HIV Treatment: monitoring, adherence and resistance

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Content of the presentation

- Introduction to the monitoring, adherence and resistance
- Adherence
- Resistance
- HIV Testing – types

What is adherence?

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Adherence to ARV

- is a strict compliance by the patient to the treatment regime as prescribed by the doctors (dose, time, combination with food)

Adherence to treatment

- part of the therapy and an element of particular importance determining the effectiveness of HIV treatment

Factors affecting the adherence to treatment

- Doctors and the trust of patient in the effectiveness of treatment
- Side effects
- Social environment
- Lifestyle
- Social conditions – problems with finances and housing
- Use of alcohol and drugs
- Depression and mental health
- etc.

What is monitoring?

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Monitoring is

Continued process of surveillance and registration of parameters of an object according to defined criteria

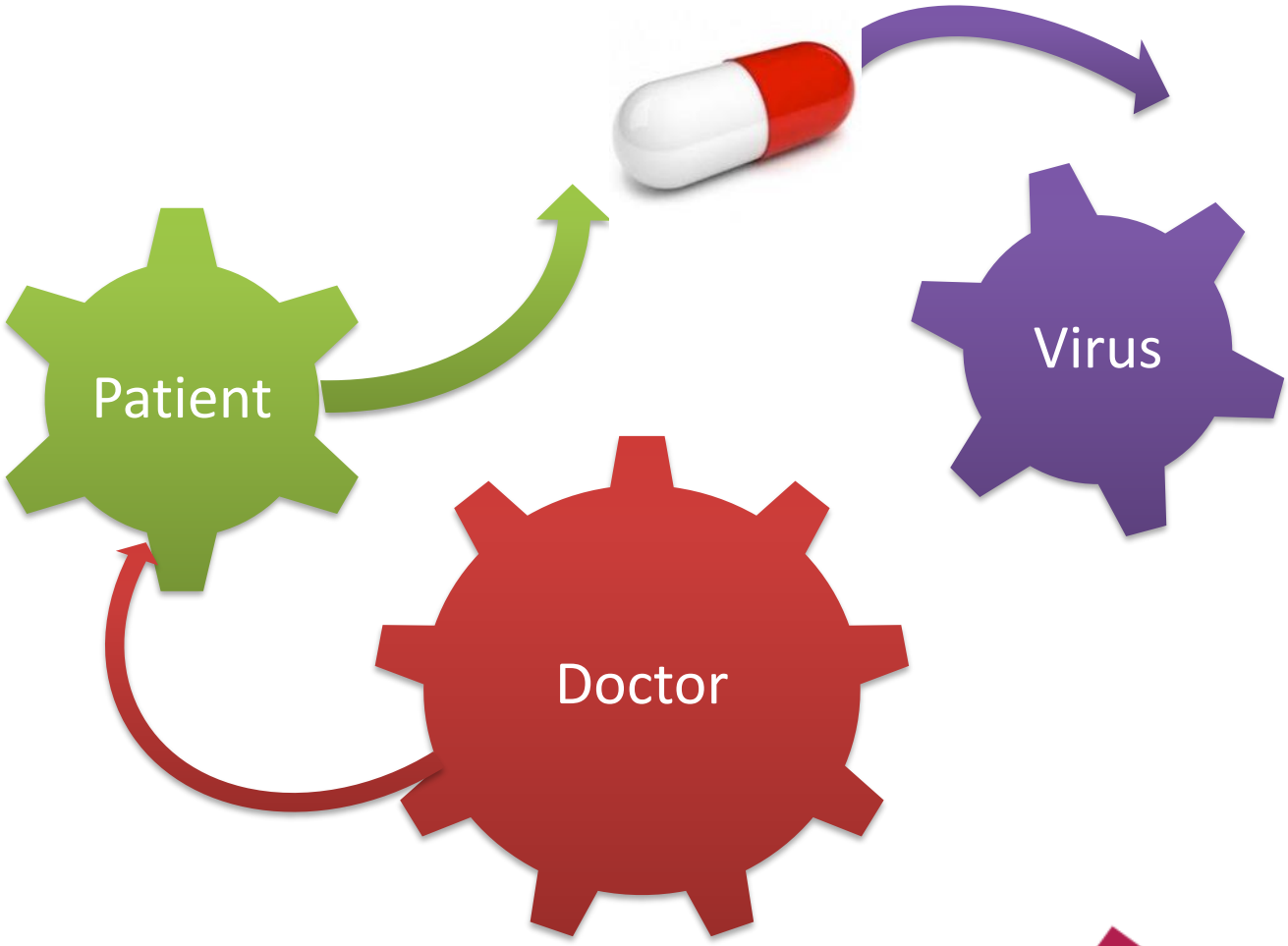
Is a system of the collection, registration, storage and analysis of data of several key symptoms/parameters to derive conclusions on the overall situation/behavior

Monitoring of ARV Therapy

implies the following:

- Formation and maintenance of adherence to ARV therapy
- Understanding of the complex system of surveillance of the patient's condition
- Assessment of adherence level by the patient
- Assessment of adherence risk factors
- Observation of lack of adherence and analysis of reasons therefore

Monitoring the adherence to ARV therapy



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Resistance

Insensitivity of a living organism towards the impacts of various factors

Types of resistance of HIV virus to ARV drugs

3 types of resistance:

1. Clinical resistance: HIV virus quickly reproduces in the organism regardless of patient taking ARV drugs

2. Phenotypic resistance: HIV virus reproduces in tubes when ARV drugs are added

3. Genetic resistance: Genetic code of HIV virus contains mutations that lead to the resistance to ARV drugs

HIV Testing
Antibody test

- Antibody tests
  - Rapid tests and home tests
    - Antibodies are produced by the immune system which is what the test looks for. Can be used in blood and oral fluid
    - 3 – 12 weeks after infection before detection
    - Rapid antibody screening test takes 30 minutes
    - OraQuick HIV test swab from the mouth takes about 20 minutes
    - Home testing kits involves a finger prick blood sample can take 7 – 10 days for results
- All positive test results will require a second conformation test

HIV testing
Fourth generation tests

- Fourth generation tests look for
  - HIV antibodies and antigens
  - Antigens are foreign substances that cause your immune system to activate
  - Antigen is part of the virus and present during acute infection
  - Antigen p24 is produced before antibodies are produced

- 2 – 6 weeks for the body to make enough antigens and antibodies for the test to detect HIV

HIV testing
nucleic acid test (NAT)

- Nucleic acid test
  - Does not look for antigens or antibodies
- It looks for the virus
- Gives a positive or negative result
  - And the actual amount of the virus

Takes 7 – 28 days for NAT to detect the virus

Very expensive and rarely used

Monitoring

- Viral load
- CD4 count
- Resistance tests
- Drug levels
- Viral tropism
- Renal function test
- Liver function tests
- Full blood count

Viral load

- The most important test once started on treatment!
- Shows how much virus is in the blood
- Result may look like 100 000 copies/mL for someone not on ART
  - For someone on ART it may look like 3 copies/mL (undetectable)
- Viral loads show if the ARV therapy is working or not

CD4 Count

- This measures how your immune system is functioning -
  - A high CD4 count means its good
    - A low CD4 count is not
      - Anything under 250 is dangerous
      - The most important test before commencing ARV therapy
- CD4 cells are lymphocyte cells (white blood cells) sometime known as T-cells
- Two types of T-cells – CD4 are helper cells and lead against infection and CD8 cells “suppressor” cells. These are also killer cells
- A normal CD4 count range would be 400 – 1600 cells per cubic millimeter
- CD4% is the total lymphocytes (white blood cells) that are CD4 cells
- Starting ARV will increase the CD4 count as the immune system recovers

Resistance test

- This shows if the HIV virus is resistant to HIV drugs
  - It shows if the chosen drug will work
- A virus that has mutated may cause drug resistance to occur
  - K103N will stop EFV and NVP from working
  - M184V will stop 3TC and FTC working
- Missing medication can cause resistance to develop
- A detectable viral load while on treatment can cause a mutation to occur

Therapeutic Drug Monitoring

- Drug level testing
- This should be done once commenced on ARV
- Detects how much drug the body is absorbing
  - For ARV's to work properly there has to be a set level of drug in the body
- Sometimes a dose adjustment maybe needed or a change of therapy if the body does not absorb the drug correctly
  - Many reasons why drugs are not absorbed
  - Adherence level is the biggest reason why drug levels maybe low….

Viral tropism

- When HIV attaches to CD4 cells it uses molecules on the cell surface

  receptors or chemokine co-receptors
- The first receptor HIV uses is the CD4 molecule

  it then uses a co-receptor CCR5 or CXCR4 molecule

- Usually uses one type of co-receptor

  CCR5 co-receptor is called CCR5 tropic or R5 tropic

- R5 tropic test used for Maraviroc

Renal function tests

- HIV Associated Nephropathy (HIVAN)
  damage caused by HIV to kidneys

- Nephrotoxicity
  toxicity or injury to the kidneys
  side effects of ARV's

- Up to 30% of HIV+ people have kidney disease

- Measures the levels of urea, creatinine and salts
  dipstick urine tests often pick up increased protein levels which indicate potential kidney damage

Liver function test

- Liver function tests check the liver is working properly
- Some drugs use the liver pathway for metabolism
  - Alanine aminotransferase (ALT).
  - Aspartate aminotransferase (AST).
  - Alkaline phosphatase (ALP).
  - Gamma glutamyl transferase (GGT).
  - Bilirubin.
  - Albumin.
- Ultrasound
- Liver biopsies
- Fibro scan

Adherence

- What is adherence?
- How much is enough?
- How can adherence be improved?
- What about missed or forgotten tablets?

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Drug resistance questions

- What is “wild-type” virus and what does it do?
- Which drugs can someone use if they have already developed resistance?
- Can drug resistance be transmitted or passed from mother to child?
- Is it possible to develop resistance to a drug even with perfect adherence?
- Are some drugs easier to become resistant to than others?
- How high does the viral load need to be to be able to use resistance testing?
- If you have developed resistance to a drug, does that mean that you are resistant to all the drugs in that class?
- If your viral load is undetectable but your CD4 still low, could that be a sign of drug- resistance? Would the doctors consider doing a drug-resistance test?
- What are the main signs of drug-resistance?
- When should you have a resistance test?

Resistance

- What is it?
  - A mutation of the virus structure
  - Low levels of drug in the body can cause resistance
  - A person can be infected with with drug resistant HIV
- When does resistance occur?
  - Most common when detectable virus levels while on ART
  - After stopping treatment if not done properly
- Cross resistance
  - When a resistance occurs with one class of drug then usually the other drugs in the same class wont work also

Treatment failure

- Virological failure
  - Never reaches undetectable or rebounds
    - The drugs are not working!
- Clinical failure
  - The drugs are not stopping a person from becoming ill with other illnesses associated with HIV
- Managing treatment failure
  - It can be complex.
    - Important to understand why this has happened
      - Drug levels, adherence drug drug interactions other
- Viral blip – is not a treatment failure

Test time!

- What does ARV stand for?
- How many drugs are usually used in ARV combination therapy?
- Name four families of drugs
- Which drug family is active before HIV enters a CD4 cell?
- How many combinations are recommended as first-line treatment by the WHO?
- Name the individual drugs used in the WHO combinations
- Give at least three reasons to delay starting treatment
- What can affect the levels of ARVs in the blood?
- What is adherence?
- Give six examples of things that could help with adherence.
- What is drug resistance?
- What is clinical failure?
- What is Virological failure?
- How low does viral load need to go to prevent resistance developing?

Thanks to

- i-base
  - http://i-base.info

- Center for disease Control and Prevention
  - http://www.cdc.gov/hiv

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