

تفريغ فارما ١

اسم الموضوع: Lecture 17

إعداد الصيدلاني / ة: نور ابوليلي



" على قَدْر الصَّبْرِ يَأْتِي الجَبْرِ "

يقطع الله أسبابك فتظنه يعجزك، ويترك اليأس يأكل قلبك بلا استجابة، لأنه يعلم حلاوة الجبر بعد اليأس فيرفعك لدرجة المضطر، فيُجيب دُعاءك ويُلبّي نداءك، فيكتب لك حينها أجر

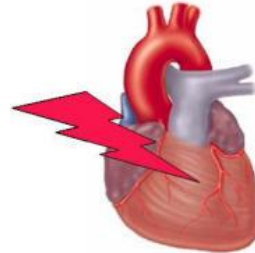
الصبر وحلاوة الجبر



لجان الترفعات

Drugs Used in Cardiac Arrhythmias

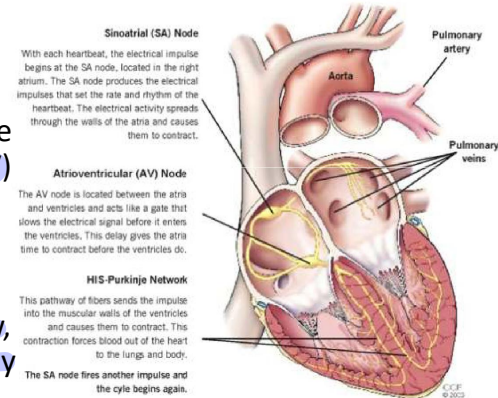
* في القلب nodes وعضو المسؤول عن ال Conduction ويوصلو ال signal لكل القلب
SA node هي التي تنج ال signal ، عند الانسان الطبيعي تنج ما بين 100-60 بال دقيقة بتطلع من ال
SA node وتنتشر في كل ال atrium وتغزو عن يصر له contraction هي ال signal بتوصل ال AV node
وظيفةها تدخل ال signal عن ال Ventricle عن يصر لهم Contraction ، من وظائف ال AV node انها
تقل ال delay ال signal مدة 0.15 sec هاد ال delaying time بطني الحال ال atrium يصر له contraction
بالا من بعد صول بتدخل ال signal ال AV node الي بتوصلها ال bundle of his + Purkinje fibres عن
يصر contraction ال Ventricle ، اذا صار في خلل بعد ال system نج نمر حالة اسمها ال Arrhythmia



Normal Sinus Rhythm

- Normal electrical cardiac function (normal sinus rhythm, NSR) is dependent on generation of an impulse in the normal sinoatrial (SA) node pacemaker usually at a frequency of 60–100 bpm.
- This impulse spreads rapidly through the atria and enters the atrioventricular (AV) node, which is normally the only conduction pathway between the atria and ventricles.
- Conduction through the AV node is slow, requiring about 0.15 seconds. (This delay provides time for atrial contraction to propel blood into the ventricles.) The impulse then propagates over the His-Purkinje system and invades all parts of the ventricles.

The Heart's Electrical System



Arrhythmia → في الـ 3 مسيات :-

- Arrhythmias (also called dysrhythmia) consist of cardiac depolarizations that deviate from the above description in one or more aspects; there is an abnormality in: (يعني الفترة بطلة ثابتة) →

- 1) • the site of origin of the impulse
- 2) • the rate or regularity of the impulse
- 3) • or the conduction of the impulse.

1) ضل في الـ site of origin impulse
شلا مشكلة بالـ SA node
صارت تطلع signal أكثر من الطبيعي.

2) يعني الـ SA node كانت تطلع الـ signal شلا كل 0.75 sec (نرتة ثابتة) بعد صاها في خلل وصاها تطلع الـ signal كل 0.75 sec
0.4 sec ← 0.5 sec ←

3) مشكلة في طريقة التوصيل : يا إما بار AV node or Bundle of his أو دي جزء من اجزاء القلب

- Many factors can precipitate or exacerbate arrhythmias: ischemia, hypoxia, acidosis or alkalosis, electrolyte abnormalities, excessive catecholamine exposure, drug toxicity (eg, digitalis or antiarrhythmic drugs).

↑ زار الـ K/Ca أو قل
في ادوية تعالج الـ Arrhythmia
بنفس الوقت الـ S.E الهم
الهم يزيرو الـ Arrhythmia

↑ Epinephrine / NE

رصد أهم الـ أسباب
زي شلا MI

Arrhythmia

Cardiac arrhythmias are a common problem in clinical practice, occurring in up to 25% of patients treated with digitalis, 50% of anesthetized patients, and over 80% of patients with acute myocardial infarction.

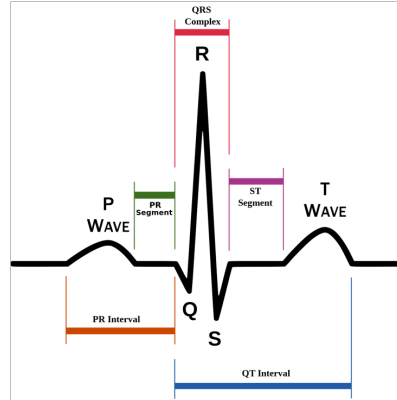
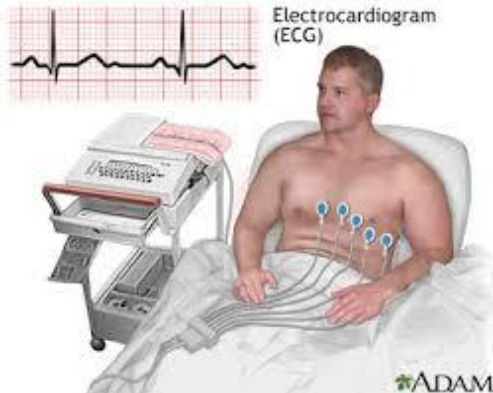
Arrhythmia may decrease cardiac output and disturb perfusion of vital organs.

Signs and symptoms that typically accompany arrhythmia:

1. Chest pain
 2. Anxiety and confusion (from reduced brain perfusion) → perfusion بالتي، ال perfusion
للكل الجسم ومن ضمنهم
 3. Abnormal pulse rate or rhythm
 4. Reduced blood pressure
- ال Brain يتقل ذراع - في
حالوا -
Anxiety and confusion

Arrhythmia

- Although some arrhythmias are silent, most produce signs and symptoms.
- Only ECG can definitively identify an arrhythmia. ← يعرف اذا الشخص مصاب بال Arrhythmia عن طريقه
- Electrocardiogram (ECG) is a test that show the electrical activity of the heart. قسطر القلب



Arrhythmia

• Types of arrhythmias:

• Atrial arrhythmias: → Atrium يتكون في ال

– Atrial fibrillation

– Atrial flutter

• Supraventricular tachycardias: → Atrium في المنطقة بين ال و Ventricle ال

– AV nodal reentry → ال delay ببطول موجود

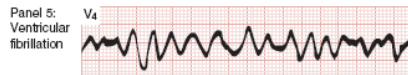
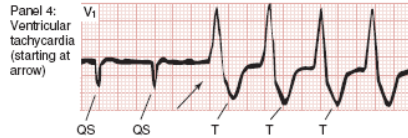
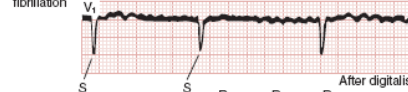
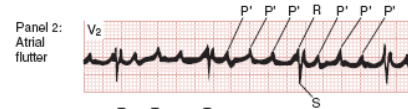
– Acute Supraventricular tachycardia

• Ventricular tachycardia: → Ventricle في ال

– Acute ventricular tachycardia

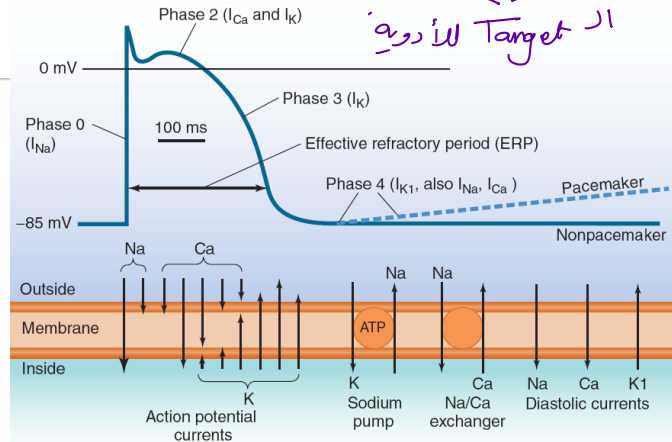
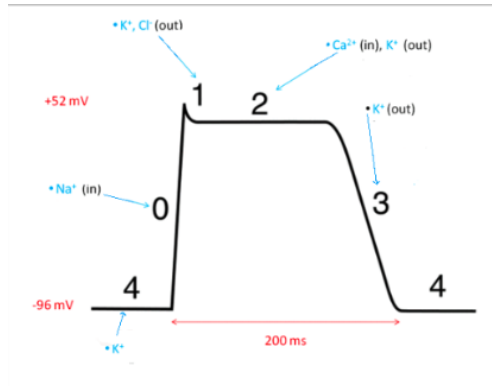
– Ventricular fibrillation

↓
أسوء حالة ممكن تسبب الوفاة .



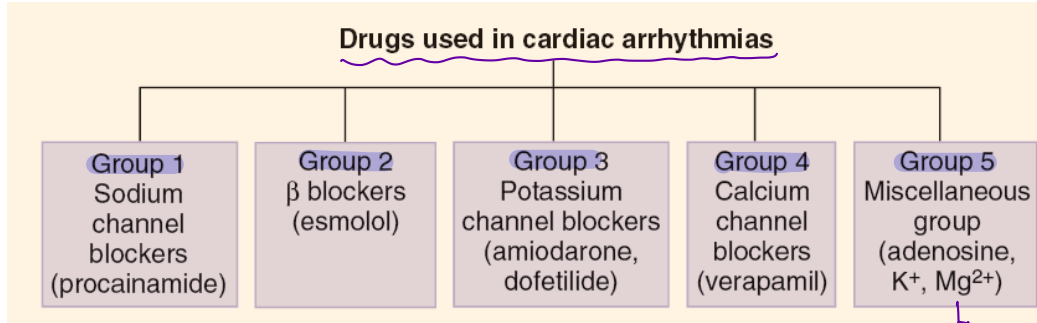
Action Potential of Cardiac Cell

- The cellular action potentials are the result of ion fluxes through voltage-gated channels and carrier mechanisms.
- Antiarrhythmic drugs act on 1 or more of the 3 major currents (I_{Na} , I_{Ca} , I_K) or on the β adrenoceptors that modulate these currents.



اللَّهُمَّ إِنِّي أَتُبِرًا مِنْ حَوْلِي وَقُوَّتِي وَالتَّجَا إِلَى حَوْلِكَ وَقُوَّتِكَ. اللَّهُمَّ أَعْنِي وَلَا تُعْنِ عَلَيَّ وَأَنْصِرْنِي وَلَا تَنْصِرْ عَلَيَّ وَاهْدِنِي وَيَسِّرْ الْهَدَى لِي.

Antiarrhythmic Drugs



لا ينتموا لمجموعة معينة .

Group 1 Antiarrhythmics (Sodium Channel Blockers) →

يُحسّل Block لـ
Na Channels

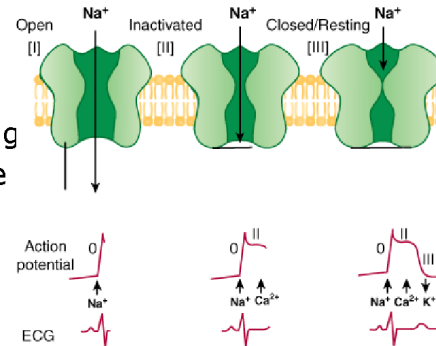
وعمليّة الـ Depolarization

مانع تغير بالتي نبضات
القلب قلت ← قلب الـ

Arrhythmia

- All antidysrhythmics in class 1 (A, B, and C) alter Na^+ conductance through cardiac voltage-gated Na^+ channels. These drugs bind to the Na^+ channels and slow their recovery from the open or inactivated state to the resting, or closed, state.
- This conversion must occur before the channel can reopen and participate in another depolarization. Consequently, as the proportion of drug-bound Na^+

channels increases, fewer of these channels are capable of reactivation on the arrival of the next depolarizing impulse. As a result, by reducing the excitability of the myocardium, abnormal rhythms are prevented.



Source: Nelson LS, Levin NA, Howland MA, Hoffman RS, Goldfrank LR

Group 1 Antiarrhythmics (Sodium Channel Blockers)

تَمَيِّز

Use-dependence:

- Na Block لا يعمل يعني يعمل
- Channel إلى صفة أصلاً فاحقة وفعالية
- ما يرتبط على الـ Na channel إلى Fully repolarized
- ↓
- القلب يحتوي على عدد كبير من الـ Na channel جزء منهم يكون نشطاً و
- جزء يكون repolarized (جاءت لإستقبال signal جديد)، الانوية هي التي يرتبط على الـ Na channel إلى حاله Depolarization و توقعها حيث ما تقدر تستقبل signal جديدة
- اما الـ Channel إلى أصلاً repolarized تقدر تستقبل signal جديدة، هيكل مماثل على الخلية بالوقت signal 150 فالتحليل تقدر تستقبل من الـ 150 (٩٥) والـ 6٥ مارح تستقبل من الـ ١٥٠ ثلاث حالات الـ Depolarization و صافى على نين القلب ضمن الـ Range الطبيعي.

Group 1 drugs bind more rapidly to open or inactivated sodium channels than to channels that are fully repolarized following recovery from the previous depolarization cycle.

Therefore, these drugs show a greater degree of blockade in tissues that are frequently depolarizing (for example, during tachycardia, when the sodium channels open often).

This property is called use-dependence (or state-dependence) and it enables these drugs to block cells that are discharging at an abnormally high frequency, without interfering with the normal, low-frequency beating of the heart.

Group 1 Antiarrhythmics (Sodium Channel Blockers)

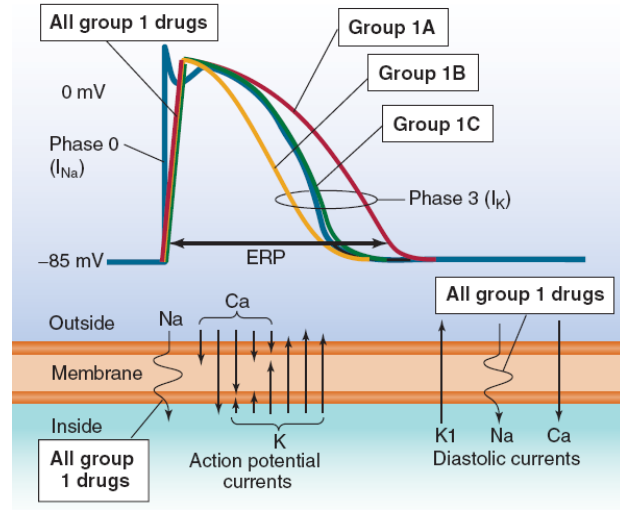
- Group 1 antiarrhythmics decreased rate of entry of sodium which slows the rate of rise of Phase 0 of the action potential.
- The group 1 drugs are further subdivided on the basis of their effects on the action potential (AP) duration:

1) Group 1A agents (prototype

procainamide) prolong the AP.

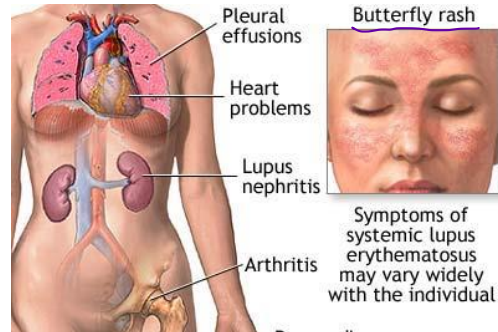
2) Group 1B drugs (prototype **lidocaine**) shorten the AP in some cardiac tissues.

3) Group 1C drugs (prototype **flecainide**) have no effect on AP duration.



Group 1A Antiarrhythmics

- **Procainamide** is effective against most atrial and ventricular arrhythmias.
بعضية ليس عند صم
- **Procainamide** may cause hypotension and with long-term use a syndrome similar to lupus erythematosus.
S.E
مع الاستخدام الطويل
S.E
* زيء الطفح الجلدي



Group 1A Antiarrhythmics

- **Quinidine** and **disopyramide** have similar effects to procainamide but are used much less frequently.
- **Quinidine** causes cinchonism (flushed skin, headache, vertigo, tinnitus) and GI upset.
- **Quinidine** reduces the clearance of digoxin and may increase the serum concentration significantly.
- **Disopyramide** has marked antimuscarinic effects and may precipitate heart failure. It is contraindicated in HF and have atropine-like side effects.

يحتبر :-

antimuscarinic

يعني إلو S.E

بشبه الـ

S.E تاعته الـ

Atropine

- **Cinchonism** or **quinism** is a pathological condition caused by an overdose of quinidine or its natural source, cinchona bark.



Group 1B Antiarrhythmics

- **Lidocaine** is useful in acute ischemic (ventricular) arrhythmias. Atrial arrhythmias are not responsive unless caused by digitalis. خِطَاة ↓ يستخدم به حالة
- **Lidocaine** is one of the least cardiotoxic of the currently used sodium channel blockers.
- **Lidocaine** is usually given intravenously, but intramuscular administration is also possible. It is never given orally because it has a very high first-pass effect and its metabolites are potentially cardiotoxic. * لا تؤخذ فمياً IV
- **Mexiletine** has similar actions and is given orally for chronic arrhythmias.
- **Phenytoin**, an anticonvulsant, is sometimes classified with the group 1B antiarrhythmic agents. It can be used to reverse digitalis-induced arrhythmias. ↓

يستخدم للأشخاص الذين يعانون من اضطراب نظم القلب
صالحه المصريح به
تشنجات ب. و ج.
إلّا تأثير على الـ
Arrhythmia

يمكننا انوار Digoxin اذا
ضربت بال Dose بصير في
Toxicity وبصير عندي
Tachycardia ممكن استخدم الـ phenytoin

Group 1C Antiarrhythmics

ينجمية في حالات

• **Flecainide** is approved only for refractory ventricular and supraventricular tachycardias.

- **Flecainide** is more likely than other antiarrhythmic drugs to exacerbate or precipitate arrhythmias (proarrhythmic effect).
- **Propafenone** has some structural similarities to propranolol and possesses weak β -blocking activity.
- The most common adverse effects are a metallic taste and constipation.

بشبه

* بعض صادر الدواء عسنان أضعف الـ supraventricular tachycardias

بـ ممكن يـبـب Arrhythmia مرة ثانية

* فهو يعتبر Antiarrhythmic و proarrhythmic

Group 2 Antiarrhythmics (Beta Blockers) → β_1 receptor Block بحمل

- Their mechanism in arrhythmias is primarily cardiac beta adrenoceptor blockade.
- **Esmolol**, a very short-acting beta blocker for ^{بسر IV} intravenous administration, is used exclusively in acute arrhythmias.
- **Propranolol**, **metoprolol**, and **timolol** are commonly used as prophylactic drugs in patients who have had a myocardial infarction.
- The toxicities of beta blockers are the same in patients with arrhythmias as in patients with other conditions.
- **Sotalol** and **amiodarone**, generally classified as group 3 drugs, also have group 2 beta-blocking effects.

شرحهم بسلايد 18

* B blocker الى تعطى orally حسب الحالة لشخص

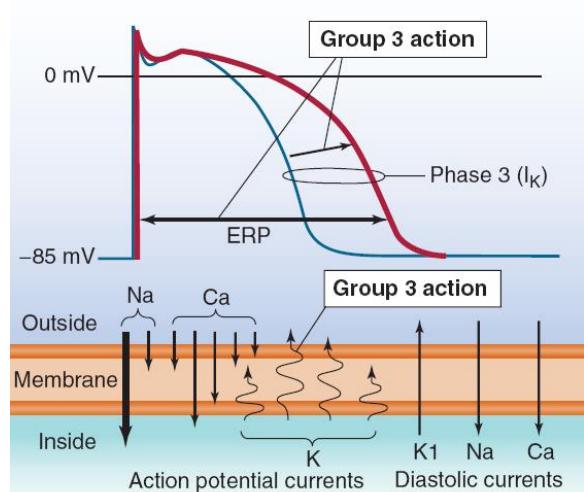
صاره Acute tachycardia لأنها بتوفد وتحت عشان تعطى المفعول

* بتكون prophylactic كحماية / وقاية للأشخاص with high risk to arrhythmia

Group 3 Antiarrhythmics (Potassium Channel Blockers)

- **Dofetilide** and **ibutilide** are typical group 3 drugs.
- The hallmark of group 3 drugs is prolongation of the AP duration. This AP prolongation is caused by blockade of potassium channels, chiefly the ones are responsible for the repolarization of the AP.

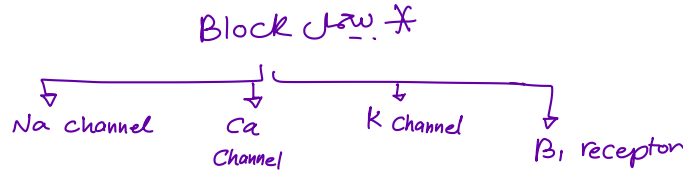
* يعمل Block ال K channel ← يمدد AP for prolongation
لما يكون ال A.P لة في الخلية ما يقدر يستقبل signal جديدة
حيل قلنا عدد مرات انقباض القلب



Group 3 Antiarrhythmics (Potassium Channel Blockers)

1 isomer
K channel blocker سَيَسْتَعْمَلُ
1 isomer
B blocker سَيَسْتَعْمَلُ

- **Sotalol** is a chiral compound (ie, it has 2 optical isomers). One isomer is an effective beta blocker, and both isomers contribute to the group 3 antiarrhythmic action. The clinical preparation contains both isomers.
- **Amiodarone** is usually classified as a group 3 drug because it blocks the same potassium channels and markedly prolongs AP duration. However, it also blocks sodium and calcium channels and beta receptors.



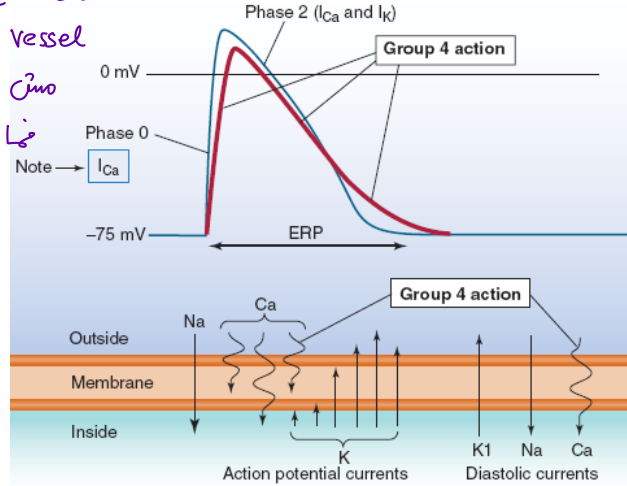
Group 4 Antiarrhythmics (Calcium Channel Blockers)

* moderate effect :- متوسطة تأثير على القلب و
 متوسطة على الأوعية الدموية blood vessel
 Arrhythmia ←

- **Verapamil** is the prototype. **Diltiazem** is also an effective antiarrhythmic drug.
- Nifedipine and the other dihydropyridines are not useful as antiarrhythmics.

* effect متوسطة على القلب
 * أكثر نوع يستخدم لحالات
 Arrhythmia لا ينو بقلل HR

لأنه تأثيرهم على
 Blood vessel
 من القلب
 فما يستعملهم



Nonpharmacologic Treatment of Arrhythmia

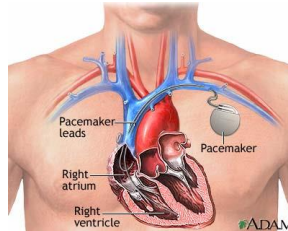
علاجات جراحية :-

- It should be noted that electrical methods of treatment of arrhythmias have become very important. These methods include:

- (1) External defibrillation ^{خارجي} → Atrial fibrillation
- (2) Implanted defibrillators ^{زرعة الجهاز جوار القلب}
- (3) Implanted pacemaker ^{كوي}
- (4) Radiofrequency ablation of arrhythmogenic foci via a catheter.

Ischemia / hypoxia ^{نقص تروية / نقص أكسجين}
مجموعة ضحايا مرسورة بالـ Ventricle تتجمع حولين بعض

وتنصير تقطع signal ، فخرج بصير في عندي لـ signal
طالعه من SA node و التجمعات هاتي خ القلب
من عارف لأي لـ signal يستصيب ، اكل : نمن عملية
Radiofrequency ablation يدخلو catheter ويوصلو
للكان الي فيه الخلايا الجديرة ويكوسا زي كأنهم يقتلوصا .



Questions??