Paediatric Society CME
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HIV infection and HIV drug resistance

Antiretroviral resistance patterns in children with HIV infection
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This is an update on the patterns of HIV drug resistance in children

1. **Name 4 classes of HIV drugs, and 1 or 2 examples of each of these**
   NNRTI – non-nucleoside reverse transcriptase inhibitors (Nevirapine, Efavirenz)
   NRTI – nucleoside reverse transcriptase inhibitors (Lamivudine, Zidovudine, Emtricitabine, Tenofovir)
   PI – protease inhibitors (Lopinavir / ritonavir)
   New drug class: INSTI - Integrase strand transfer inhibitor (Raltegravir, Dolutegravir)

2. **Define what Acquired Drug Resistance, Transmitted Drug Resistance, and Pre-treatment Drug Resistance mean**
   Acquired drug resistance – develops when HIV mutations emerge due to viral replication in individuals on ART
   Transmitted drug resistance – detected in ART drug naïve individuals, occurs when previously uninfected individuals become infected with virus that has drug resistance mutations (DRMs)
   Pre-treatment HIV drug resistance – detected in ARV drug-naïve individuals initiating ART

3. **What is the WHO resistance threshold for changing to a different empiric first-line ART therapy, and why?**
   WHO considers a national pre-treatment resistance of >10% to an ARV drug or drug class as an indication to transition to a different empiric first-line ART regimen. The presence of PDR is a strong predictor of treatment failure on first-line ART in infants and children, this has especially been shown with NNRTI DRMs.
   Some countries have regular surveillance for drug resistance that can be performed on dried blood spots as part of early infant diagnosis (EID) testing in PMTCT programs.

4. **What class of HIV drugs has the highest rates of resistance in children worldwide?**
   NNRTIs, especially in children exposed to Nevirapine as part of PMTCT. The main response to this has been for WHO to recommend use of PIs (such as ritonavir-boosted lopinavir) instead of NNRTIs in regimens (2010). Now, there are some PI resistance, and WHO are introducing new Integrase strand transfer inhibitors such as Dolutegravir (2017).

5. **What is WHO's recommended second-line treatment now?**
   It depends on what the first-line therapy has been. (a) If it has been NNRTI based (Nevirapine or Efavirenz) then 2nd line therapy can either be:
   Integrase strand transfer inhibitor, such as Dolutegravir *plus* 2 NRTIs,
   or
   A Protease inhibitor such as Lopinavir/ritonavir plus 2 NRTIs
   (b) If it has been a PI-based first-line therapy, then WHO suggests Raltegravir *or* Dolutegravir plus 2 NRTIs.

6. **When should a child be changed from first-line therapy to second-line therapy?**
   If there is evidence of viral, immunological or clinical failure, despite adequate adherence:
   Viral failure is defined by a persistently detectable viral load exceeding 1000 copies/mL (that is, two consecutive viral load measurements within a 3-month interval with adherence support between measurements) after at least 6 months of starting a new ART regimen.
   Immunological failure is defined as: Younger than 5 years: Persistent CD4 levels below 200 cells/mm3; Older than 5 years: Persistent CD4 levels below 100 cells/mm3.
   Clinical failure: New or recurrent clinical event indicating advanced or severe immunodeficiency (WHO clinical stage 3 and 4 clinical condition with the exception of TB) after 6 months of effective treatment