Genetic Inheritance

وراثت ژنتیکی

مقدمه

- از قدیم الایام می دانستند که وراثت از هر دو والد است.
- ولی تصور بر این بود که این وراثت مثل مخلوط شدن مایعات است.
  - اما امروزه می دانیم که این روش مخلوط شدن نمی تواند برخی صفات را توضیح دهد (مثل یک اسب سیاه و یک اسب سفید باید اسبهای خاکستری تولید کنند ولی در عمل اینچنین نیست!)

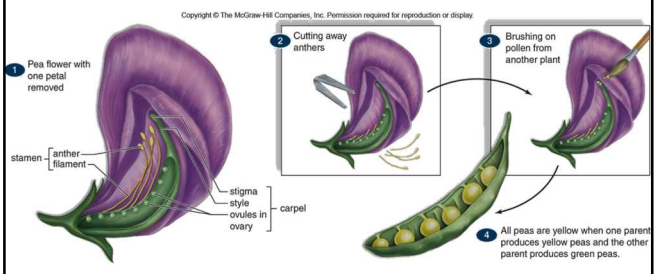
GREGOR MENDEL (گِرِگور مِندِل)

- Prior to Mendel's work (1860s) it was thought that off-spring represented an intermediate (i.e., equal mix) of the parental characteristics.
- Austrian monk **Gregor Mendel** developed the fundamental laws of heredity after performing a series of experiments with pea plants
- Math, physics, botany at University of Vienna

GREGOR MENDEL

- Studied *Pisum sativum*, garden pea plant (نخود فرنگی)
  - Self-fertilizes (خودگرده افشانی)– produces both male & female gametes
  - Can cross-fertilize (دِگرگرده افشانی)– done by plant breeders
- Observed that white-flowered parent plants produce white flowers
- Observed that when bred w/ different-colored plant, different traits emerged.

مندل آزمایشاتش را خوب طراحی کرد



Garden pea anatomy and the cross-pollination (دِگرگرده افشانی) **procedure Mendel used**

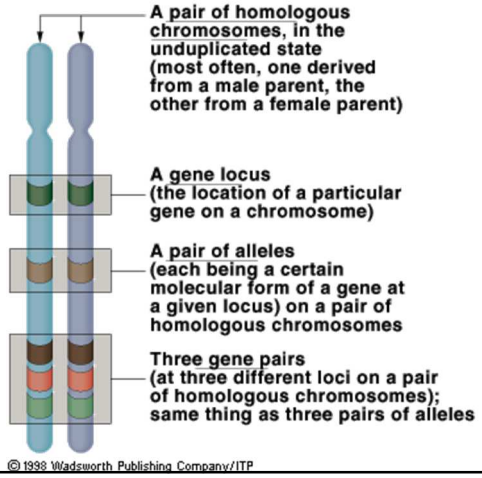
صفات نخودفرنگی
و آمیزش های (CROSSES) مطالعه شده توسط مندل

Trait	Characteristics				F_2 Results*	
	Dominant		Recessive		Dominant	Recessive
Stem length	Tall		Short		787	277
Pod shape	Inflated		Constricted		882	299
Seed shape	Round		Wrinkled		5,474	1,850
Seed color	Yellow		Green		6,022	2,001
Flower color	Purple		White		705	224
Pod color	Green		Yellow		428	152

*All of these results give an approximate 3:1 ratio of dominant to recessive. For example, $\frac{787}{277} = \frac{3}{1}$.

واژه ها

- Genes—sequence of DNA on a chromosome that gives information on inheritable traits *(i.e. hair color gene)*
- Allele—all forms of the same gene. Reside at the same location (locus) on homologous chromosomes. *(i.e. alleles for red, brown, blonde, and black hair)*
- Locus—location of a gene on a chromosome
- Hybrid—offspring of two "parents" who each breed true for different forms of a trait



واژه ها

- Homozygous—identical alleles on homologous chromosomes (AA, aa)
- Heterozygous—non-identical alleles on homologous chromosomes (Aa)
- Dominant allele—masks effect of recessive allele when paired
  - Capital letter for dominant ("A")
  - Lower-case letter for recessive ("a")

واژه ها

- **Homozygous-** an organism has two identical alleles at a gene locus
  - Homozygous dominant— **AA**
  - Homozygous recessive— **aa**
- **Heterozygous-** an organism has two different alleles at a gene locus
  - Heterozygous— **Aa**
- True-breeding parents— **P**
- First-generation offspring— $\mathbf{F_1}$
- Second-generation offspring— $\mathbf{F_2}$

- Genotype— particular alleles in an individual; genetic make-up
- Phenotype— Individual's observable traits (what they look like)

PEA PLANT (نخودفرنگی)

- Sperm in pollen grains, originate in stamen
- Carpel: female flower part, has eggs, fertilization, seed development
- Brush pollen onto carpel for artificial fertilization

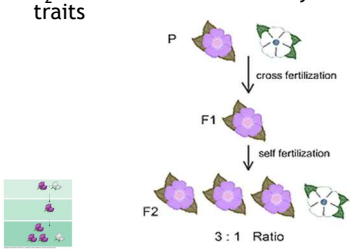
TEST CROSSES (آزمون های تلاقی) SUPPORT MENDEL'S LAWS AND INDICATE THE GENOTYPE

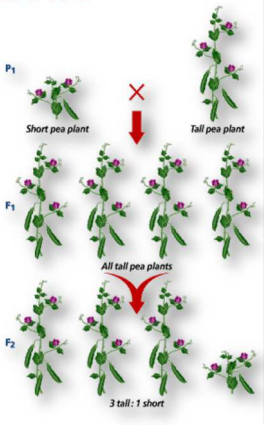
Testcross: intentional breeding (زادگیری تعمّدی) in order to determine underlying genotypes

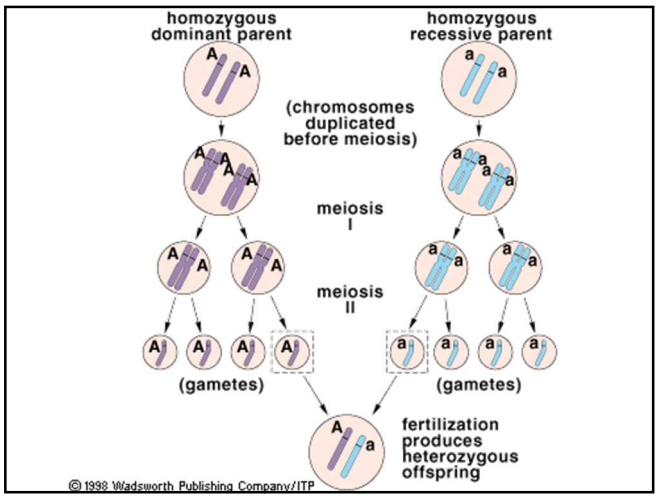
- **One-trait Testcross** - When a heterozygous individual is crossed with one that is homozygous recessive, the results are always a 1:1 phenotypic ratio

MONOHYBRID EXPERIMENTS

- Assume each P was homozygous
  - AA for one trait, aa for other trait
  - Breed true for a phenotype
- F_1 only show "A" trait, not "a" trait
- F_2 show 1 "a" trait for every 3 "A" traits

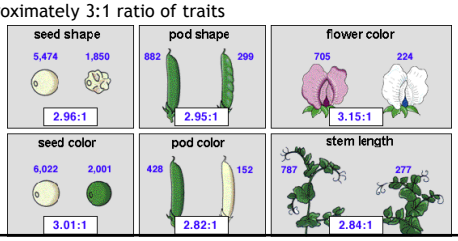






MONOHYBRID EXPERIMENTS

- Mendel tracked 7 observable traits on pea plants
  - Seed shape (round or wrinkled)
  - Seed color (yellow or green)
  - Pod shape (inflated or wrinkled)
  - Pod color (green or yellow)
  - Flower color (purple or white)
  - Flower position (on stem or at tip)
  - Stem length (tall or dwarf)
- Noted that F_1 had all same trait, some of F_2 had different trait
- Approximately 3:1 ratio of traits



MENDEL & CHROMOSOMES

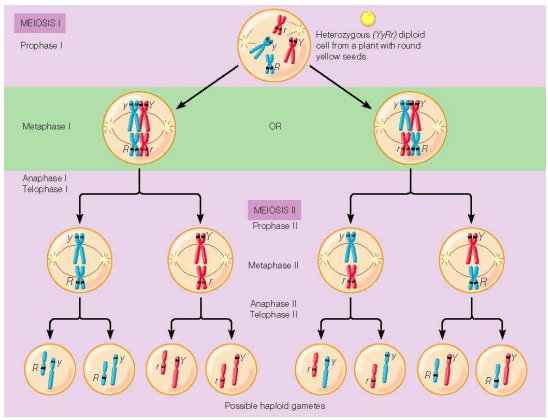
- Law of Segregation (قوانین تفرّق)
  - Each parent has two factors for each trait
  - The factors segregate (separate) during the formation of the gametes
  - Each gamete or egg contains only one factor (allele) from each pair of factors
  - Each homologous chromosome carries one allele. During meiosis, these chromosomes separate so that only one ends up in each gamete.
  - Fertilization gives each off-spring two factors for each trait

THE UNITS OF INHERITANCE ARE ALLELES OF GENES

Traits are controlled by **alleles** - alternate forms of a gene
- Found on homologous chromosomes at a particular **gene locus**

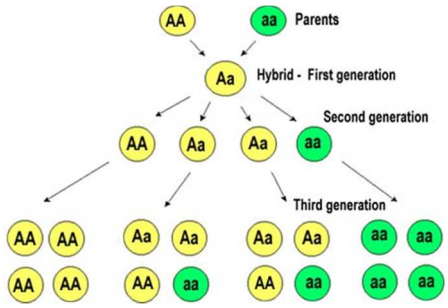
The **Dominant Allele (آلل غالب)** masks expression of the other allele:
- the **Recessive Allele (آلل مغلوب)**

MENDEL & CHROMOSOMES



MENDEL & CHROMOSOMES

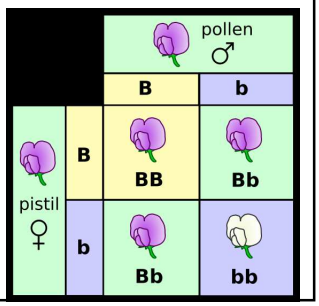
- ژنوتیپ غالب (A) مانع بروز فنوتیپ مغلوب (a) می شود



PUNNETT SQUARE (مربعات پونت)

- Monohybrid cross (تلاقی تک آمیزه، تلاقی تک دورگه): a single phenotype ("Mono" = 1)

	G	g
G	GG	Gg
g	Gg	gg



TEST CROSSES SUPPORT MENDEL'S LAWS AND INDICATE THE GENOTYPE

Test cross - intentional breeding in order to determine underlying genotypes

- **Two-trait Test cross** - when an individual is heterozygous for two traits is crossed with one that is recessive for the traits, the offspring have a 1:1:1:1 phenotypic ratio

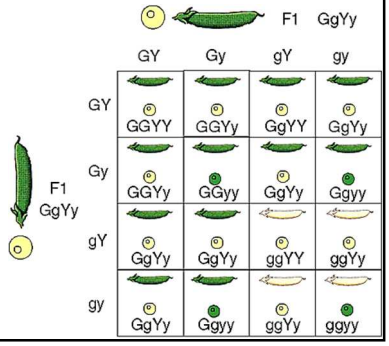
AaBb x aabb

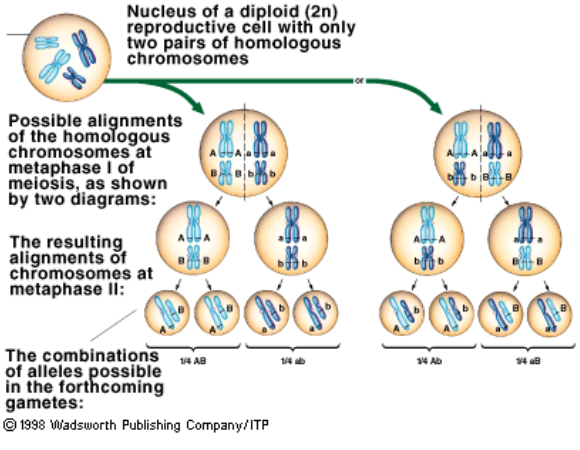
25% = AaBb
25% = aaBb
25% = Aabb
25% = aabb

PUNNETT SQUARE

- Dihybrid cross—two phenotypes ("Di" = 2)

	RT	Rt	rT	rt
RT	RRTT	RRTt	RrTT	RrTt
Rt	RRTt	RRtt	RrTt	Rrtt
rT	RrTT	RrTt	rrTT	rrTt
rt	RrTt	Rrtt	rrTt	rrtt





MENDEL & CHROMOSOMES

- Law of Independent Assortment
  - "Each pair of alleles segregates independently of other pairs of alleles during gamete formation."
  - The alleles for a given trait (on homologous chromosomes) separates during meiosis independently of other traits.
    - E.g. Hair color alleles will segretate during meiosis independently of eye color alleles

شجره نامه ها می تواند اُلگوهای توارثی را آشکار سازند

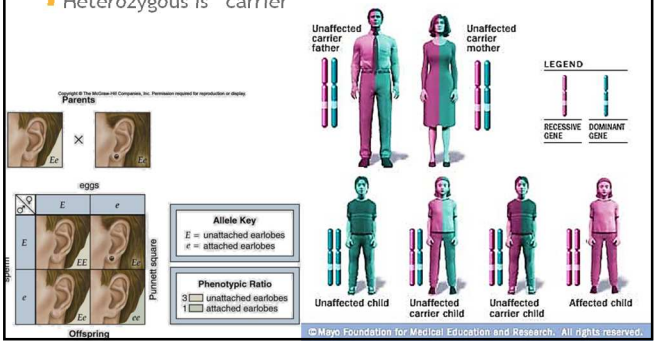
Some genetic disorders are medical conditions inherited from parents

Some may be due to the inheritance of abnormal alleles on **autosomal chromosomes** (all the chromosomes except the sex chromosomes)

- **Carriers (ناقل ها):** those individuals that carry the abnormal allele but do not express it

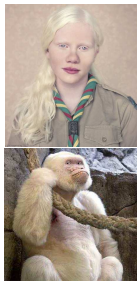
AUTOSOMAL INHERITANCE

- Autosomal Recessive
  - Recessive phenotype only shown with homozygous recessive
  - Heterozygous is "carrier"



AUTOSOMAL RECESSIVE

- Albinism (زالی)
  - Lack of normal amounts of melanin (pigment) in body
- Cystic fibrosis (فیبروز کیستیک)
  - Thick mucus in lungs & digestive tract
  - Breathing & digestion difficult
  - Most common lethal genetic disorder among Caucasians in U.S.
  - Genetic testing for the recessive allele is possible
- Tay-Sachs Disease - uncontrollable seizures, and paralysis prior to dying
  - در گروه بیماری‌های اختیاس **لیزوزوم (LSD)** قرارمی‌گیرد. یک بیماری اتوزومال است.افراد مبتلا به این بیماری دارای نقص ارثی در **هگزوزامیندار** اند. در اثر نقص این آنزیم، ماده **گانگلیوزید** (یک لیپوساکارید سرامیدی با حداقل یک واحد سیالیک) در نورون تجمع می‌یابد. بچه‌ای که مبتلا به این بیماری است در همان ماه‌های اول عمرش اختلالات سیستم عصبی را نشان می‌دهد. او طرفی کارکردهای فیلی را نیز ازدست‌می‌دهد.اشکالات به صورت کیست‌زده در قشر مغز، شبکیه چشم و نخاع دیده‌می‌شود. نورون‌های این افراد متورم و دفالوذ است. به علت تجمع و عدم متابولیزه ماده گانگلیوزید بیماران مبتلا به تای ساکس دارای لیزوزوم‌های نرکی هستند. این افراد معمولا در دوسالگی یا حداکثر سه سالگی از دنیا می‌روند.



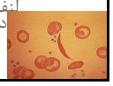
AUTOSOMAL RECESSIVE HUMAN GENETIC DISORDERS

Phenylketonuria - most commonly inherited metabolic disorder affecting nervous system
- Many diet products have warnings that they contain phenylalanine

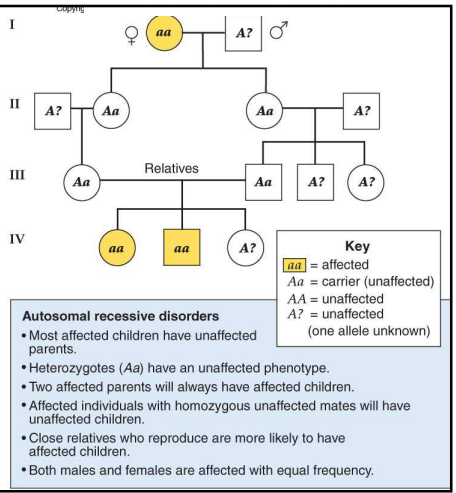
- **فنیل کتونوری**: تجمع اسید آمینه **فنیل آلانین** در مایعات بدن و سیستم عصبی است. تجمع این اسید آمینه به دلیل عدم وجود آنزیم **فنیل آلانین هیدروکسیلاز** برای تبدیل فنیل آلانین به **تیروزین** رخ می‌دهد. تجمع غیرطبیعی این اسید آمینه در بدن کودک، خطرناک است و منجر به بروز اختلالاتی در مغز و پوست می‌شود.

Sickle-cell Disease - genotype Hb^S Hb^S has many symptoms from anemia to heart failure
- Individuals who are Hb^A Hb^S have sickle-cell trait

- **کم‌خونی سلول داسی‌شکل**: یک اختلال خونی ارثی که باعث کم‌خونی، حملات درد شدید، کاهش مقاومت بدن نسبت به عفونت و وضعیت نامطلوب سلامت به‌طور مزمن می‌گردد. این بیماری سرطانی نیست. این اختلال مغز استخوان، غدد لنفاوی طحال، کبد و تیموس را درگیر می‌سازد، معمولاً حوالی ۶ ماهگی بارز شده در تمام طول زندگی تداوم می‌یابد.

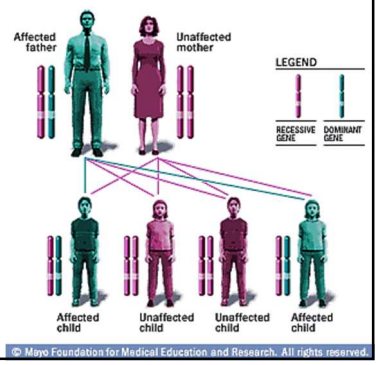


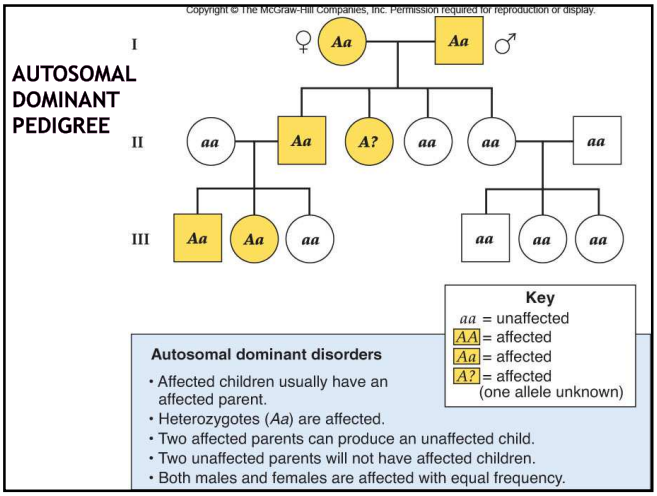
AUTOSOMAL RECESSIVE PEDIGREE



AUTOSOMAL INHERITANCE

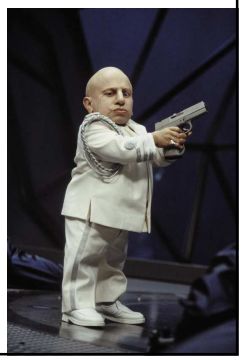
- Autosomal Dominant
  - Allele expressed in heterozygotes
  - AA or Aa show dominant phenotype





AUTOSOMAL DOMINANT

- **Achondroplasia**
  - Embryonic cartilage in skeleton doesn't develop properly (a defect in the growth of long bones)
  - "Dwarf", average 4' tall
- **Neurofibromatosis -**
  - many children with neurofibromatosis have learning disabilities and are hyperactive
- **Huntington's Disease**
  - a neurological disorder that leads to progressive degeneration of brain cells (Nervous system deteriorates)
  - Symptoms often not seen until after 30
  - Die in 40s or 50s

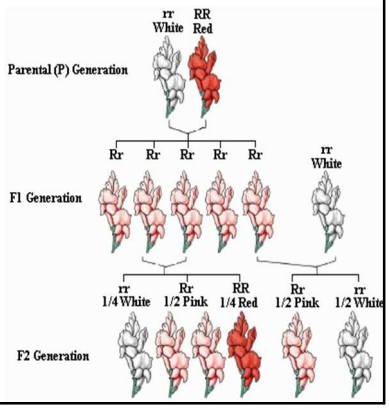


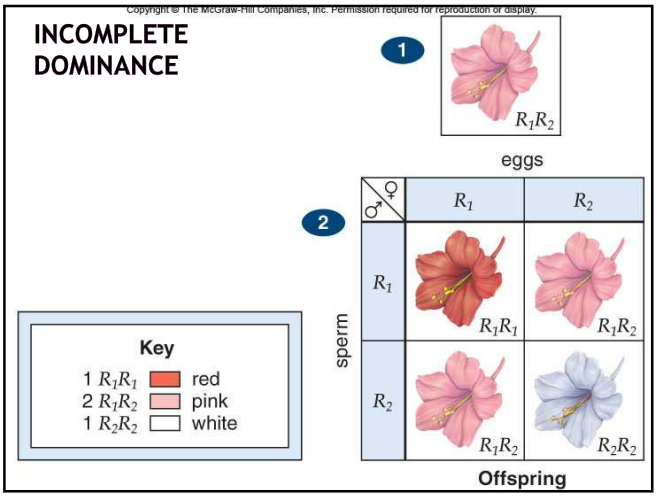
HUMAN GENETIC DEVELOPMENTS

- Phenotype treatments
  - Phenylketonuria (PKU)—lack of enzyme, can't convert certain amino acid, brain function problems
  - Restrict intake, can lead normal life
- Genetic screening
  - Detect alleles that can cause disorders
- Prenatal diagnosis
  - Amniocentesis—collect fluid from around fetus
  - Cells in fluid from fetus, can analyze for certain disorders

INCOMPLETE DOMINANCE

- Heterozygous phenotype between the two homozygotes
- One trait doesn't completely dominate the other
- Hybrid is a blend of the two phenotypes



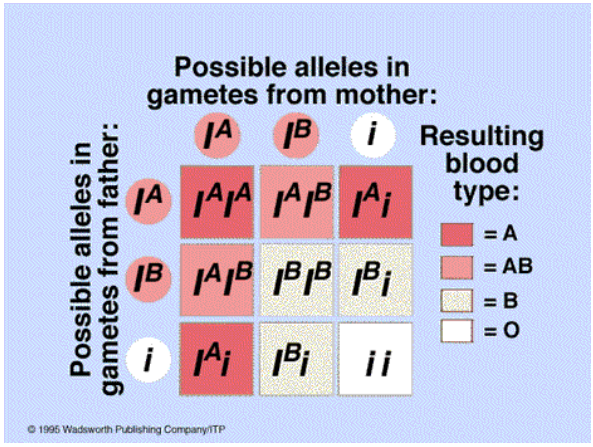


CODOMINANCE

- Nonidentical alleles expressed at same time
- Multiple allele system—3 or more alleles for a single gene locus
- Blood types

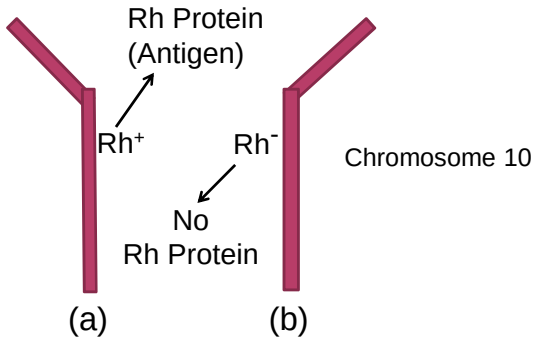
	I^A	I^B
i	I^Ai	I^Bi
i	I^Ai	I^Bi

Phenotype	Posible Genotypes
O	ii
A	I^AI^A, I^Ai
B	I^BI^B, I^Bi
AB	I^AI^B



Rh Factor – is a protein on surface of the red blood cell

Can be an antigen (i.e., cause the immune system to react.

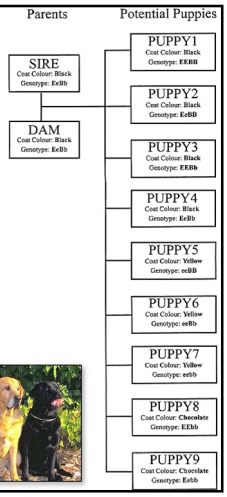


HEMOLYTIC DISEASE OF THE NEWBORN

1. Rh^+ father.
2. Rh^- mother carrying her first Rh^+ fetus. Rh antigens from the developing fetus can enter the mother's blood during delivery.
3. In response to the fetal Rh antigens, the mother will produce anti-Rh antibodies.
4. If the woman becomes pregnant with another Rh^+ fetus, her anti-Rh antibodies will cross the placenta and damage fetal red blood cells.

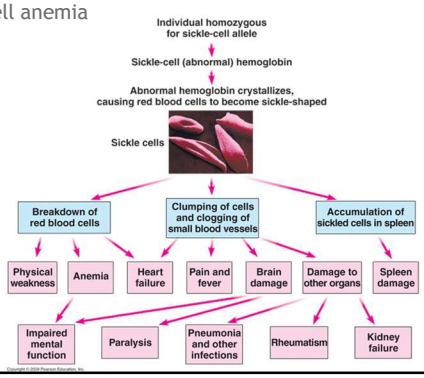
EPISTASIS

- Phenotype results from interaction among products of 2 or more gene pairs
- Labrador retriever colors
  - B (black) & b (brown)
  - EE or Ee—melanin (pigment) production. Black or brown
  - ee—no melanin produced. Always yellow!



PLEIOTROPY

- One gene may affect multiple systems or traits
  - Sickle-cell anemia



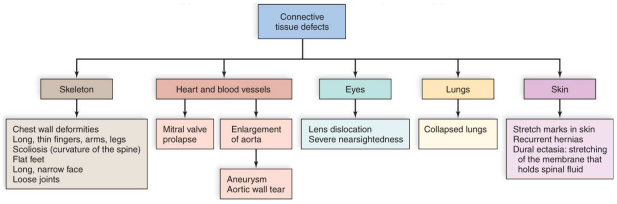
MARFAN SYNDROME ILLUSTRATES THE MULTIPLE EFFECTS A SINGLE HUMAN GENE CAN HAVE

Linked to mutation in FBN_1 Gene on chromosome 15

FBN_1 is gene for a protein called Fibrillin.

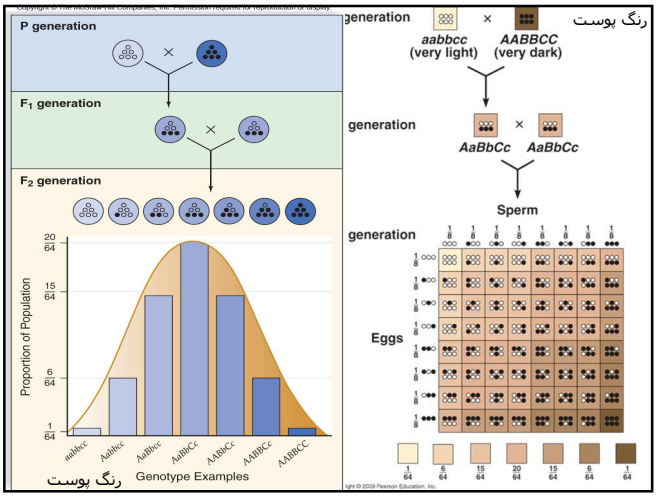
Protein that is essential for elastic fibers in connective tissue.

MARFAN SYNDROME ILLUSTRATES THE MULTIPLE EFFECTS A SINGLE HUMAN GENE CAN HAVE



COMPLEX VARIATION

- Continuous variation—range of small differences in a trait
  - Due to **polygenic inheritance**—inheritance of multiple genes that affect the same trait
  - In Humans: Eye, Skin, Hair color
  - Skin color—due to different kinds & amounts of melanin

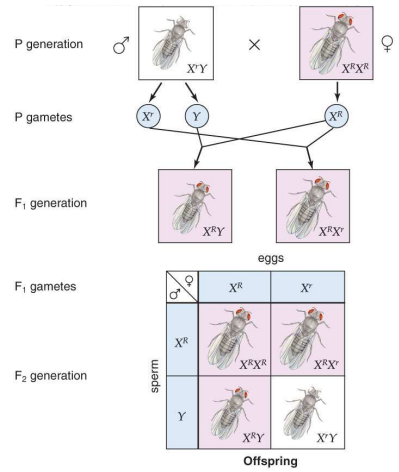


TRAITS TRANSMITTED VIA THE X CHROMOSOME HAVE A UNIQUE PATTERN OF INHERITANCE

X-linked alleles have a different pattern of inheritance than autosomal alleles

- The Y chromosome cannot offset the inheritance of an X-linked recessive allele

Affected males always receive their X-linked recessive mutant allele from the female parent



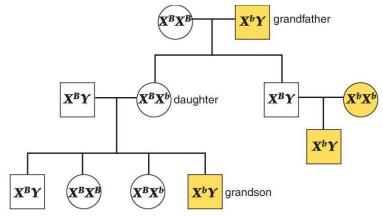
X-LINKED INHERITANCE

HUMANS HAVE X-LINKED DISORDERS

Color Blindness - the alleles for the red- and green-sensitive proteins are on the X chromosome

Muscular Dystrophy - occurs in males but the recessive allele remains in the population through passage from mother to daughter

Hemophilia - 1 in 10,000 males is affected by both external and internal bleeding



X-LINKED RECESSIVE PEDIGREE

Key
X^BX^B = Unaffected female
X^BX^b = Carrier female
X^bX^b = Color-blind female
X^BY = Unaffected male
X^bY = Color-blind male

X-linked Recessive Disorders
- More males than females are affected.
- An affected son can have parents who have the normal phenotype.
- For a female to have the characteristic, her father must also have it. Her mother must have it or be a carrier.
- The characteristic often skips a generation from the grandfather to the grandson.
- If a woman has the characteristic, all of her sons will have it.

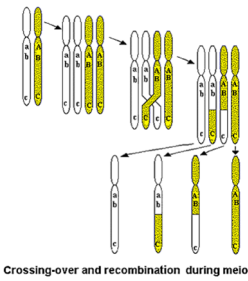
THE GENES ON ONE CHROMOSOME FORM A LINKAGE GROUP

Gene linkage (پیوستگی ژنی)- the existence of several genes on the same chromosome
- Genes on a single chromosome form a **linkage group** because they tend to be inherited together

- Sometimes linkage groups split, and entire linkage group is not transferred in the cross-over.
  - This is known as ***Incomplete Linkage***

CROSSING OVER (کراسینگ اُور)

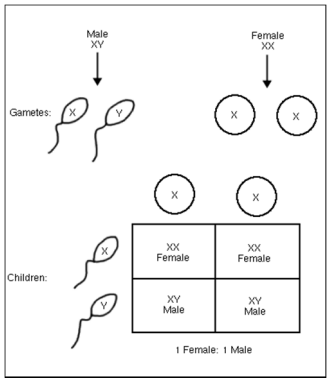
- Responsible for genetic variation
- Can result in nonparental combinations
- The closer the genes on a chromosome, the more likely to stay together
  - Linked genes



Crossing-over and recombination during meiosis

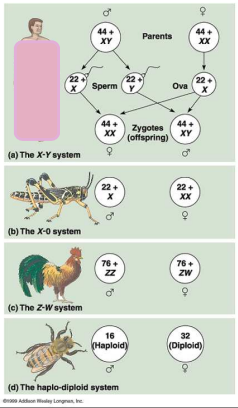
SEX DETERMINATION (تعیین جنسیت)

- Humans
  - XX = Female
  - XY = Male



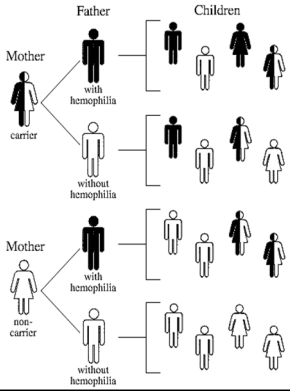
SEX DETERMINATION (تعیین جنسیت)

- گونه های مختلف، سیستم های مختلفی دارند
- X-Y
  - XX = Female, XY = Male
  - انسان
- X-O
  - XX = Female, X = Male
  - ملخ، سوسک، بسیاری از حشرات
- Z-W
  - ZW = Female, ZZ = Male
  - ماهی، پروانه، پرنده
- Haplo-Diploid
  - 2n = Female, n = Male
  - مورچه، زنبور



X-LINKED INHERITANCE

- Recessive, found on X chromosome
- Only present if X^AY or X^AX^A, Not X^AX
- Baldness
- Red-Green Color Blindness
- Hemophilia A
  - Lack of certain clotting factors
  - Blood cannot clot, bleed uncontrollably



X-LINKED INHERITANCE

X^B = Bald, recessive trait

X, Y = Non-bald, dominant trait

	X^B	Y
X	XX^B	XY
X	XX^B	XY

	X^B	Y
X^B	X^BX^B	X^BY
X	XX^B	XY

	X	Y
X^B	XX^B	X^BY
X	XX	XY

X^BX^B = bald woman
XX^B = carrier woman
XX = normal woman
X^BY = bald man
XY = normal man