46%

بسم الله الرحمن الرحيم

DOPAMINE SCIENTIFIC TEAM

Trophoblastic diseases

FINAL | Lecture 4

﴿قُلْ بِفَضْلِ ٱللَّهِ وَبِرَحْمَتِهِۦ فَبِذَٰلِكَ فَلْيَفْرَحُوا۟ هُوَ خَيْرٌ مِّمَّا يَجْمَعُونَ﴾

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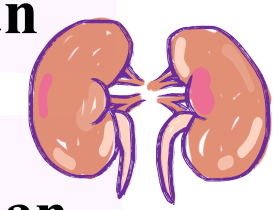

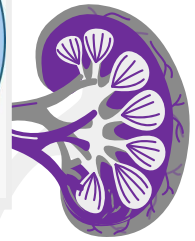

Trophoblastic diseases

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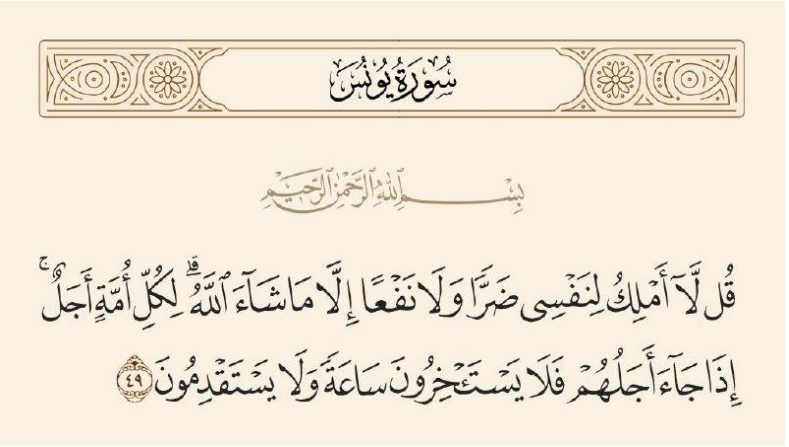

سُورَةُ يُونُسَ

بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ

قُل لَّآ أَمۡلِكُ لِنَفۡسِي ضَرّٗا وَلَا نَفۡعًا إِلَّا مَا شَآءَ ٱللَّهُۚ لِكُلِّ أُمَّةٍ أَجَلٌۚ
إِذَا جَآءَ أَجَلُهُمۡ فَلَا يَسۡتَـٔۡخِرُونَ سَاعَةٗ وَلَا يَسۡتَقۡدِمُونَ ٤٩

Trophoblastic diseases

• A group of rare diseases that involve **abnormal growth of cells inside a woman's uterus.**
• They develop from **trophoblasts** (the cells that would normally form the placenta during pregnancy).
• During early embryo development, trophoblasts form tiny projections called "chorionic villi". In time, these will develop into **placenta** that will protect and nourishes the growing fetus.
• Trophoblastic diseases consist of several types; they can be **benign or malignant.**

- **Trophoblast** = outer layer of blastocyst cells present about **4 days after fertilization**.
- Function:
  provides nutrients to embryo
  Forms a large part of the placenta

Types of trophoblastic diseases

- Hydatidiform mole
- Invasive mole
- Choriocarcinoma
- Placental- site trophoblastic tumor
- Epithelioid trophoblastic tumor

In this lecture we will only discuss the Hydatidiform mole and Choriocarcinoma

Trophoblastic ??

- Trophoblast: is the outer layer of cells of the blastocyst, are present four days after fertilization in humans.
- Trophoblasts provide nutrients to the embryo and develop into a large part of the placenta.
- They may be involved in different types of disorders
- Today we will be discussing 2 types of trophoblastic diseases:

1 **Hydatidiform Mole (**Molar pregnancy)

2 **Gestational Choriocarcinoma**

Hydatidiform Mole

- 2 forms of abnormal gestational processes, result from **abnormal fertilization**:
- 2 types:
- **complete mole:** an empty egg is fertilized by two spermatozoa (or a diploid sperm), yielding a **diploid** karyotype composed of entirely paternal genes
- **partial mole:** a normal egg is fertilized by two spermatozoa (or a diploid sperm), resulting in a **triploid** karyotype with a predominance of paternal genes

To understand each type check the next slide first

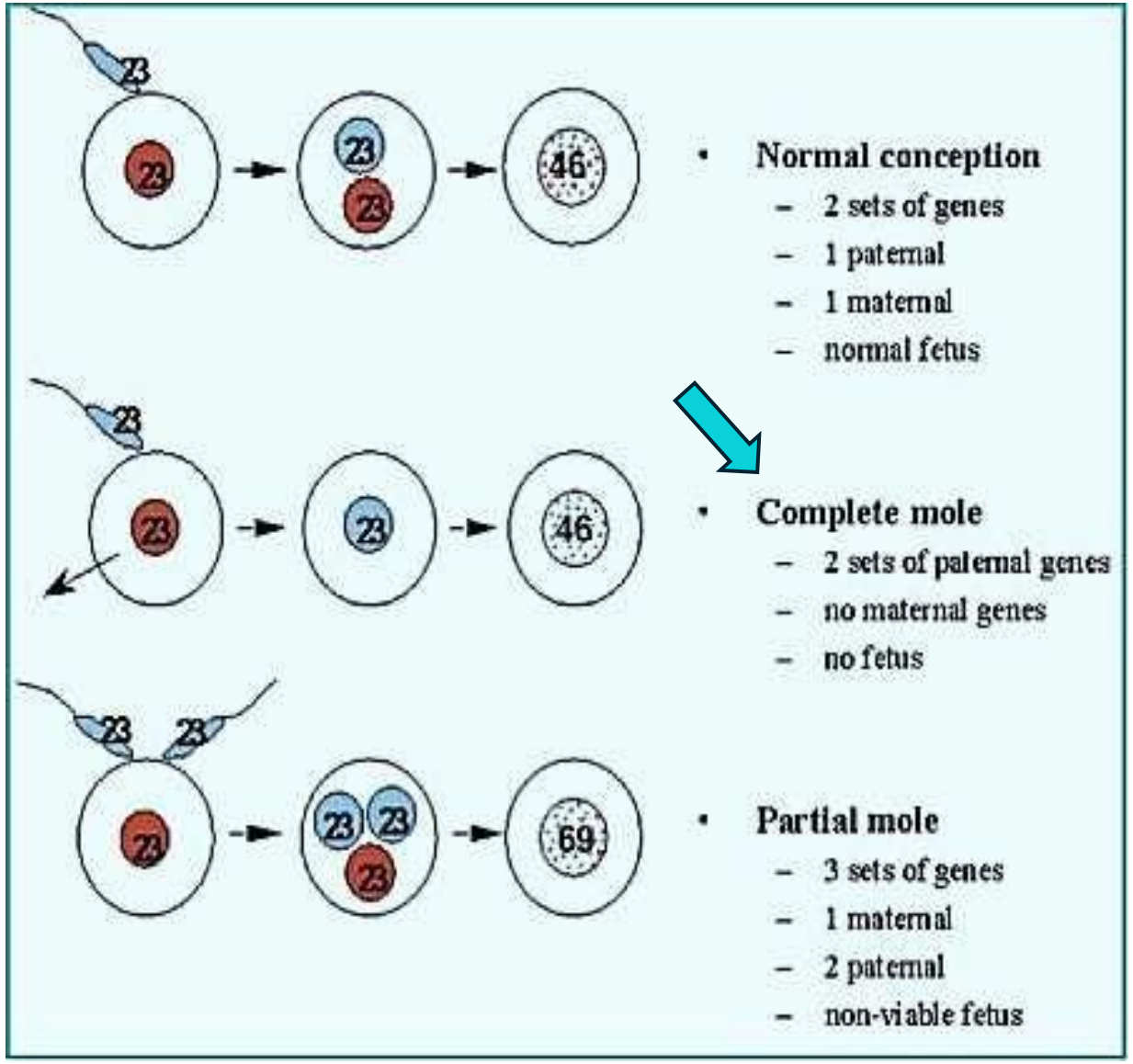
Normal Fertilization :

In normal gestation, a single haploid sperm (23 chromosomes) fertilizes a single haploid ovum (23 chromosomes). This results in a diploid zygote with a total of 46 chromosomes—23 of paternal origin and 23 of maternal origin.

Abnormal Fertilization:

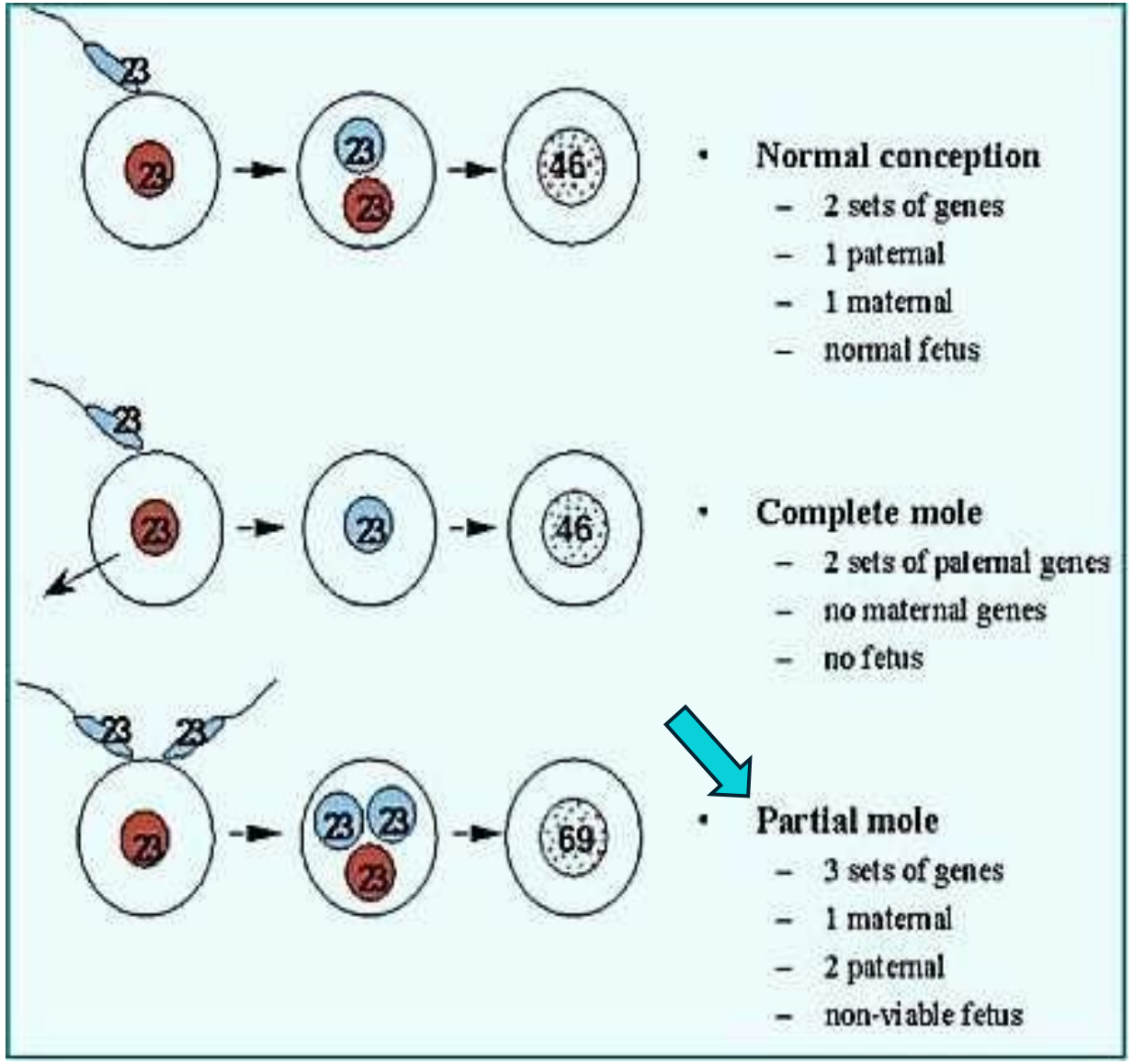
1- Complete Hydatidiform Mole:

In the case of a complete mole, a haploid sperm fertilizes an **empty ovum** that lacks maternal DNA (contains zero chromosomes=NO DNA material). Following fertilization, the paternal chromosomes (23) undergo duplication, resulting in a diploid set of 46 chromosomes, all of **paternal origin** , no maternal genes at all . As a result**, no fetus will develop.**



2- Partial Hydatidiform Mole:

In a partial mole, **two** haploid sperms(each contain 23 chromosomes) fertilize a single normal haploid ovum 23 chromosomes (dispermic fertilization). This results in a **triploid zygote** containing three sets of chromosomes—two paternal and one maternal—for a total of 69 chromosomes which is not normal in human being (the normal human being have 46 chromosomes) . This chromosomal abnormality leads to the development of a non-viable fetus that does not continue to develop.



· From a genetic perspective, the possible karyotypes in a **complete** hydatidiform mole include the following:

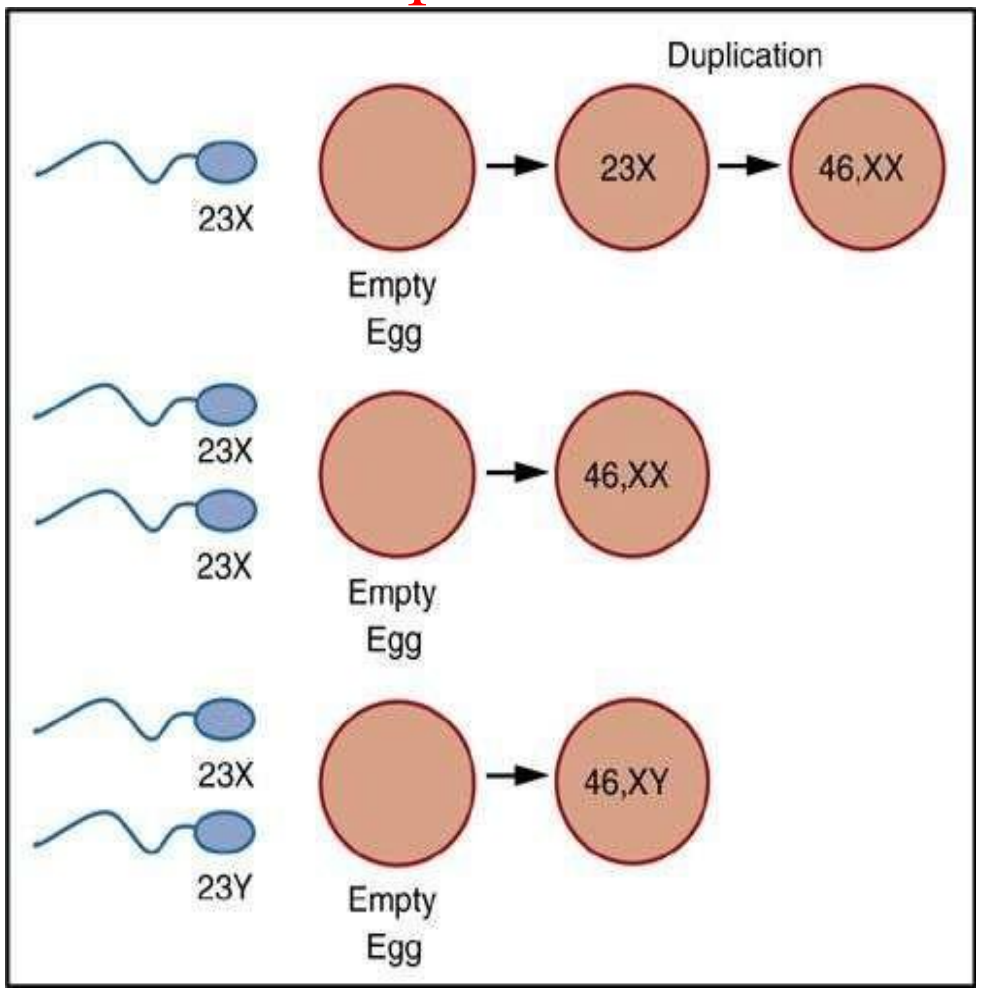
· An empty egg is fertilized by a single haploid sperm, which subsequently **duplicates** its genetic material, resulting in a **46**, composed entirely of **paternal** chromosomes. In the example shown in the image, the sperm carried 23,X and after duplication, it became 46,XX.

· An empty egg is fertilized by two sperms —either one carrying 23,X and the other 23,Y, resulting in a 46,XY karyotype, or both carrying 23,X, resulting in a 46,XX karyotype. In both cases, all genetic material is of **paternal origin.**

- There is no YY type , because Y chromosome is so small and can't generate a small tissue .
- karyotype is an individual's complete, organized set of chromosomes, typically arranged by size, number, and shape in a laboratory-produced image (karyogram).

For further explanation do your own search .

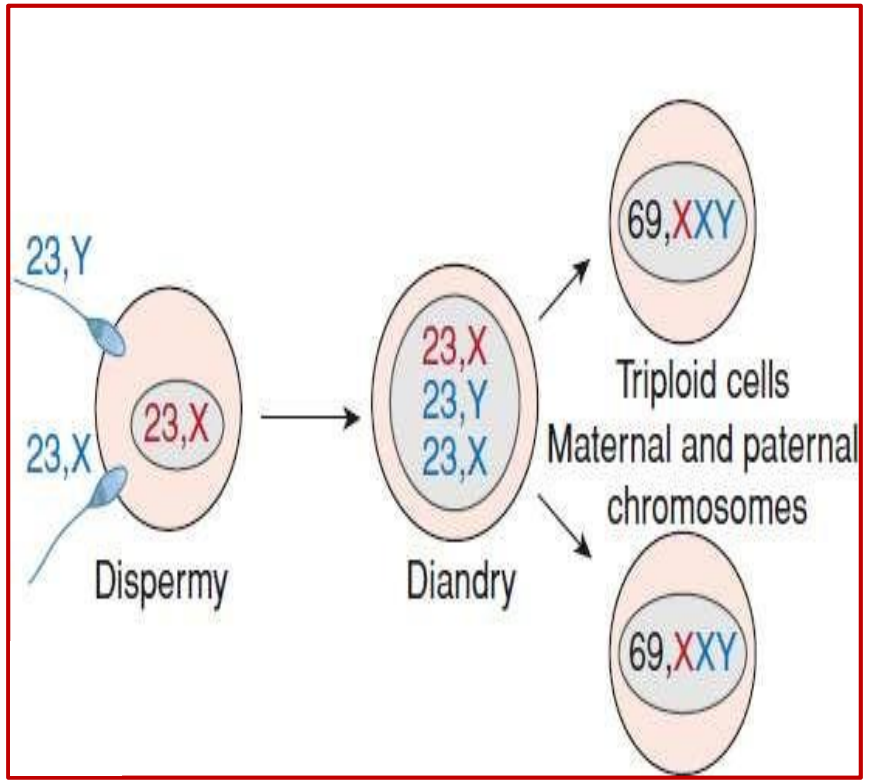
Complete mole



· In the case of a **partial** hydatidiform mole, two haploid sperms fertilize a single normal haploid ovum, resulting in a triploid zygote. The possible karyotypes include:

- 69,XXX
- 69,XXY
- 69,XYY

Partial mole

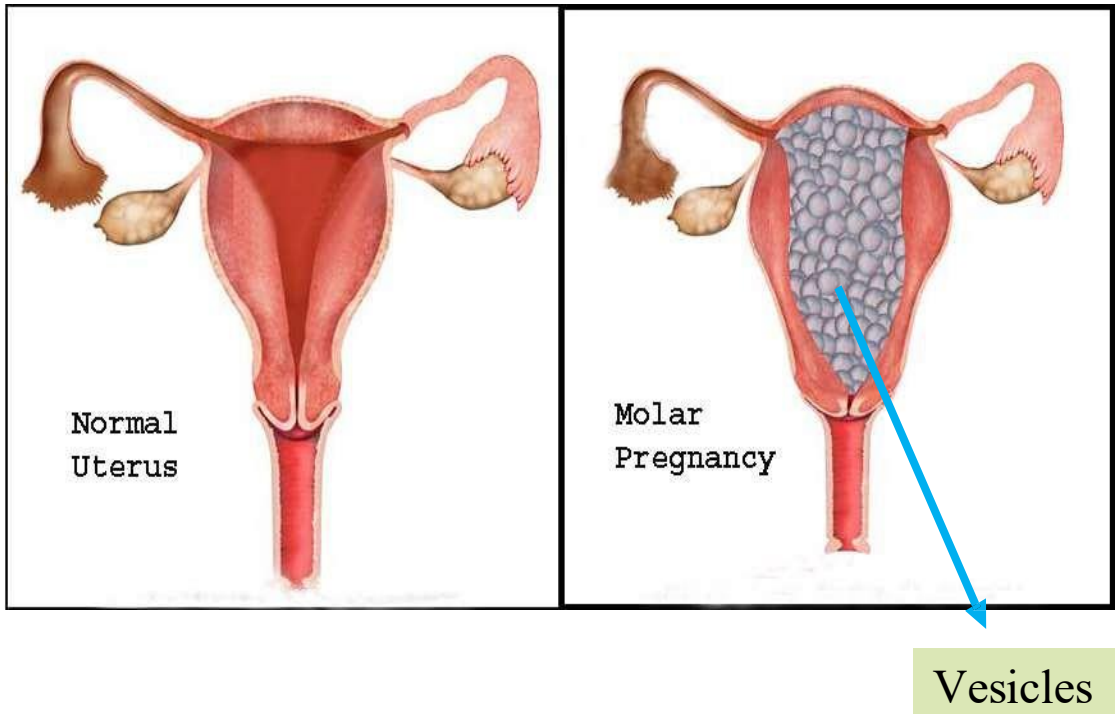


- ***complete*** **hydatidiform mole→** does not permit embryogenesis = never contains fetal parts, and the chorionic epithelial cells are diploid (46,XX or, uncommonly, 46,XY).

- ***partial*** **hydatidiform mole →** compatible with early embryo formation and may contain fetal parts, has some normal chorionic villi, and is almost always triploid (e.g., 69,XXY).

- Complete hydatidiform mole: no embryo develops, so no fetal tissues or body structures are found.
- Partial hydatidiform mole: an abnormal embryo may begin to develop, so some fetal tissues or body structures may be found.

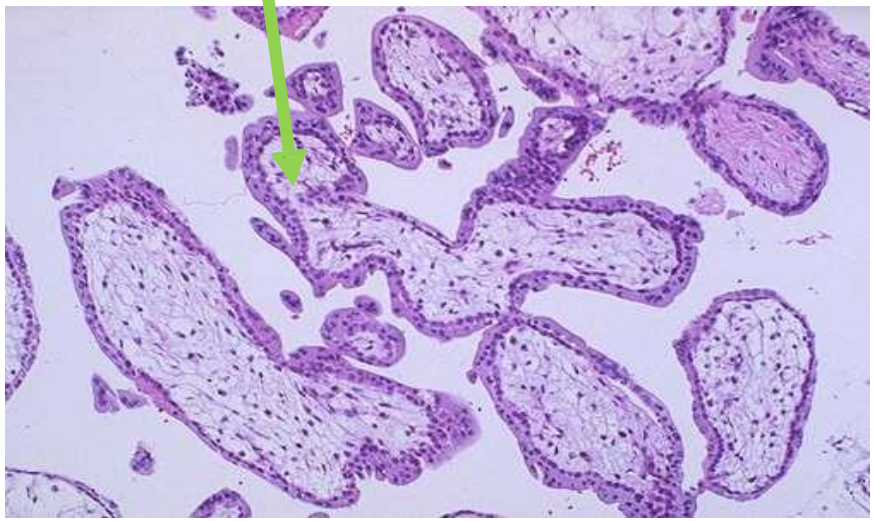
Normal uterus vs mole pregnancy

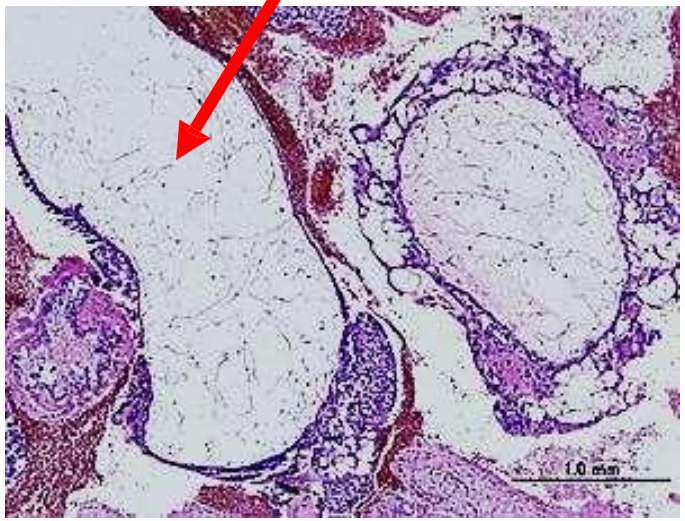


This figure illustrates the difference between a normal uterus and one affected by a molar pregnancy.

In a **molar pregnancy**, the uterine cavity is filled with swollen, abnormal chorionic villi that resemble clusters of grape- like vesicles.

Normal Pregnancy versus Mole – histology

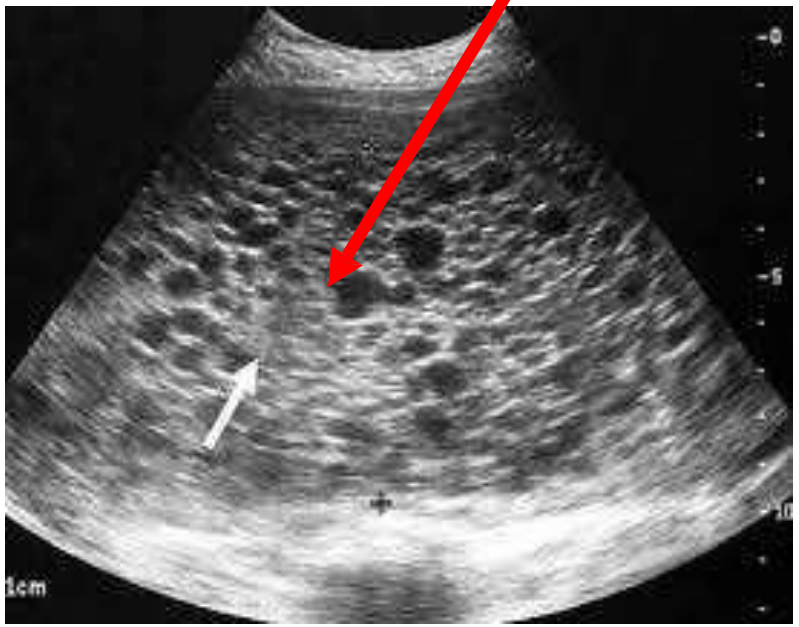




The major difference is the **size of chorionic villi**

Mole pregnancy markedly swollen, abnormal chorionic villi that resemble clusters of grape-like vesicles.

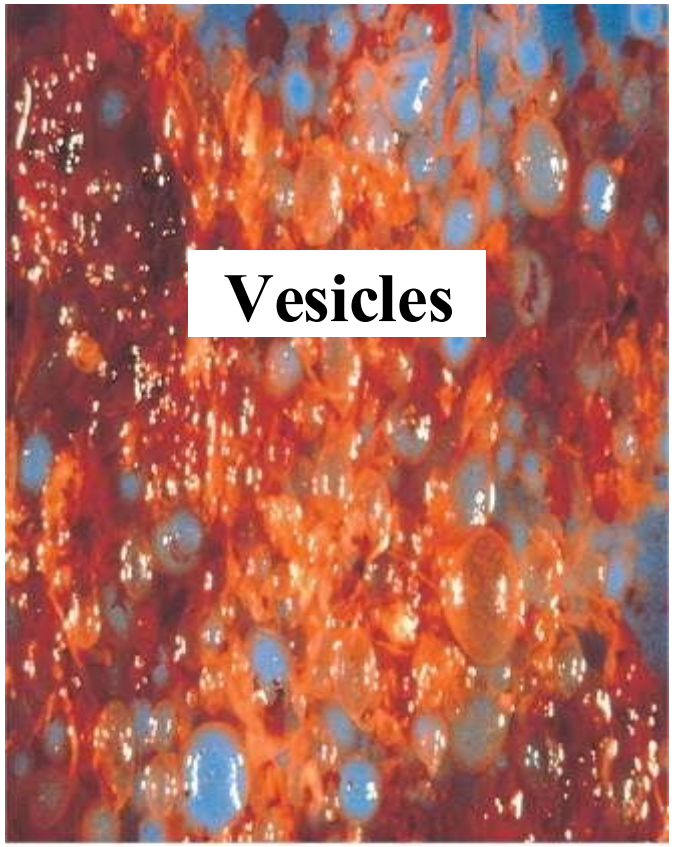
Normal Pregnancy versus Mole – Ultrasound

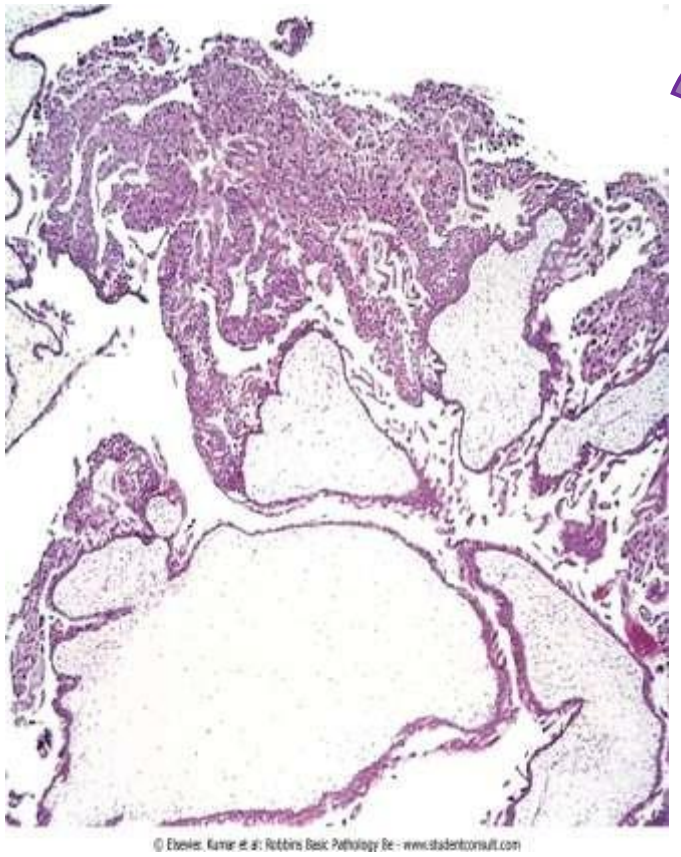


Vesicles
"Snow storm"

- This image compares a normal pregnancy and a molar pregnancy at the 12th week of gestation.
- In a normal pregnancy, the ultrasound shows a well-formed fetus with identifiable features such as the head, facial details, developing trunk, and limb buds.
- In a molar pregnancy, the ultrasound reveals only **multiple vesicles without any fetal structures**. These vesicles create a characteristic appearance known as a "snowstorm" pattern.

<u>Morphology</u>: cystically dilated chorionic villi (**grapelike structures**); villi are covered by varying amounts of mildly to highly atypical chorionic epithelium





- If we examine one of these vesicles under the microscope, we would observe **dilated, swollen chorionic villi lined by large amounts of atypical and abnormal chorionic epithelium.**

Comparison between Complete and Partial Mole

Feature	Complete Mole	Partial Mole
Karyotype	46,XX (46,XY)	Triploid (69,XXY)
Villous edema	All villi "More marked"	Some villi
Trophoblast proliferation	Diffuse; circumferential	Focal; slight
Trophoblastic Atypia	Often present	Absent
Serum hCG	Elevated	Less elevated
hCG in tissue	++++	+
Behavior & Prognosis	The prognosis is slightly worse due to a 2% risk of developing Choriocarcinoma	Rare choriocarcinoma "better prognosis"

hCG: human chorionic gonadotropin.

- **Incidence of Molar Pregnancy** → 1 to 1.5 per 2000 pregnancies (uncommon); higher incidence in **Asian** countries.
- Moles are most common **before maternal** age 20 years and **after** age 40 years
- Early monitoring of pregnancies by ultrasound →early diagnosis of hydatidiform mole, during the first trimester of pregnancy.
- Clinically: Elevations of hCG in the maternal blood and absence of fetal parts by ultrasound

Signs and Symptoms

- The ***most common presentation*** is vaginal bleeding during 1st trimester of pregnancy.
- Elevation of hCG in maternal blood and urine.
- Hyperemesis: severe nausea and vomiting.
- Absence of fetal parts by ultrasound.
- Passage of vaginal tissue described as grape-like vesicles.
- Pre-eclampsia. (تسمم الحمل)
- Uterus size looks larger than expected for a normal pregnancy. (Especially in Complete-Mole Pregnancy)
- **All above signs and symptoms are less dramatic in partial mole compared to complete mole.**

Treatment

- First stabilize patient condition, in severe hemorrhage, stabilize the patient and transfuse blood if necessary. If preeclampsia occurs due to a molar pregnancy, manage and control blood pressure.
- Then surgical evacuation of uterine contents should be Performed.
- Close monitoring of serum hCG levels→ if persistently high→ further evaluation to role out invasive mole or malignancy. (*hCG is considered a tumor marker for trophoblastic diseases.(*

Prognosis:

- **complete moles:**
  - 80% to 90% → Cured by surgical management, with no recurrence occurring.
  - <10% → invasive mole (invades myometrium).
  - 2% to 3% → choriocarcinoma.

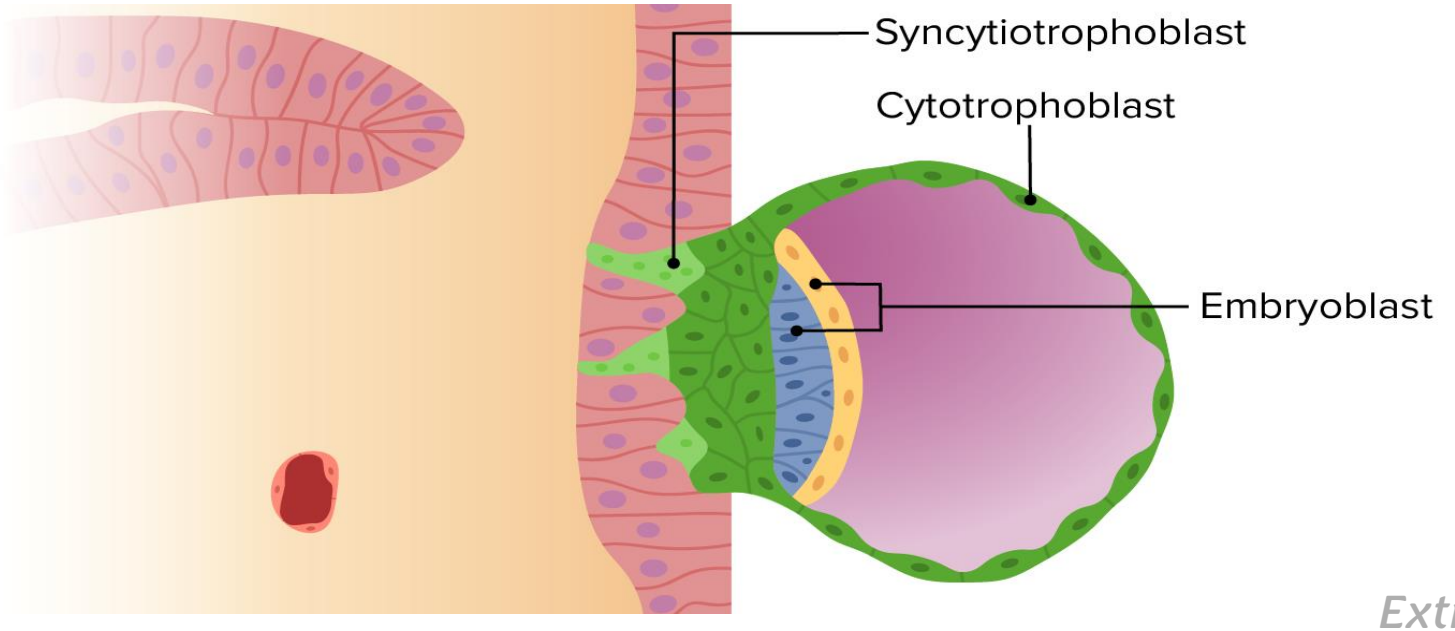
- **Partial moles:**
  - Better prognosis and rarely give rise to choriocarcinomas.

Choriocarcinoma

- Very aggressive malignant tumor arises from ***gestational chorionic epithelium*** or from *gonads*.
- Rare (1 in 30,000 preg); more common in Asian and African countries.
- Risk greater before maternal age 20 and after age 40.
- 50% arise in ***complete hyaditidiform*** moles; 25% arise ***after an abortion***, and a few (20%-25%) in ***normal pregnancy.***

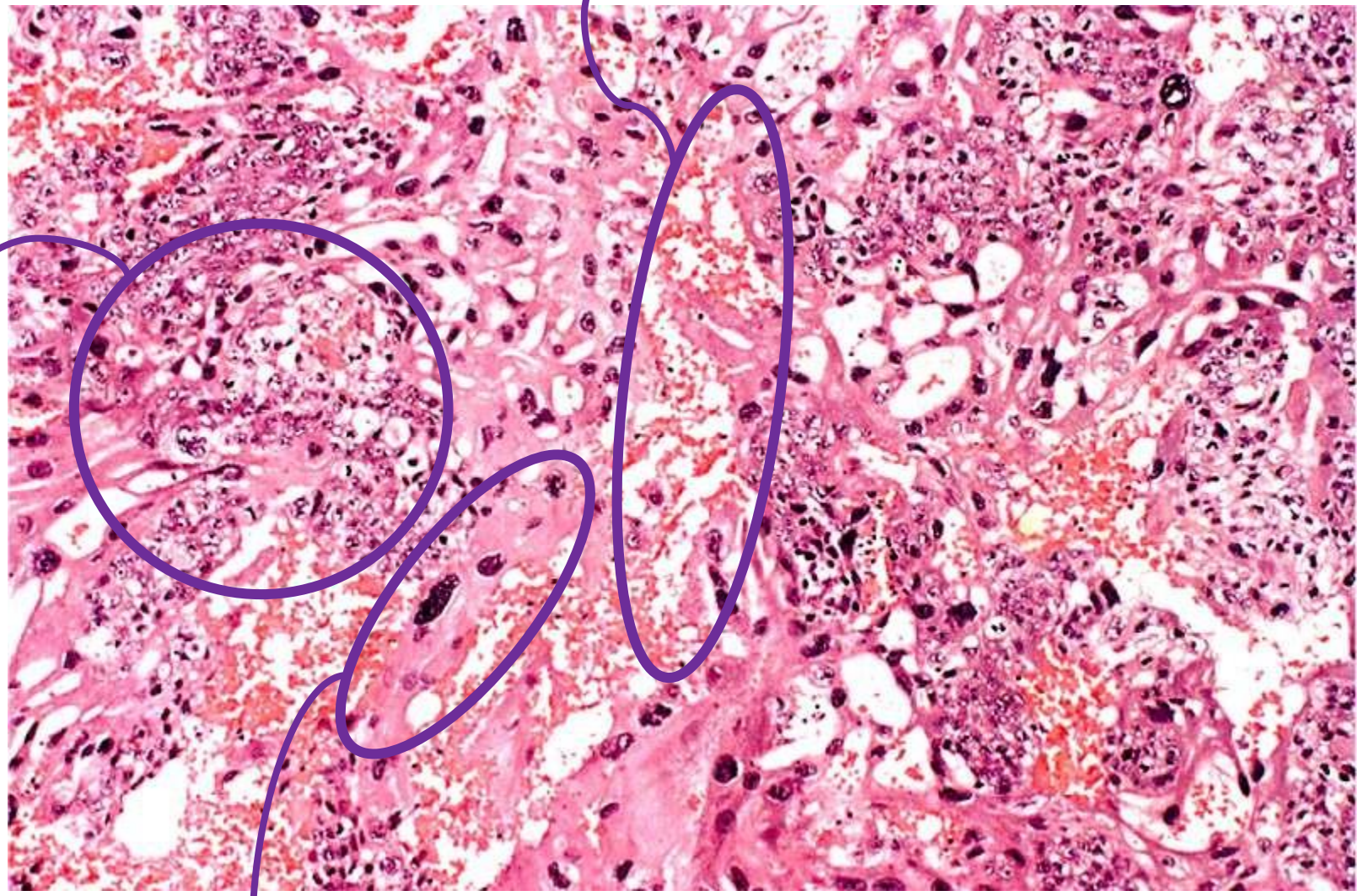
In this lecture, we will focus only on gestational choriocarcinoma.

- Clinically: **bloody, brownish discharge** and **very high titer of hCG** in blood and urine.
- Very **hemorrhagic**, **necrotic** masses within the myometrium.
- Chorionic villi are not formed; tumor is composed of anaplastic clusters of cytotrophoblast and syncytiotrophoblast. (Layers of the trophoblast)



Extra figure

•Areas of hemorrhage separating the masses.



- Cytotrophoblast: small, mononuclear cells (single nucleus) that are arranged in clusters and are surrounded by the syncytiotrophoblast layer.

- Syncytiotrophoblast cells are large multinucleated cells (have multiple nuclei) formed by the fusion of cytotrophoblast cells.

Prognosis of Gestational Choriocarcinoma:

- Aggressive disease.
- Widespread dissemination via **blood** to lungs (50%), vagina, brain, liver, and kidneys.
- Lymphatic invasion is **uncommon**.
- Despite extreme aggressiveness, **good response to chemotherapy.**
- Increased survival rate.

سبحانك اللهمَّ وبحمدِك
أشهدُ أنْ لا إلهَ إلا أنت
أستغفرُكَ وأتوبُ إليك

summary

Hydatidiform Mole

Complete Mole

- Empty ovum + 2 sperms
- Diploid: usually 46,XX
- Entirely paternal genes
- NO fetus or fetal parts
- All villi swollen (diffuse edema)
- Diffuse trophoblastic proliferation
- hCG very high
- "Snowstorm" appearance on ultrasound
- Higher risk of malignancy
- 2–3% → choriocarcinoma

Partial Mole

- Normal ovum + 2 sperms
- Triploid: usually 69,XXY
- Fetal parts may be present
- Some villi swollen only
- Mild/focal trophoblastic proliferation
- hCG less elevated
- Rarely becomes choriocarcinoma
- Better prognosis

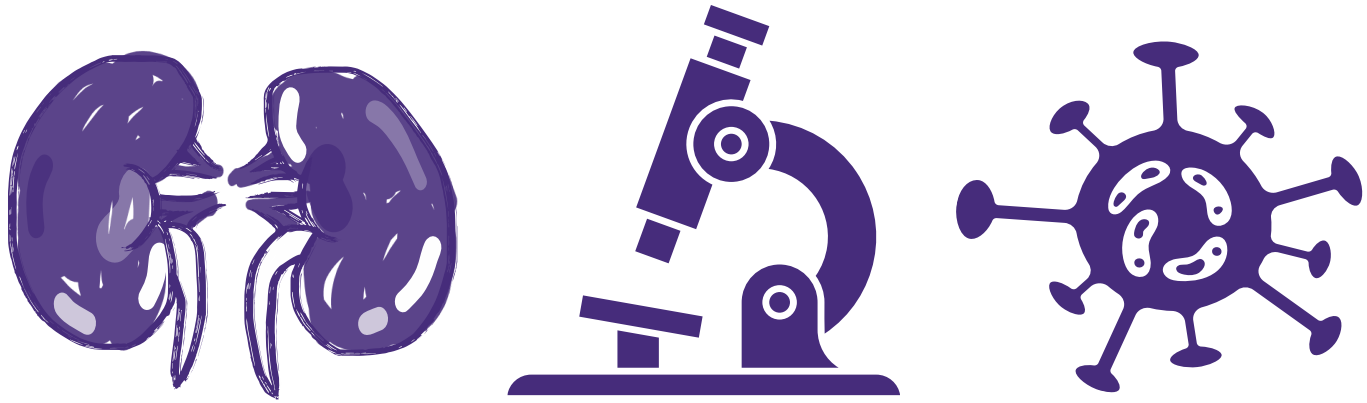
Clinical Features of Mole

- Vaginal bleeding
- Elevated hCG
- No fetal parts on ultrasound
- "Snowstorm" ultrasound appearance

Risk Factors

- Maternal age <20 or >40
- More common in Asian countries

- Gestational choriocarcinoma is a highly aggressive malignant trophoblastic tumor. It most commonly develops after a complete hydatidiform mole, but it may also occur after abortion or even a normal pregnancy.
- Patients usually present with bloody brown vaginal discharge and very high levels of hCG in blood and urine.
- Histologically, the tumor is composed of malignant cytotrophoblasts and syncytiotrophoblasts. An important exam point is that chorionic villi are absent.
- The tumor spreads mainly through the blood (hematogenous spread). The lungs are the most common site of metastasis, but spread can also occur to the brain, liver, and vagina.
- Despite being highly aggressive and rapidly metastatic, gestational choriocarcinoma responds very well to chemotherapy



PATHOLOGY
QUIZ
LECTURE 10

رسالة من الفريق العلمي

اللهم اكشف الكرب عن إخواننا في غزة، اللهم داوِ جريحهم، وارحم شهداءهم، واجبر كسيرهم، وارفع عنهم البأس والضرّ.

اللهم أطعم جائعهم، وآمِن خوفهم، وآوِ مشرّدهم، وخفف عن المحاصرين منهم يا أرحم الراحمين.

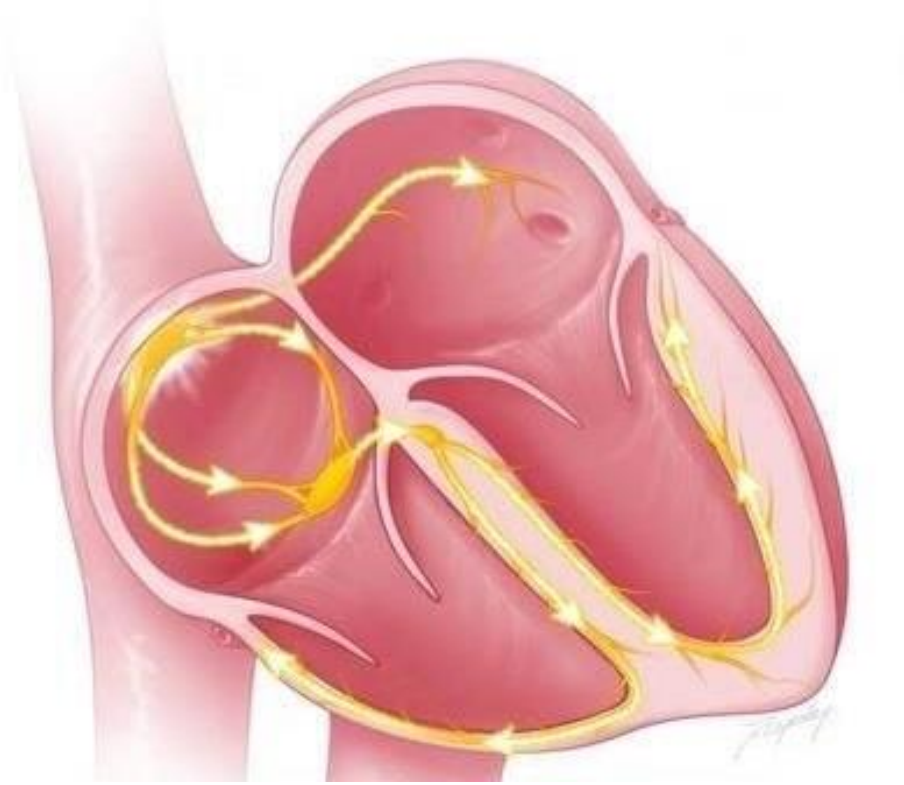
اللهم كن لهم عونًا ونصيرًا، واحفظ رجالهم ونساءهم وأطفالهم، وثبّت قلوبهم، واربط على صدورهم، وأنزل عليهم سكينتك ورحمتك.

اللهم اجعل الدائرة على عدوهم، وخالف بين كلمتهم، وأدرِ عليهم دائرة السوء، وأتِهم من حيث لا يحتسبون، وغرّهم بإمهالك حتى يأخذهم أخذك العزيز المقتدر.

اللهم انصر دينك وكتابك وعبادك المؤمنين، وطهّر المسجد الأقصى ومسرى رسولك ﷺ من الظلم والعدوان.

اللهم عجّل لغزة بالفرج والنصر والطمأنينة، واجعل لهم من كل ضيق مخرجًا، ومن كل همّ فرجًا، إنك على كل شيء قدير

اللهم إن عمر عطية في ذمتك وحبل جوارك، فقِه من فتنة القبر وعذاب النار، أنت أهل الوفاء والحق، فاغفر له وارحمه إنك أنت الغفور الرحيم.



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Corrections from previous versions:

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V1 → V2			