

## Antimicrobial drug use in combination

- **Additive (indifferent) effect:** the activity of two drugs in combination is equal to the sum (or a partial sum) of their independent activity when studied separately .
- **Synergistic effect:** the activity of two drugs in combination is greater to the sum of their independent activity when studied separately .
- **Antagonistic effect:** the activity of two drugs in combination is less to the sum (or a partial sum) of their independent activity when studied separately .

Antimicrobial combinations are used widely, although most infections in patients with normal defenses can be treated with a single antimicrobial agent. Few reasons justify the use of antimicrobial combinations: (1) broad-spectrum coverage for the initial therapy of severely infected patients; (2) polymicrobial infections; (3) prevention of selection of resistant microorganisms when a high mutation rate of the causal organism exists to the antibiotic indicated; (4) reduction of dose-related toxicity – this concern is rare and mostly of historical interest, related to the use of sulfonamides; and (5) antimicrobial synergistic activity. It is appealing to use combinations and treat two types of infections— infections resulting from resistant or relatively resistant organisms and infections requiring a bacterial eradication (high bactericidal effect), considering the site of infection and the host defenses.

Example of antibiotic combination :

**Amoxicillin/clavulanic acid** or **co-amoxiclav** is an antibiotic useful for the treatment of a number of bacterial infections . It is a combination antibiotic consisting of amoxicillin trihydrate, a  $\beta$ -lactam antibiotic, and potassium clavulanate, a  $\beta$ -lactamase inhibitor. This combination results in an antibiotic with an increased spectrum of action and restored efficacy against amoxicillin-resistant bacteria that produce  $\beta$ -lactamase.

**Ampicillin/sulbactam** is a combination of the common penicillin-derived antibiotic ampicillin and sulbactam , an inhibitor of bacterial beta-lactamase. Two different forms of the drug exist.

### Procedure :

#### A\\ Double disc test :

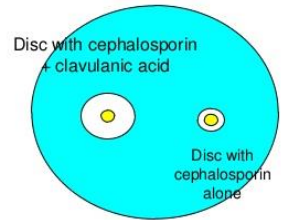
1. Prepare bacterial suspension and standardization with 0.5 McFarland standard .
2. Swab a Mueller-Hinton plate with the bacteria . Dip a sterile swab into the broth and express any excess moisture by pressing the swab against the side of the tube or add 0.1  $\mu$  of bacteria suspension .
3. Spreading the surface of the agar completely with L- shape spreader or swap it . (you do not want to leave any un swabbed agar areas at all).
4. After completely swabbing the plate, turn it 90 degrees and repeat the swabbing process. (It is not necessary to re-moisten the swab.) Run the swab around the circumference of the plate before discarding it in the discard bag.
5. Allow the surface to dry for about 5 minutes before placing antibiotic disks on the agar.
6. Place the appropriate two antibiotic discs on the surface of the agar using sterile forceps .

7. Incubate the plates in 35 -37° C for 16-18 hr.



• **1- Combination disk**

- Uses 2 disks of 3<sup>rd</sup> cephalosporin alone and combined with clavulanic acid
- An increase of  $\geq 5$  mm in zone inhibition with use of the combination disk



**B\\ Well method :**

1. Pour Muller Hinton Agar Medium in plates at depth 4 mm .
2. Spread a broth culture of an isolated bacterium in to an agar plates by spreader or by cotton swab .
3. After drying the plate at 37 °C for 30 minutes , make a well in the plate ( several wells when used many concentration of a certain antibiotic or several antibiotic for the same bacteria ) by using a sterile cork borer in appropriate diameter ranging from (5-10) mm under aseptic condition ,
4. Fill the well with a tested antibiotic(combine two tested antibiotics ,by weigh each drug and dissolve both in D.W ) .
5. Incubation the plates at 37 °C for 18-24 hr.
6. Measure the inhibition zone around the wells .