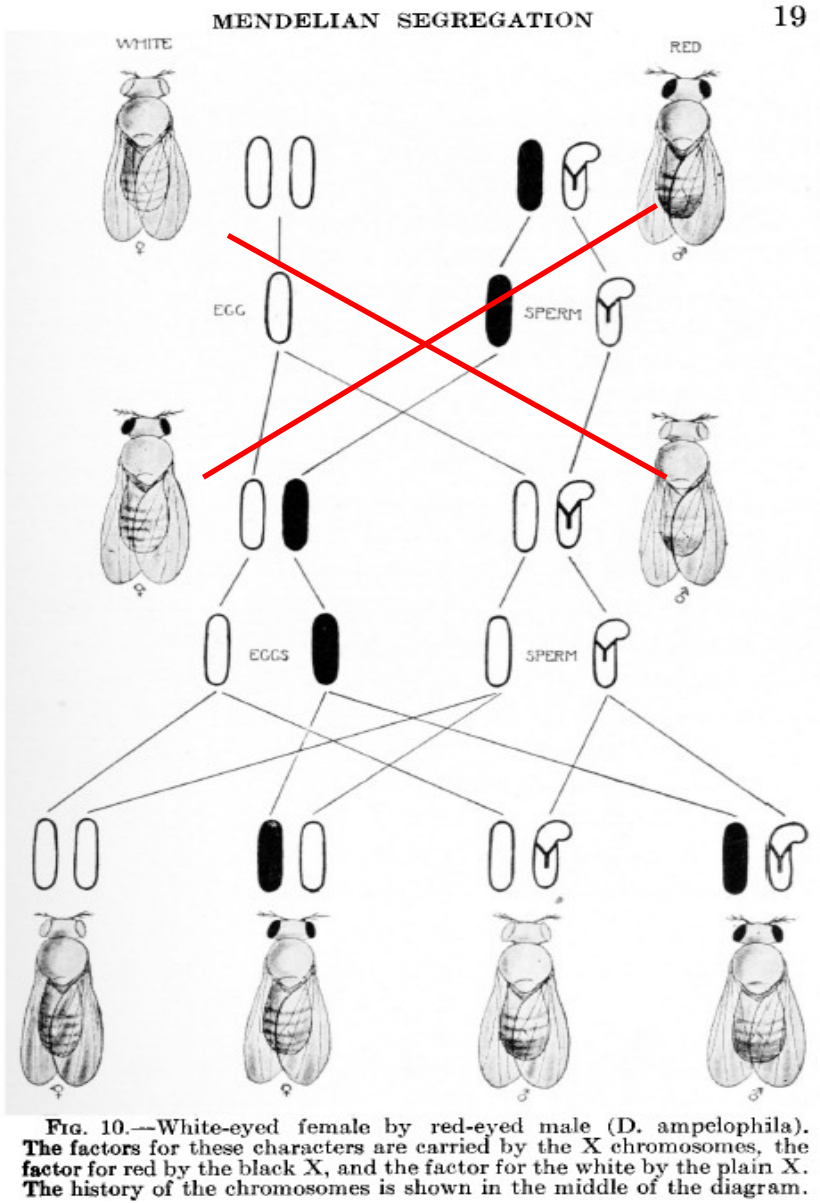
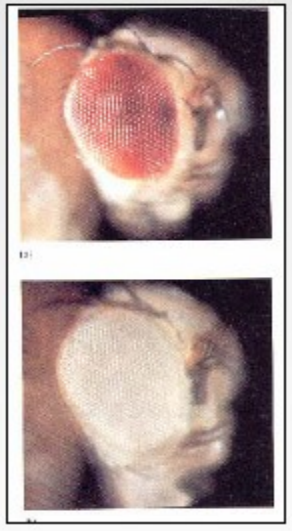
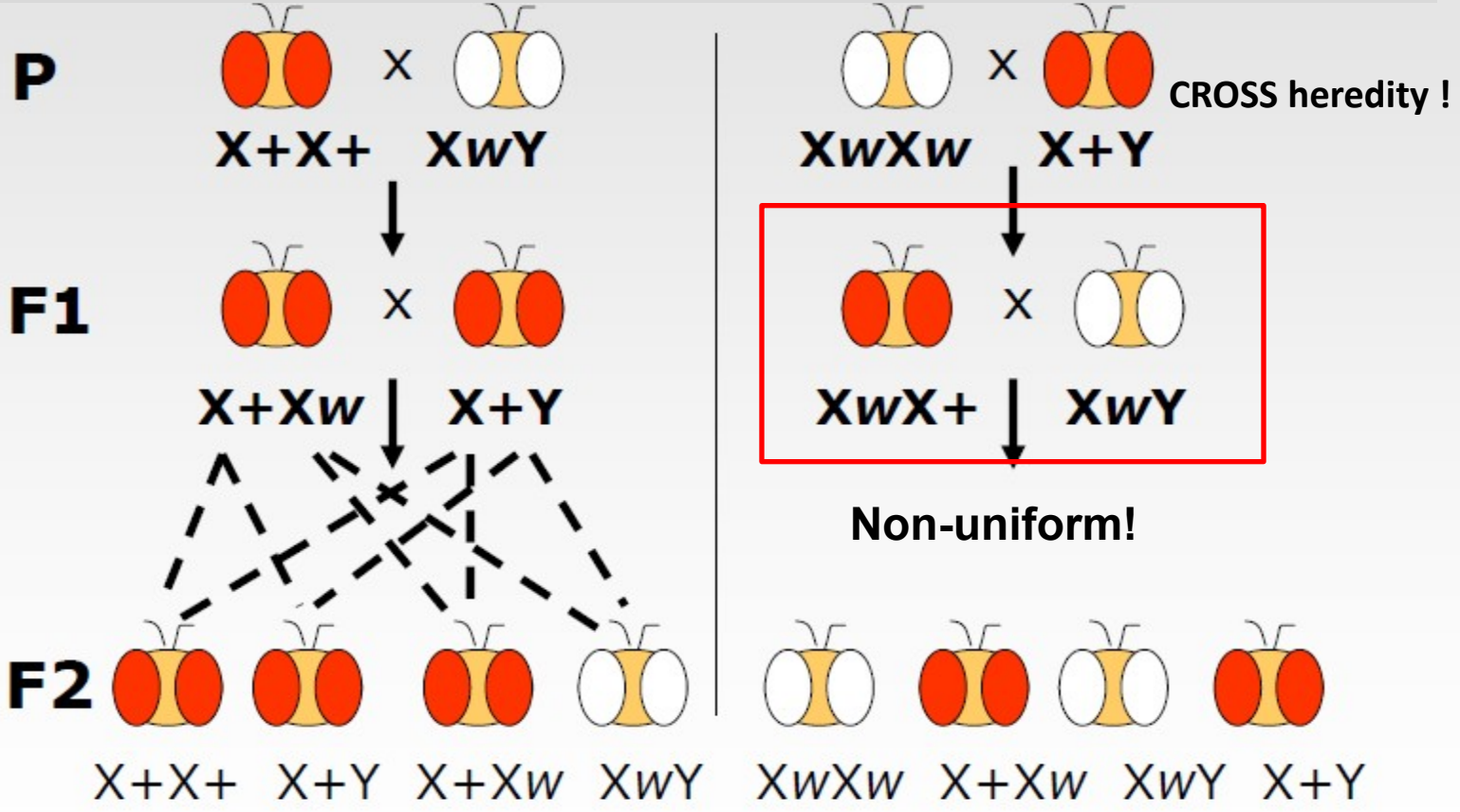


FIG. 10.—White-eyed female by red-eyed male (D. ampelophila). The factors for these characters are carried by the X chromosomes, the factor for red by the black X, and the factor for the white by the plain X. The history of the chromosomes is shown in the middle of the diagram.

Sex-linked heredity
D. melanogaster

Genes located on non-homologous region of chromosome Y





Mendel s law of uniformity of F1 hybrids and identity of reciprocal cross does not apply here !!!

Rules of sex-linked inheritance (Morgan 1910)

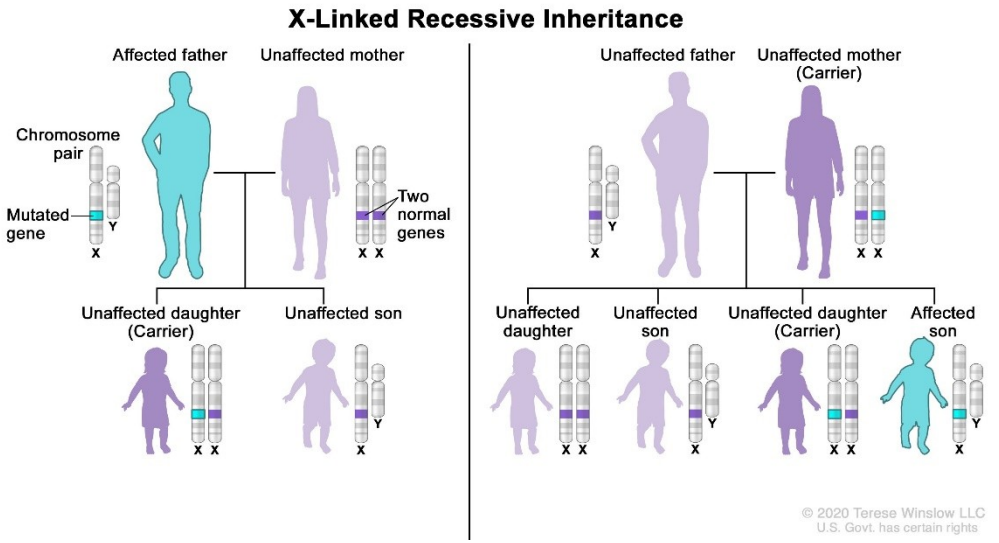
1. If an individual carry **dominant sex-linked trait (gene),** whole F1 population will show **same trait** as dominant parent regardless of sex. In F2 there will **be ratio 3:1** in this trait and individuals carrying recessive variant (allele) will be **same sex as recessive**

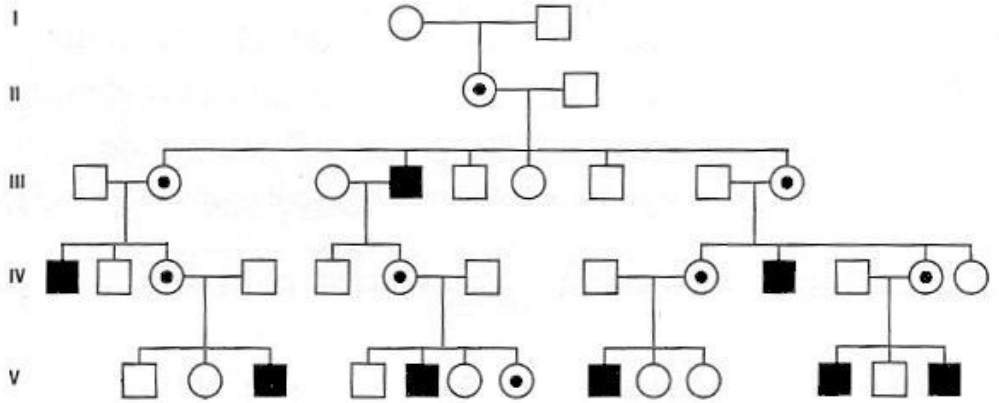
2. If individuals with **homogametic sex** carry **recessive sex-linked trait** (gene), there will be shown both dominant and recessive variants but in **opposite sex** than in parents. In F2 regeneration the both variants will manifest with **same frequency** in whole population and in population of given sex

X-linked recessive inheritance

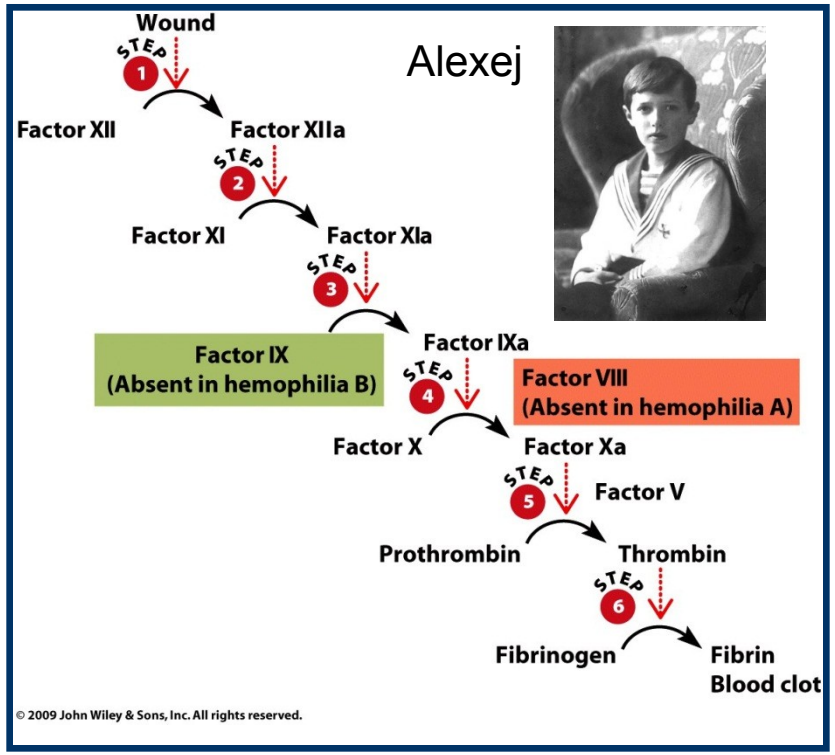
- Recessive allele in males – hemizygous (only one member of chromosome pair)
- Produce affected males in most times

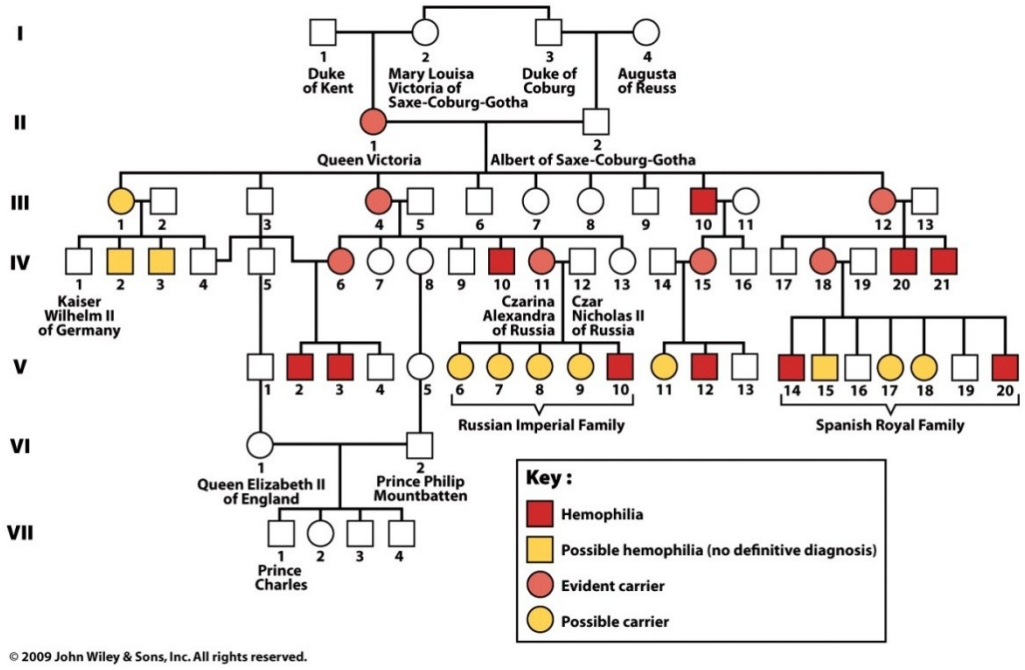
1) X^AX^A x X^aY (women healthy)
   - Healthy sons; daughters = carriers of the disease
- X^AX^a x X^AY (women carrier, man healthy)
   - ½ sons affected, ½ carriers
   - Rare cases in women: daughters of affected man + woman carrier; women with 45,X karyotype
- Examples: DMD, Hunter disease





Haemophilia: 1/10000 in men; 1/100 000 in women žen – pedigree of europeanm ruling houses





Porucha koagulace – deficit srážlivého faktoru v krvi !