Management Caveats For Physicians Caring For Children With HIV In Pakistan 2024

The Aga Khan University Karachi
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Ministry of National Health Services, Regulations and Coordination
Government of Pakistan

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Acknowledgements

This booklet was planned in 2021 when two years had passed since establishment of two new pediatric ART Treatment Centers in Larkana District and we had received almost daily feedback on problems faced by newly inducted physicians on the ground which were not addressed adequately in existing reference materials.

As reference we had an excellent Manual on pediatric HIV care and treatment for district hospitals: addendum to the Pocket book of hospital care of children (WHO) (2011) which consolidated principles of IMNCI with HIV care. We also had the Consolidated Training Manual for Antiretroviral Therapy (ART) Centers: A Guide for the Staff (commissioned by UNDP) (2018) which added more detail in perspective and knowledge.

We wanted to develop a short flip-through booklet where physicians dealing with children with HIV or pregnant women with HIV could use a problem-based approach to resolve their patients' medical needs. We also needed the booklet to reflect available diagnostic and treatment resources in most provincial program ART Treatment Centers and public sector hospitals and devise a functional system of identifying a 'sick' child and referring in a timely fashion to a higher center of care closest to the patient's place of residence. We hope that this product will be helpful and used daily in clinics for patient management.

This effort is dedicated to the beautiful children of Pakistan and remaining South Asia (Iran, Afghanistan, India, Bangladesh, Nepal) who are vulnerable to or living with HIV infection, their families who traverse various vertical programs for healthcare and, the dynamic HIV Program Physicians and Personnel who work hard to manage their patients well despite resource constraints.

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1. 3TC - Lamivudine
2. ABC - Abacavir
3. ABG - Arterial Blood Gas
4. AB – Antibody
5. ACE - Angiotensin-converting enzyme
6. AEM – Asian Epidemic Model
7. AFB – Acid-Fast Bacilli
8. AFASS - Acceptable, Feasible, Affordable, Sustainable and Safe
9. AFP – Alpha fetoprotein
10. AG – Antigen
11. AHC - Acute Hepatitis C
12. AIDS - Acquired Immunodeficiency Syndrome
13. AKI - Acute kidney injury
14. AKU – Aga Khan University
15. ALT – Alanine Aminotransferase
16. AOM - Acute otitis media
17. AIN - Anal Intraepithelial Neoplasia
18. APRI – Aspartate aminotransferase to Platelet Ratio Index
19. APTT - Activated partial thromboplastin time
20. ARDS - Acute Respiratory Distress Syndrome
21. ART - Antiretroviral Therapy
22. ARV – Antiretroviral
23. ASH – Abbasi Shaheed Hospital
24. ATT – Antituberculous Therapy
25. ATV – Atazanavir
26. AVD - Atherosclerotic Vascular Disease
27. AZT - Zidovudine (Azidothymidine)
28. BAL - Bronchoalveolar Lavage
29. BACP - Balochistan AIDS Control PrograM
30. BCG- Bacillus Calmette–Guérin
31. bid - bis in die
32. BMC - Bolan Medical College
33. BMI - Body Mass Index
34. BNP - Brain Natriuretic Peptide

35. BUN – Blood Urea Nitrogen
36. CCR5 - C-C chemokine receptor type 5
37. CABG - Coronary Artery Bypass Grafting
38. CHK – Civil Hospital Karachi
39. Ca – Calcium
40. cART - combination antiretroviral therapy
41. CBO – Community Based Organization
42. CBD - Chronic Bone Disease
43. CBC- Complete Blood Count
44. CDC - Centers for Disease Control and Prevention
45. CD4 - Cluster of Differentiation 4
46. CFR - case fatality rate
47. CHB - Chronic Hepatitis B
48. CHC - Chronic Hepatitis C
49. CKD - Chronic Kidney Disease
50. CLD - Chronic Lung Disease
51. CLHIV – Children Living with HIV
52. CIN - Cervical Intraepithelial Neoplasia
53. cm - centimeter
54. CMV – Cytomegalovirus
55. CMCL– Chandka Medical College Larkana
56. CNS – Central Nervous System
57. COPD - Chronic obstructive pulmonary disease
58. CPT - Cotrimoxazole Preventive Therapy
59. CRP - C-reactive Protein
60. CRT - Cardiac Resynchronization Therapy
61. CSF - Cerebrospinal Fluid
62. CT – Computed Tomograp
63. CXR - Chest X-Ray
64. CXCR4 – C-X-C chemokine receptor type 4
65. DAA - Directly Acting Antivirals
66. DCV - Delcatasavir
67. DOTS - directly-observed therapy, short-course
68. d4T – Stavudine
69. ddI - Didanosine
70. DNA - Deoxyribonucleic Acid

71. DLT – Dolutegravir-Lamivudine-Tenofovir
72. DR – Detailed Report
73. DRM - Drug Resistance Mutations
74. DTG - Dolutegravir
75. DRV - Darunavir
76. EBV – Epstein Barr Virus
77. ECG - Electrocardiography
78. EFV – Efavirenz
79. EGD - Esophagogastroduodenoscopy
80. eGFR – estimated Glomerular Filtration Rate
81. EIA - Enzyme Immunoassays
82. EID - Early Infant Diagnosis
83. ELISA – enzyme-linked immunosorbent assay
84. EMB – Ethambutol
85. EMRO - Eastern Mediterranean Region Office
86. ETV - Entecavir
87. FATA – Federally Administered Tribal Areas
88. FDA – Federal Drug Authority
89. FDC - Fixed Dose Combination
90. FH - Family History
91. FI – Fusion Inhibitors
92. FIB-4 - fluorescent treponemal antibody absorption
93. FP – Family Planning
94. FSW – Female Sex Worker
95. FTA-ABS - Fluorescent treponemal antibody absorption
96. FT4 – Free Thyroxine (T4)
97. FTC – Emtricitabine
98. G-CSF - Granulocyte Colony-Stimulating Factor
99. GERD - Gastroesophageal reflux disease
100. GFR - Glomerular Filtration Rate
101. GFATM - Global Fund for AIDS, Tuberculosis and Malaria
102. GI – Gastrointestinal
103. GIT – Gastrointestinal Tract
104. GMMMCH - Ghulam Muhammad Mahar Medical College Hospital
105. GT – Genotype testing
106. GT3 – Genotype 3

107. GUD - Genital ulcer disease
108. HAND - HIV-associated neurocognitive disorders
109. Hb- Hemoglobin
110. HBIG – Hepatitis B Immunoglobulin
111. HBV - Hepatitis B Virus
112. HbsAg – hepatitis B surface antigen
113. HBsAb – hepatitis B surface antibody
114. HCC – Hepatocellular Carcinoma
115. HCG - Human Chorionic Gonadotropin
116. HCP – Healthcare Provider
117. HCV - Hepatitis C Virus
118. HHV-8 – Human Herpes Virus 8
119. HIV - Human Immunodeficiency Virus
120. HIV-NRD - HIV-associated neuroretinal disorder
121. HIV-DR – HIV- Drug Resistance
122. HIVAN - HIV-associated nephropathy
123. HLA – Human leukocyte antigens
124. HMC – Hayatabad Medical Complex
125. HPI - History of the presenting illness
126. HPV – Human Papilloma virus
127. HSV - Herpes Simplex Virus
128. HSW – Hijra Sex Worker
129. HPV - Human Papillomavirus
130. HR – Isoniazid-Rifampicin
131. HRG - High-Risk Groups
132. HSR - Hypersensitivity Reaction
133. HRZE – Isoniazid-Rifampicin-Pyrazinamide-Ethambutol
134. IBA – Ibalizumab
135. IBD - Inflammatory bowel disease
136. ICD - Implantable cardioverter-defibrillators
137. IGRA - Interferon-Gamma Release Assay
138. ID – Infectious Disease
139. IDU – Intravenous Drug User
140. IgG – Immunoglobulin G
141. IgM – Immunoglobulin M
142. IMNCI - Integrated Management of Neonatal and Childhood Illnesses

143. INH – Isoniazid
144. INSTI - Integrase Strand Transfer Inhibitor
145. INF – Interferon-
146. IRIS - Immune Reconstitution Inflammatory Syndrome
147. ISBN – International Standard Book Number
148. IUCD – Intrauterine Contraceptive Device
149. JPMC - Jinnah Postgraduate Medical Centre
150. KG – Kilogram
151. KICS - Kaposi sarcoma inflammatory cytokine syndrome
152. KP - Key Population
153. KS - Kaposi Sarcoma
154. KSAL - Kaposi sarcoma-associated lymphedema
155. KSHV - Kaposi sarcoma-associated herpesvirus
156. LANA - Latency-Associated Nuclear Antigen
157. LFT – Liver Function Test
158. LGH – Lahore General Hospital
159. LIP - Lymphoid Interstitial Pneumonitis
160. LMIC – Low-Middle-Income Country
161. LN – Lymph Node
162. LPV/r - Lopinavir/Ritonavir
163. LUMHS - Liaquat University of Medical & Health Sciences
164. MAC - Mycobacterium Avium Complex
165. MAM - Moderate Acute Malnutrition
166. MCV - Molluscum Contagiosum Virus
167. MDR- Multi drug resistant
168. Mg – Magnesium
169. ml – Milliliter
170. MNCH - Maternal, Neonatal and Child Health
171. MOTT- Mycobacterium Other Than Tuberculosis
172. MoNHSRC - Ministry of National Health Services Regulation and Coordination
173. MRI – Magnetic Resonance Imaging
174. MSM - Men who have sex with men
175. MSW - Male Sex Worker
176. MTB – Mycobacterium Tuberculosis
177. MTCT- Mother to Child Transmission
178. MUAC- Mid-upper arm circumference

179. NA - Not Applicable
180. NAT – Nucleic Acid Test
181. NAAT – Nucleic acid amplification tests
182. NACP - National AIDS Control Program of Pakistan
183. NCD - Non-Communicable Diseases
184. NFV - Nelfinavir
185. NGO – Non-governmental organization
186. NLZ – Nevirapine-Lamivudine-Zidovudine
187. NNRTI - Non-Nucleoside Reverse Transcriptase Inhibitor
188. NRTI - Nucleoside Reverse Transcriptase Inhibitor
189. NSP – Nutritional Support Program
190. NSAID - Nonsteroidal Anti-Inflammatory Drugs
191. NTM – Non-tuberculous Mycobacteria
192. NVP – Nevirapine
193. OCP – Oral Contraceptive
194. OCT - Optical coherence tomography
195. OD – Once Daily
196. OFC – Occipito-frontal Circumference
197. OI – Opportunistic Infections
198. PA-I - Post-attachment Inhibitors
199. PACP - Provincial AIDS Control Program
200. PAS – Pakistan AIDS Strategy
201. PCR - Polymerase chain reaction
202. PCP – Pneumocystis Carinii Pneumonia
203. PEP - Post Exposure Prophylaxis
204. PH - Past History
205. Ph – Phosphorus
206. PI - Protease Inhibitors
207. PJP - Pneumocystis Jirovecii Pneumonia
208. PLHIV - People Living with HIV
209. PML - Progressive Multifocal Leukoencephalopathy
210. PMTCT - Prevention of Mother-to-Child Transmission
211. PPA – Pakistan Paediatric Association
212. PPTCT - Prevention of Parent-to-Child Transmission
213. POC - Point-of-Care
214. PREP – Pre-exposure Prophylaxis

215. PT - Phenotypic Testing
216. PT - Prothrombin Time
217. PTH – Parathyroid Hormone
218. PW – Pregnant Woman
219. PWID - People Who Inject Drugs
220. PZA – Pyrazinamide
221. qPCR - Quantitative PCR
222. RAL – Raltegravir
223. RDT - Rapid Diagnostic Test
224. RIF – Rifampicin
225. RNA - Ribonucleic acid
226. RPR - Rapid Plasma Reagin
227. RSV - Respiratory syncytial virus
228. RTV – Ritonavir
229. RUTF - ready-to-use therapeutic food
230. SAM - Severe Acute Malnutrition
231. SD – Standard Deviation
232. SH - Social History
233. SIRS - Systemic Inflammatory Response Syndrome
234. SOF - Sofosbuvi
235. SR - Systems Review
236. SRH - Sexual Reproductive Health
237. STD – Sexually Transmitted Diseases
238. STI – Sexually Transmitted Infections
239. SVR - Sustained Viral Response
240. SW – Sex Workers
241. SZCHL – Sheikh Zayed Children Hospital Larkana
242. TAF – Tenofovir alafenamide
243. TAM - Thymidine analogue mutations
244. TB – Tuberculosis
245. TBM – TB Meningitis
246. TDF - Tenofovir Disoproxil Fumarate
247. Tdap - tetanus, diphtheria, and pertussis
248. TG – Transgender
249. THR – Taluka Hospital Ratodero
250. TIH – The Indus Hospital

251. TLD - Tenofovir-Lamivudine- Dolutegravir
252. TM - Thalassemia Major
253. TMJ - Temporomandibular joint
254. TMP - SMX - Trimethoprim-Sulfamethoxazole
255. TPT - TB Preventive Therapy
256. TP-PA - Treponemal Pallidum Particle Agglutination
257. TSH - Thyroid-Stimulating Hormone
258. TST - Tuberculin Skin Test
259. TSW - Transgender Sex Worker
260. UNAIDS - United Nations Programme on HIV/AIDS
261. UNDP - United Nations Development Programme
262. UNICEF - United Nations Children's Fund
263. UTI - Urinary tract infection
264. VAD - Ventricular Assist Device
265. VCA - Viral Capsid Antigen
266. VCT - Voluntary Counselling and Testing
267. VDRL - Venereal Disease Research Laboratory
268. VL - Viral Load
269. VZV - Varicella Zoster Virus
270. VZIG - Varicella-Zoster Immune Globulin
271. WAZ - Weight for Age Z score
272. WHO - World Health Organization
273. WHZ - Weight for Height Z score
274. WLHIV - Women Living with HIV
275. WRA - Women of Reproductive Age
276. ZDV - Zidovudine

Chapter 01

Key Concepts in Epidemiology of HIV in Pakistan

Learning Objectives:

The learner should be able to

- Name Key Populations (KPs) or High-Risk Groups (HRGs) for HIV
- Recognize 'vulnerable' groups and 'bridging' populations
- Identify modes of transmission in Pakistan
- List attributable risk of acquiring HIV per high-risk exposure
- Discuss the context of 'outbreaks' in Pakistan
- Identify the lack of knowledge on 'high' prevalence districts

HIV can affect anyone regardless of sexual orientation, race, ethnicity, gender, age or where they live. However certain groups in Pakistan are more likely to get HIV infection than others due to increased exposure to risk factors.

What is 'general population' in Pakistan?

People with standard/low risk of acquiring HIV because of no high-risk behaviors. This group usually has an HIV prevalence of less than 0.1%.

What is a generalized epidemic?

Epidemics are termed "generalized" if transmission is sustained by sexual behaviour in the general population (typically defined on the basis of population prevalence of >1%). Eg. Southern and parts of eastern Africa have 'generalized' epidemics.

What is a 'Key Population'/'High-Risk Group' in Pakistan?

Key Populations (KP) are defined groups in the population who due to specific higher-risk behaviors, are at higher risk of acquiring HIV infection irrespective of the epidemic type or local context. KPs generally have a high prevalence of HIV and have high potential for transmission of infection due to repeated high-risk behaviors. They may also have legal and social issues which contribute to risk of getting infected through poor access to preventive and therapeutic resources.

Examples of KP/HRGs in Pakistan include Intravenous Drug users (due to contaminated needle-sharing), male and female and transgender sex workers (repeated unprotected sexual exposure) and Men who have Sex with Men (repeated unprotected sexual exposure). Both terms are used interchangeably.

What is a concentrated epidemic?

Epidemics are termed 'concentrated' if transmission largely occurs in clearly defined high risk groups such as men who have sex with men (MSM), people who inject drugs (PWIDs) and sex workers (SWs) eg. The epidemic in Pakistan is categorized as a 'concentrated epidemic' in Key Populations (meaning: prevalence in KPs >1%).

What is a 'vulnerable' population in Pakistan?

People in the population whose living conditions are prone to factors which place them at risk of contracting HIV but not 'as high' as 'Key Populations'. Examples in Pakistan include long-distance drivers, displaced populations, deportees, immigrants, adolescents or orphans on the street (street children), women and children with repeated exposure to unsafe injection apparatuses/blood transfusion in high prevalence districts.

What is a 'bridging' population in Pakistan?

People who may or may not belong to Key Populations but have the potential to act as a 'bridge' for introducing HIV infection into the general population. Classically this group was composed of spouses, partners, clients or those who network with KPs (overlapping high-risk behaviors). Example: a bisexual MSM who has had sex or shared needle with an IDU may act as 'bridge' for transmission of HIV to his spouse and children or male sexual partner, a Pakistani deportee from Middle East who has had sexual exposure to a female or male sex worker may act as 'bridge' for transmission to his wife and children, street youth with exposure to IDU or sexual abuse may act as 'bridge' when sharing needle with non-street youth.

Bridging in the context of horizontal transmission (unsafe injections) is not well understood in Pakistan.

Modes of HIV Transmission in Pakistan

Multi-modal Transmission of HIV holds true for Pakistan too like the rest of the world.

Adult men, adult women and transgender individuals can acquire the infection by the following routes

Multi-modal Transmission of HIV holds true for Pakistan too like the rest of the world.

Adult men, adult women and transgender individuals can acquire the infection by the following routes:

1. Sexual transmission
    a. Unprotected sex with an infected individual
2. Horizontal Transmission
    a. Unsafe Blood Transfusion from an infected individual
    b. Minor or major surgical procedures with unsterilized instruments
    c. Repeated needle-sharing with an infected individual
3. Vertical Transmission

a. Born to an infected mother who was undiagnosed and/or untreated during pregnancy or puerperium

Children (0 to less than 18 years) can acquire the infection by the following routes:

1. Horizontal Transmission

Unsafe Blood Transfusion from an infected adult

Repeated exposure to contaminated injection and infusion apparatus used for medications and intravenous fluids as part of medical treatment

2. Vertical Transmission

a. In-utero or peripartum transmission from infected mother who was undiagnosed and/or untreated during pregnancy

b. Breastfeeding by an infected mother who is undiagnosed and/or untreated and/or on treatment but not virally suppressed

3. Sexual Transmission

a. Unprotected sex (± abuse) with an infected adult remains a largely theoretic but nevertheless important risk factor to explore in positive children

Each exposure above has an attributable risk of HIV acquisition per episode. Repeated episodes multiply risk of acquisition.

Table 1: Attributable Risk of Acquiring HIV per exposure

Type of Contact	Risk per episode
Vertical (no prophylaxis)	24%
Blood Transfusion 1 (no. units transfused) 10 20	 1/99000 1/10000 1/5000
Receptive Anal intercourse	1%
IDU Needle sharing	0.67%
Percutaneous (blood)	0.3%
Receptive vaginal intercourse	0.1-0.2%
Mucocutaneous (blood)	0.09%
Insertive anal intercourse	0.06%
Receptive oral intercourse (male)	0.06%
Insertive vaginal intercourse	0.03-0.14%

Prevalence in General Population

Pakistan has an estimated population of 231 million, one of the highest population growth rates (1.7% annual growth since 2020) and one of the highest fertility Rates (3.4 children per woman) in South Asia. No population-based HIV prevalence survey has been done however estimated prevalence in general population in Pakistan is 0.2%.

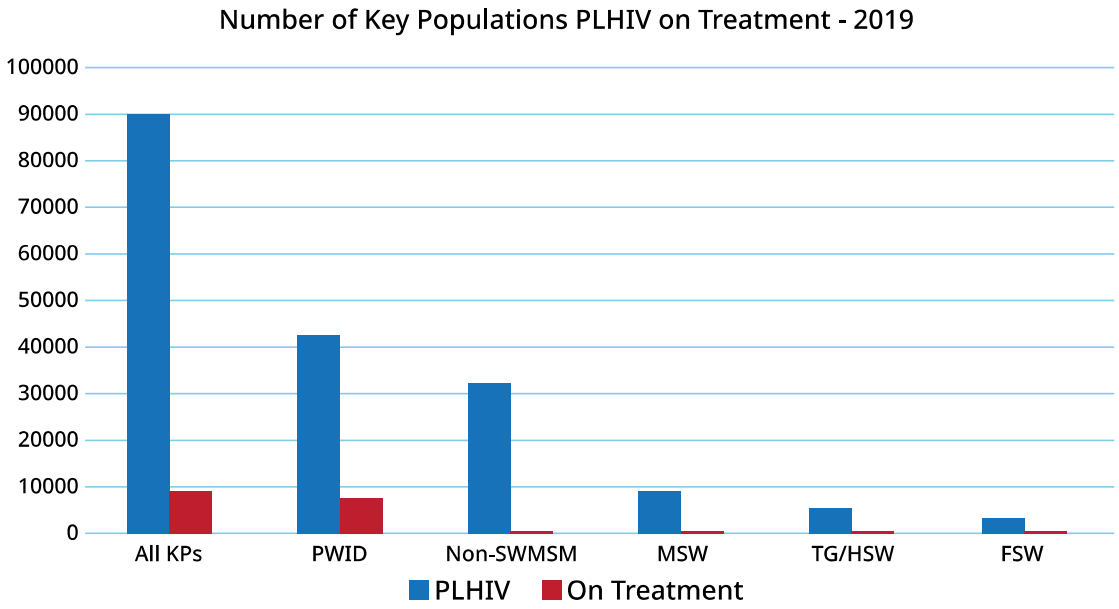
Concentrated Epidemic in Key Populations

Pakistan has a concentrated epidemic in its Key Populations (prevalence >1% in KPs).

According to Pakistan's fifth Integrated Biological and Behavioral Surveillance Round (2016-2017), HIV prevalence is rising steadily among key populations, including PWIDs (38.4%), transgender sex workers (7.5%), transgender individuals (7.1%), male sex workers (5.6%), men who have sex with men (5.4%), and female sex workers (2.2%). (10) Sex workers (especially female) are experiencing the fastest increase in prevalence.

Despite these alarming trends, treatment coverage remains critically low at 12.5% of estimated KPs, and prevention program coverage varies significantly, from a mere 3% for non-sex worker men who have sex with men to 27-29% for PWIDs, underscoring the insufficient impact on controlling the epidemic.(11)

Figure 1: Number of Key Populations PLHIV on Treatment 2019



Fifty-three percent of total estimated 270000 PLHIV are from key populations: 25 % among Men who have sex with men (MSM), 24% People who inject drugs (PWIDs), 2% female sex workers (FSWs), 2% transgender (TGs).

The HIV epidemic in Pakistan follows the Asian Epidemic Model (AEM) pattern, where initial stabilization among people who inject drugs (PWIDs) is now overshadowed by rising transmission through sexual networks and bridging groups into the general population. (7)

Where are 'new infections' happening in Pakistan?

In 2019, 77% of new infections occurred through male-to-male sex (45%), needle sharing among PWID (26%), and sex work (6%). A further 19% of new infections were likely transmitted from married MSM, PWID, and clients of sex workers to their female spouses. This means that, according to the model, currently 90% of transmissions are coming from key populations and sex worker clients and, the majority of these transmissions are occurring in the context of male-to-male sex and needle-sharing for drug use.

Programmatic coverage of Key Populations, however, remains abysmally poor.

Figure 2 New Infections by Mode of Transmission (2019)

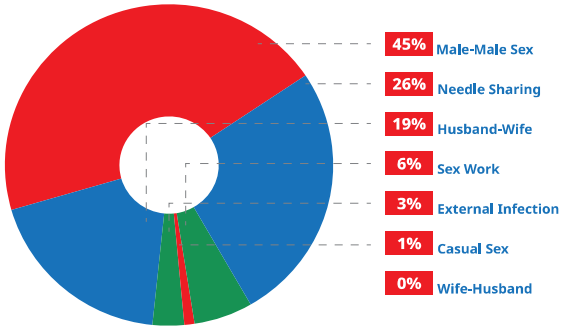


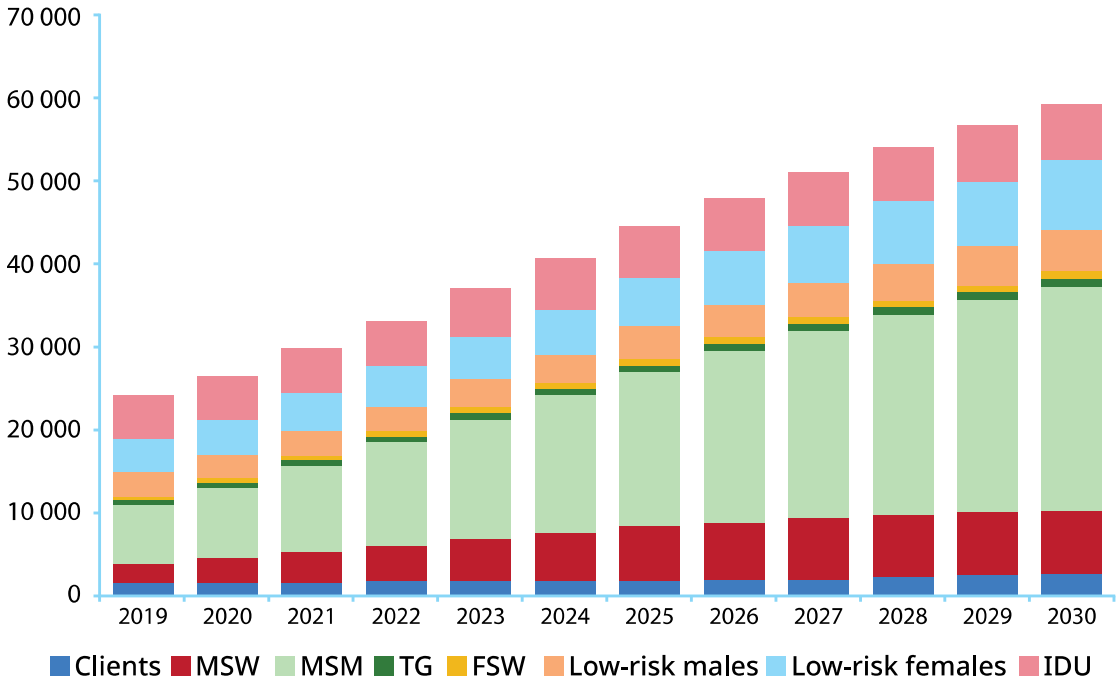
Table 2: Coverage of HIV Care in consecutive Pakistan AIDS Strategies 2-4

Key PAS 3 Indicators	2015 (PAS 2)*	2019 (PAS 3)**		2025 (PAS 4)***
	Achieved%	Target%	Achieved%	Target %
% PWID reached with HIV prevention	18	44	29	73%
% MSM (now-SW) reached with HIV prevention	4	19	9	70%
% MSW reached with HIV prevention	15	43	23	86%
% TG reached with HIV prevention	17	44	27	86%
% FSW reached with HIV prevention	8	33	4	76%
% People living with HIV currently receiving ART	7	27	12	72%

- Pakistan AIDS Strategy 2: covered activities 2007-2012
- Pakistan AIDS Strategy 3: covered activities 2015-2021
- Pakistan AIDS Strategy 4: covers activities 2021-2025

Given this coverage, and without any new effort to achieve key population programme scale-up, the model below projects the distribution of new infections to increase as follows:

Figure 3 Annual New HIV Infections: by risk population, 2019-2030
Melesse et al. JOGH 2018, 8:1



This modeling exercise has shown that the proportion of new infections accounted for by MSM increases significantly. This is why the low coverage of this population is of great concern. As the 'new' epidemic driver in Pakistan, meaningful research to increase understanding of this population, its dynamics, its barriers to access, and how to tailor interventions to its needs is of national priority.

Attempts to gauge incidence and prevalence among KPs have been made through modeling exercises. Prevalence among all KPs in Pakistan is projected to increase from 16% in 2015 to 25% in 2025.

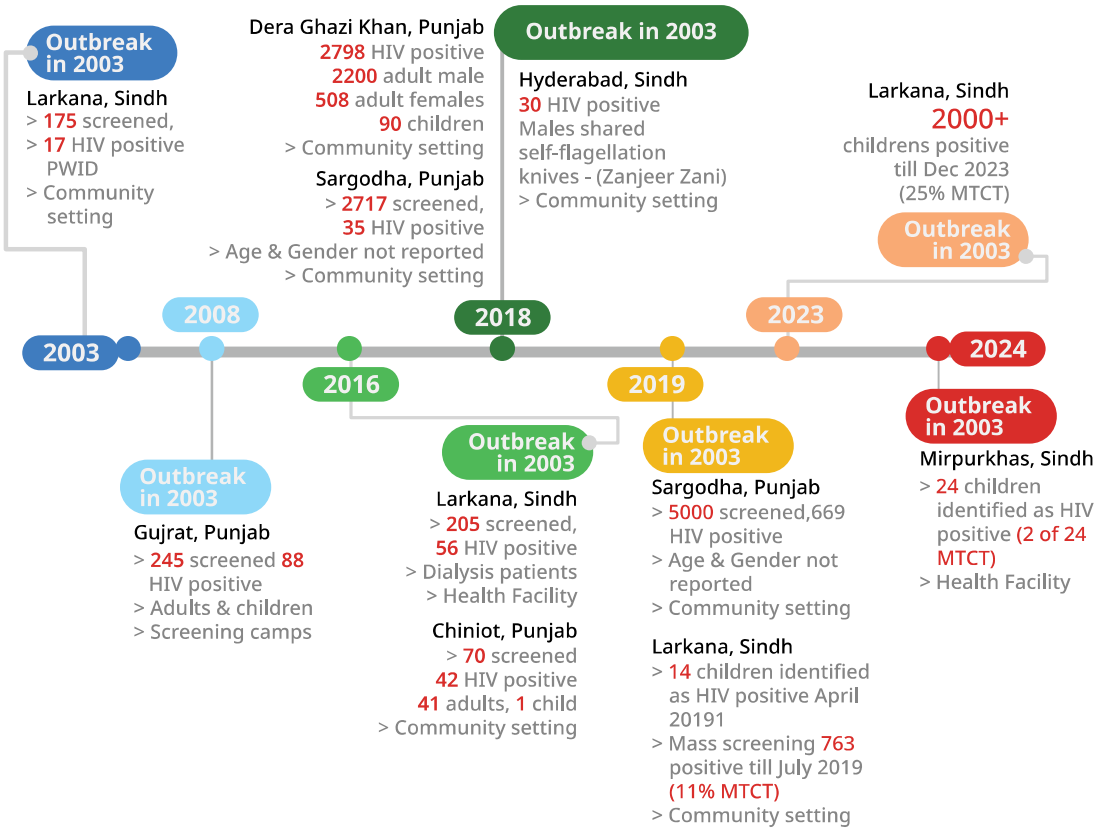
Similarly, HIV incidence among all KPs combined was projected to increase rising from 15 in 2015 to 18 per 1000 person-years by 2025. The increase is attributed to rising incidence among H/MSWs and FSWs.

Rising Incidents of Bridging and Outbreaks in General Population

Of the total estimated number of PLHHIV in Pakistan, **47% PLHIV** belong to either 'bridging' populations (non-key populations with close proximity to key populations- spouse/sexual partner/ needle-sharer belonging to KP) or belonging to 'general' population (no known risk factor identified).

The past decade has shown an increase in parenteral outbreaks of HIV in districts with a high prevalence of HIV in Key Populations.

Figure 4: Parenteral HIV Outbreaks in Pakistan



The most devastating example of bridging into the general population was the 2019 Larkana Outbreak where a large number of children tested positive (only 9% had positive mothers). Women and children are now considered a 'vulnerable' group in Pakistan especially in districts where the epidemic among Key populations is not in control and bridging populations exist. This is because of the 'higher than standard' risk of HIV acquisition associated with their health-seeking behavior (exposure to contaminated needles, blood transfusions, surgical procedures including childbirth with unsterilized instruments) especially if they reside in districts with high HIV prevalence among Key Populations. There is no data on population-based prevalence among the general population in Pakistan.

Table 3 Districts in Pakistan with the highest proportion of positive HIV testing (the order reflects the availability of testing rather than the prevalence in area)

Sindh	Punjab	Federal	KPK and GB	Baluchistan
Larkana	Lahore	Islamabad	Peshawar	Quetta
Karachi Central	Faisalabad		Mardan	Pishin
Karachi South	Gujrat		Swat	Kila Abdullah
Karachi West	Sargodha		Charsadda	Jafferabad
Hyderabad	Rawalpindi		Lakki Marwat	Loralai
Korangi	Sheikhupura		North Waziristan	Zhob
Malir	Gujranwala		Lower Dir	Ziarat
Dadu	Multan		Swabi	Kila Saifullah
Shikarpur	DG Khan		Abbottabad	Nushki
Qambar-Shahdad	Kasur		Kohat	
Karachi East	Bahawalpur		Nowshera	
Jacobabad	Sahiwal		Mansehra	
Khairpur	Okara		Khyber Agency	

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Chapter 02

HIV Testing and Counselling (HTC)

Learning Objectives:

The learner should be able to

- Understand principles of counselling (5Cs)
    - Consent, confidentiality, counseling, correct test results, and connections to prevention, treatment, care, and services
- **Discuss** the correct HIV test and timing of the **test for the patient**
- Interpret HIV test results correctly
- **Recall** Risk-based Testing criteria
    - Children
    - Women of Reproductive Age (WRA)
- Understand **the** concept of Early Infant Diagnosis (EID)

Ideally, all forms of HIV testing and **counseling** even for a child with HIV should adhere to the five C's:

Consent, confidentiality, counseling, correct test results, and connections to prevention, treatment, care, and services.

Guiding Principles:

1. Consent:

The age of consent for HIV Testing is 18 years.

For testing children under this age, consent has to be sought from their parents or guardians. The parent/guardian has the right to decline or defer the test (opt-out approach).

Caveat: The HIV Prevention and Treatment Act 2007 protects and does not allow screening of children when lodged in government facilities including crisis **centers**, orphanages, Darul Aman, prisons, etc.

Information **that** is needed by parents/guardians before they consent on the child's behalf should cover all/some of the following:

What is HIV? (a viral infection which can enter the body and remain in the body for a long time)

How does HIV infect children? (Enters the body through contaminated injections/blood/vertical transmission/reasons we were unable to find)

How does HIV affect children? (Weakens child's ability to fight infections so children with HIV can be completely well but get sicker and sicker over years)

How will the test be done? (A blood sample **collected** from a vein, preferably **the** mother will also be tested if **the** child is positive)

What will a positive test mean? (The child needs to be registered at the nearest ART Treatment Center and started on HIV medicines after additional investigations)

What will a negative test mean? (This child is not infected but needs to be careful about risk factors for getting HIV (**eg.** repeated injections, repeated blood transfusions)

What will an indeterminate test mean? (This means we could not confirm if the child was truly positive or negative and need repeat testing in two weeks to confirm negative status)

2. Confidentiality

HIV testing and counseling services are confidential. In other words, the HIV testing and counseling provided will not be disclosed to anyone else without the expressed consent of the person being tested. Sometimes in clinics, a separate space is not available for a confidential conversation. Physicians can customize their facilities to provide as safe an environment to their patients as possible. Disclosure to children under 18 about their HIV status should only be made after the consent of the parents/guardians.

3: Counselling

While written consent is not required, **counseling** must still be performed regarding risk reduction behavior and linking to care. Extensive pre-test counseling **is not** required; however, pre-test information should be provided regarding the benefits of the tests and the available services for HIV. Children and their parents must also be allowed to ask questions and clarify any concerns. Parents with children who test positive should be **counseled** regarding the disease, the need for maternal and family testing, and the potential of encountering stigma on disclosure within **the** wider family, community**,** and school circles and linkages to care for rapid initiation of therapy. The messages must be clear and concise and repeated. The parents must be allowed to ask any questions worrying them.

4: Correct test results

HIV testing and counselling providers should strive to provide high-quality testing services, and quality assurance mechanisms should be in place to ensure the provision of correct test results. Physicians ordering the tests should consider age of the child and potential interpretation of the test done (Table 4).

Table 4 HIV Testing (timing, type of test, purpose).

Who	When	How	Purpose
HIV-exposed infant	As soon as possible after birth if high risk of transmission	Viral Load test	Early Infant Diagnosis. To confirm positive diagnosis as soon as possible to facilitate decision making (shifting from 'triple prophylaxis' to ART)
	At 6 weeks if standard risk of transmission	Viral Load test	Early Infant Diagnosis. To confirm negative diagnosis (within 2 months of age))
	At 9 months	Viral Load test	To re-confirm the negative HIV status
	At 18 months of age or 3 months after cessation of breastfeeding, whichever is later	RDT (as per WHO algorithm)	To re-confirm the negative status at cessation of remaining risk factor (breastfeeding)
Infant or child suspected of HIV	As soon as clinical suspicion	Viral Load test if <18 months of age RDT if ≥ 18 months of age	To diagnose HIV infection
Adolescent or adult suspected of HIV	As soon as clinical suspicion	RDT	To diagnose HIV infection
Woman of Reproductive Age suspected of HIV	As soon as possible	RDT	To diagnose HIV infection

Quality assurance of diagnostic kits used may include both internal and external quality assurance mechanisms and should include support from the national reference laboratory as and when needed.

Care must be taken to use WHO-prequalified test kits in the order recommended

Connections to prevention, treatment, and care services

Connections to prevention, treatment, and care services should include the provision of effective referral to appropriate follow-up services as indicated, including long-term prevention and treatment support. For reference, download Table 4: For Linkage Services-ART Centers, from: https://www.nacp.gov.pk/whatwedo/treatment.html)

Retesting before enrolment in care

Given the consequences of HIV diagnosis and treatment, all people who are diagnosed to be HIV positive before enrolment in HIV care should be retested to verify their status. This will prevent the rare cases in which people may be misdiagnosed due to possible technical or clerical errors (including

specimen mix-up through mislabeling and transcription errors) as well as a random error (either by the provider or the test device). Retesting should be done on a new sample, ideally at the treatment center.

Who and when to test

HIV Risk based Testing and Counselling in infants, children and adolescents

Children (ages 0-18 years) are a 'vulnerable' group in Pakistan due to excessive exposure to unsafe injections (injectable medications/fluids) and unsafe blood transfusions. The vertical transmission rate in children in Pakistan is not known.

Universal testing for children is not recommended nor implemented in the country.

Despite lack of a validated algorithm, we strongly recommend testing children for HIV if there is a history of >1 of the following:

- Mother is known HIV+
- Any family member is HIV+ (same household)
- Mother or father belong to KP (IDU, MSM, Sex worker) OR have died recently from severe acute illness regardless of HIV status
- Child is a resident of areas with prior outbreak
- Child is diagnosed or being treated empirically for Tuberculosis
- Child is diagnosed with Hepatitis B or C
- Child has had minor or major surgery
- Child has had blood transfusions (≥1)
- Child has recurrent illnesses or acute moderate to severe weight loss
- Child has uncommon opportunistic infections suggesting immune compromise

HIV Risk Based Testing and Counselling in Women of Reproductive Age (WRA)

Women of reproductive age (15-45) are a 'vulnerable' group in Pakistan. Universal testing for HIV and Syphilis is not implemented throughout the country.

We strongly recommend **universal testing** for HIV/Hepatitis B and Syphilis at least in districts with likelihood of high prevalence (See Chapter 1, Table 3) with the aim for 'triple' elimination of mother to child transmission of three infections during pregnancy or puerperium.

Despite lack of a 'validated' **risk assessment** algorithm, we strongly recommend 'risk-based' testing in WRA for HIV if there is a history of >1 of the following: Spouse is HIV+ or from Key Population (IDU/MSM/Sex worker)

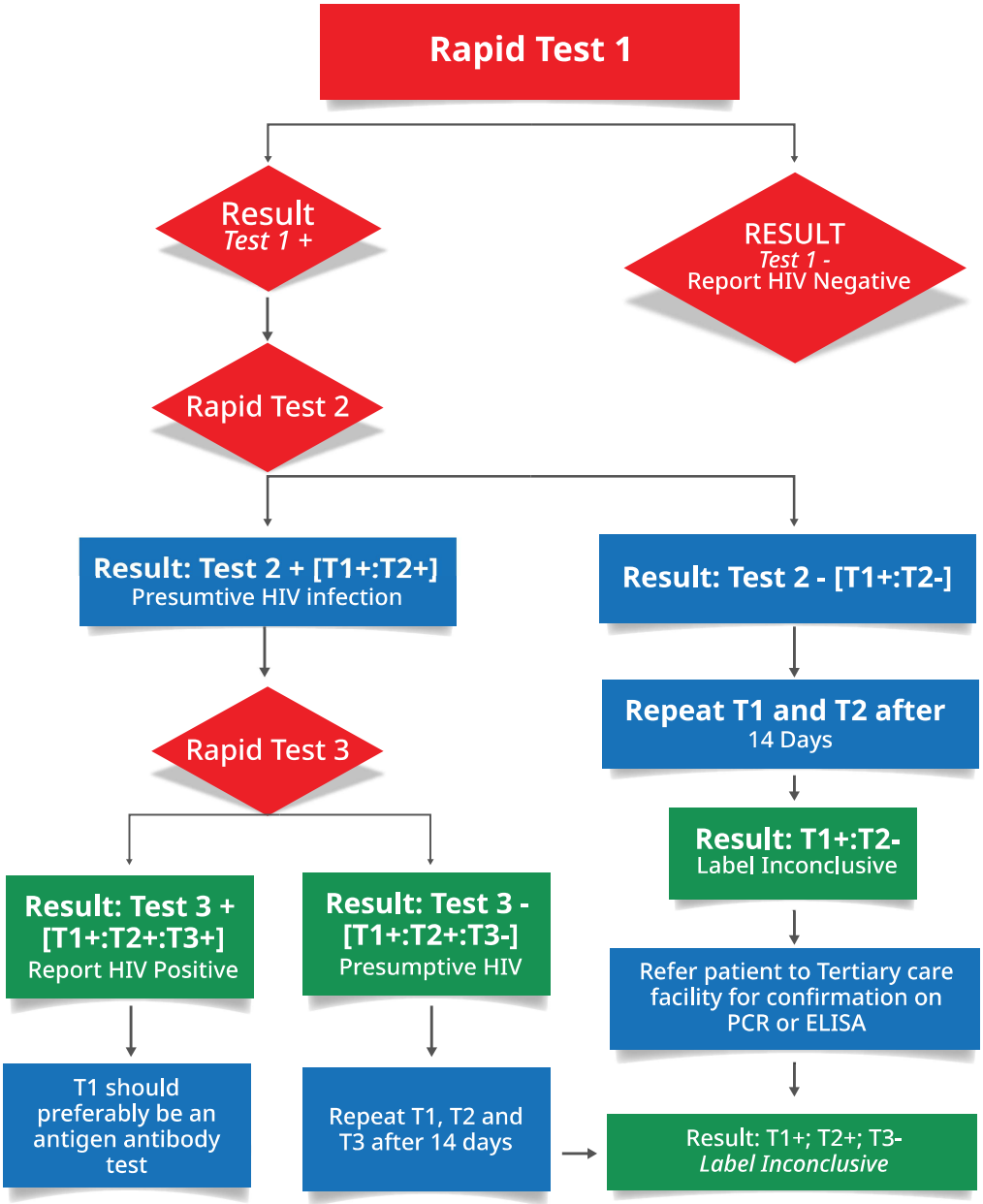
- Any family member is HIV+ (same household, non-spouse)
- Diagnosed or being treated empirically for Tuberculosis
- Diagnosed with Hepatitis B or C

- History of minor or major surgery, obstetric procedures or blood transfusions
- Recurrent illnesses or acute moderate to severe weight loss
- Uncommon opportunistic infections suggesting immune compromise

Diagnostics for HIV

The use of a single HIV test is not sufficient to diagnose HIV infection and must be confirmed. WHO recommends standardized testing strategies to maximize the accuracy of test results while minimizing costs.

Figure 5: Sequence of HIV Testing using Rapid Diagnostic Tests (RDTs)



In each of these strategies, **3** different assays are used to confirm the diagnosis, while any of the available assays may be used, care should be taken so that only WHO-approved kits are used in the correct order. Also, each of the assays should be checking antibodies against a different antigen to prevent shared false non-reactivity or false reactivity.

Finally, if one of the assays is a 4th generation test (i.e. checks for the HIV-1 p24 antigen as well as antibodies against HIV-1/2) this should be the first test done. In Pakistan, the first RDT is generally the Alere Determine (HIV-1/2 Ag/Ab Combo), the second the SD Bioline and the third Uni-Gold.

Early Infant Diagnosis (EID)

Early Infant Diagnosis is a term which specifically refers to HIV diagnostic tests used for a specific population: babies born to HIV-positive women within two months of life.

HIV progresses more quickly in infants. Up to half of vertically infected children can die within the first two years of life in the absence of ART. One of the major barriers in early initiation of ART in all HIV-infected children less than 2 years is poor access to early infant diagnosis.

Functional EID services are an important component of a functional Prevention of Parent to Child Transmission Program (PPTCT). They are associated with lower perinatal infection rates among the successfully 'prophylaxed', earlier initiation of ART (among the early diagnosed), and therefore, lower mortality rates among the infected:

1. Target Population: HIV-exposed infants (regardless of receiving appropriate prophylaxis)
2. Target Outcome: Confirmation of Successful Interruption of Vertical Transmission
3. Target Intervention:
    a. Assess Risk of Vertical Transmission (See Figure 2.2 below)
        i. 'STANDARD-RISK' of HIV transmission during in-utero, labor, or puerperium phase.
        ii. 'HIGH-RISK' of HIV transmission during in-utero, labor, or puerperium phase.
    b. Decide on timing of Viral load testing (preferably HIV DNA/TNA)
        i. First test at 6 weeks for all infants born to HIV-positive mothers with 'STANDARD-RISK' of HIV transmission (virally suppressed, on ART)
        ii. First test AS SOON AS POSSIBLE after birth for all infants born to HIV-positive mothers with 'HIGH-RISK' of HIV transmission (recent diagnosis, inadequate duration of ART, virally unsuppressed)

Figure 6 HIV-exposed infant risk Assessment Algorithm

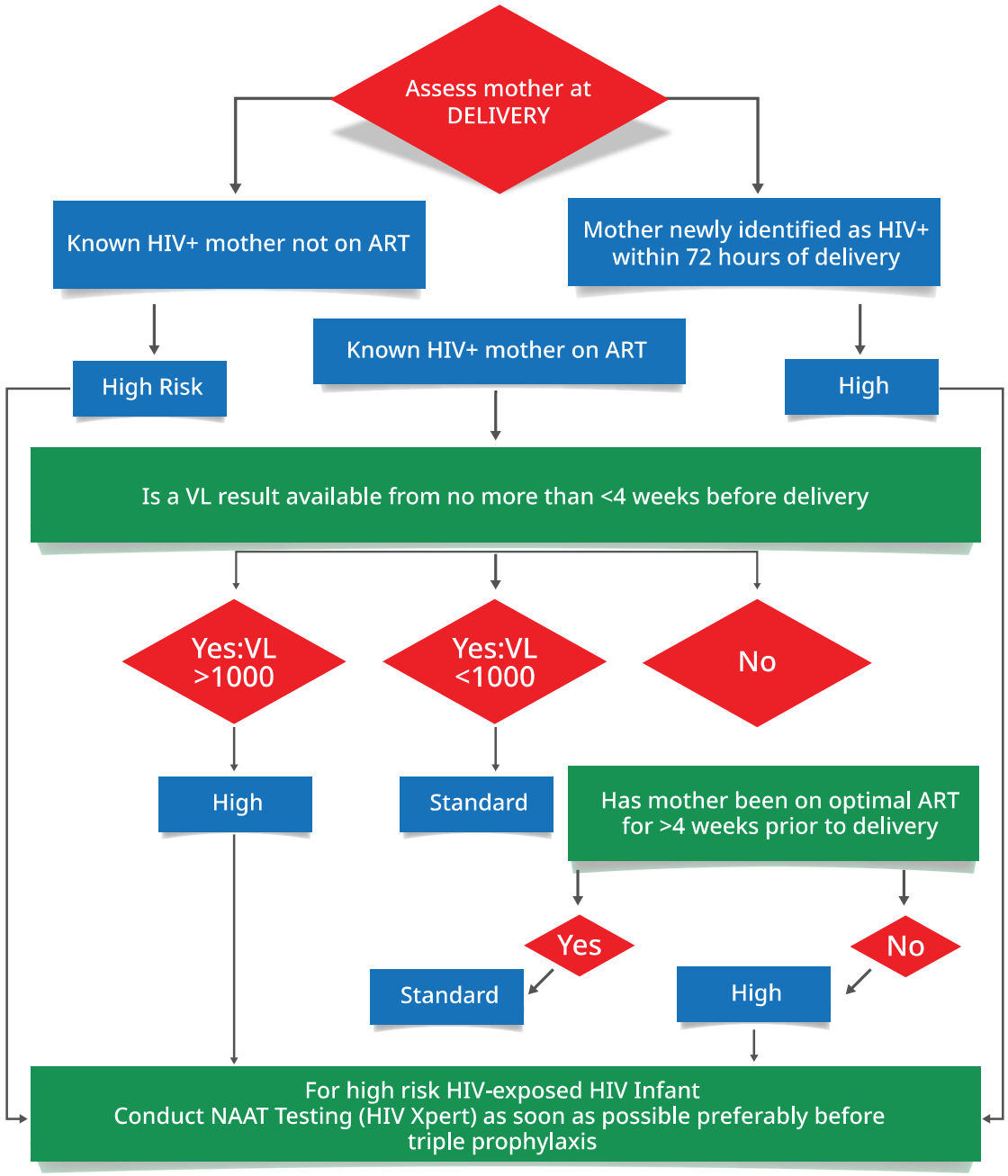
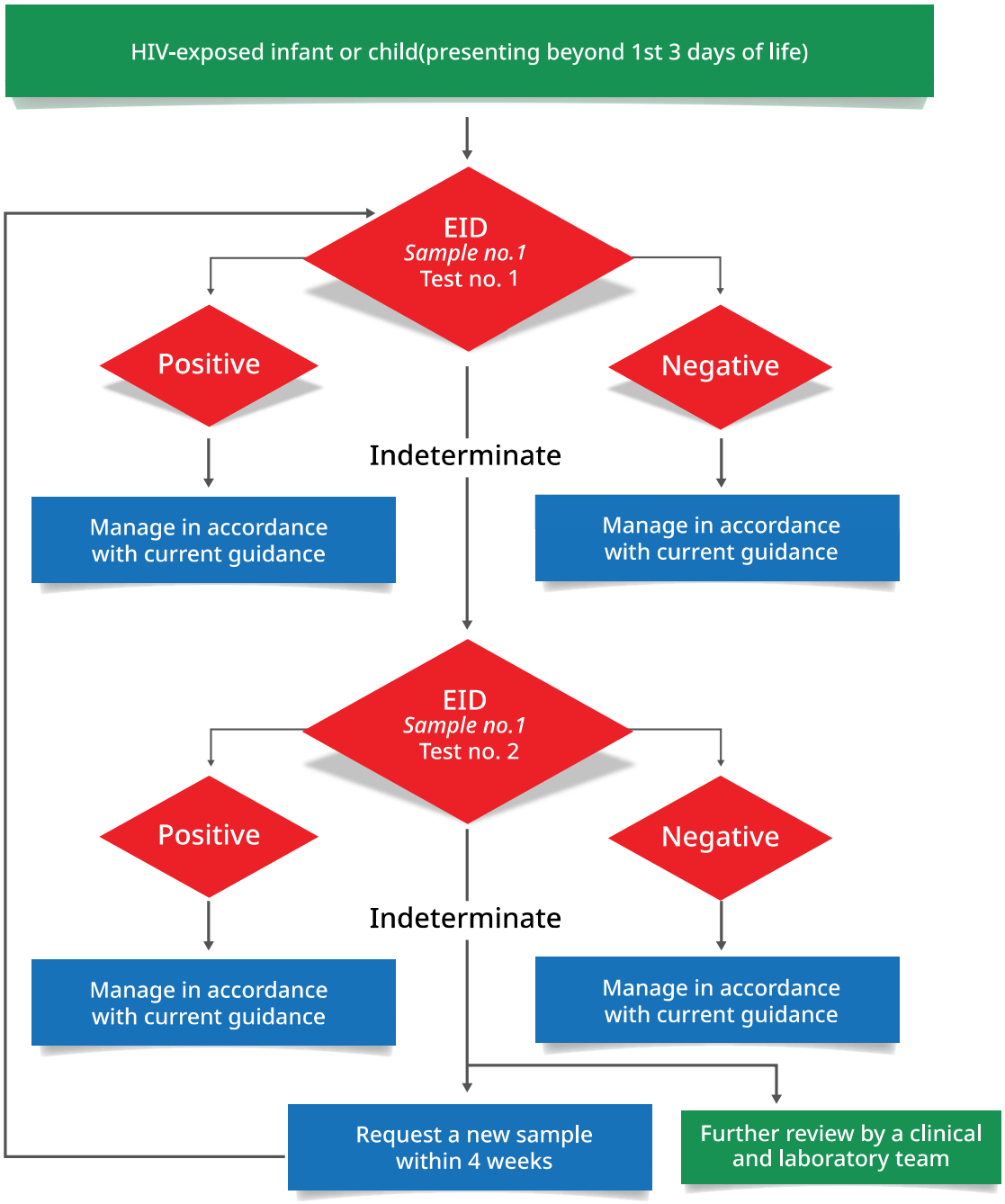


Figure 7 Simplified Early Infant Diagnosis (EID) Algorithm



Notes:

a. See the 2016 WHO consolidated ARV drug guidelines.

b. Do not report as positive or initiate ART but maintain prophylaxis in accordance with current guidance.

c. Repeat samples should be given priority in the laboratory.

d. A team of laboratories, clinicians or pediatricians, complex case experts (if possible) and caregivers should review repeated indeterminate results in two separate samples together with clinical information. Infants should be actively treated to ensure follow-up and retention.

4. Service Delivery:
    a. Testing should ideally be available at point-of-care (POC)
    b. Technique is as per availability through provincial program
        i. Dried Blood Spot Preparation and transportation
        ii. HIV-DNA Testing and Reporting (two positive or negative tests from two different samples collected on two different dates confirm diagnosis)
    c. Test-turn-around should ideally be quick
5. Outcome Overlap of EID Service and PPTCT Program:
    a. Rate of Perinatal Infection
        i. All HIV-exposed infants must be tested at least once within first two months of birth (HIV-exposed infants testing positive/Total tested)
    b. Linkage to care
        i. All HIV-exposed infants who test positive must be initiated on ART as soon as possible
            1. Median duration from EID Reporting to ART Initiation

All infants who undergo EID at 6 weeks or earlier must undergo subsequent testing at 9 months, 18 months or 3 months after cessation of breastfeeding (whichever occurs last). After 18 months of age, an RDT can be used to confirm diagnosis.

Diagnosis in older infants and children

Diagnosis in infants for whom a history of maternal exposure is not known and older children should follow the same principle as outlined in Table 4.

Diagnosis in Adults and Adolescents

The choice of tests used for young infants with HIV exposure (during in-utero life or labour) and older infants and children suspected to have infection can vary (Table 4).

References:

Content modified from Training Workshops for HIV National and Provincial Program Physicians (WHO/UNICEF)

(Mir, Mahmood)

Consolidated Guidelines for Prevention and Treatment of HIV in Pakistan. National AIDS Control Program Pakistan. WHO 2023

Chapter 03

Approach to child with HIV in first clinical visit

Learning Objectives:

The learner should be able to

1. To obtain an HIV-relevant history and exam
    a. probe for family testing status
    b. explore likely mode of transmission
    c. assess growth status
    d. assess nutritional status
    e. assess vaccination coverage gaps
    f. assess the presence of co-infections and/or opportunistic infections (Clinical Staging)
        i. Label as 'Advanced Disease' (Clinical Stages 3-4) or relatively 'Early/Stable disease' (Clinical Stages 1-2)
2. To map out an investigation plan
    a. Baseline Investigations and Special Investigations
        i. Document HBV and HCV positive or negative status
        ii. Screen for Pulmonary TB
        iii. Assess Immunological Status (CD4 absolute count and/or percentage)
        iv. Screen for likely Opportunistic Infections if Clinical Stage 3-4 and/or severe immune suppression (CD4<100)
3. To map out a treatment plan
    a. Patient
        i. ART as per Program
        ii. Prophylaxis (cotrimoxazole preventive therapy (CPT), MAC Prophylaxis, TB Preventive Therapy (TPT)) as per Program
        iii. Macronutrient Supplements (if Severe Acute Malnutrition
        iv. Micronutrient Supplements (Iron, Vitamin D)
        v. Treatment of acute common childhood infections
        vi. Treatment of uncommon opportunistic infections and co-infections
        vii. School and Home Plan (Psychosocial Support)
        viii. Other needs (referral to a higher specialized centre for suspected advanced disese: motor delays etc)
    b. Family
        i. Recommend family testing (mother, father, siblings, extended family in same household) and check for compliance on every visit till complete

History Taking for the Program

The medical files provided by the Program contain deliverables required by the funding agencies (The Global Fund/UNDP) in a sequence relevant to the agency and not the treating physician. For example referral history, diagnostics, family history and HIV exposure history precedes chief complaints followed by physical examination which is again followed by treatment history.

This abrupt jumping from history to examination and back again may obstruct the flow of thought for the treating physician. It is important to be aware of the irregularity in the documentation sequence and make an effort to not miss collecting essential clinical data.

Follow the sequence that makes the best sense to you as a physician and document at the end of the visit if easier. Else follow the sequence in the booklet.

Referral/Family/Personal History

1. Institution/Date of Registration/PLHIV ID/Contact details of Caretakers or guardians

2. Referral: this multiple-choice question gives options such as self, NGO/CBO, hospital, physician, VCT, media, peer, and others.

3. HIV Diagnostics: the physician is called to document the type of testing done and where before the patient arrived at the center. Options include rapid test, ELISA, Western blot and PCR (VL) with lab and date of test space. Aim is to repeat test at the ART center if diagnostics are from a non-program laboratory and especially if quality of its testing is not known.

4. Family History: This option is not applicable to children as it establishes marital status and number of spouses

5. HIV Status of spouse: This table though adult-centered can be used to document family testing status of the child. The first two columns document names of parents and their testing status (positive, negative, untested). The next two columns probe into whether the mother is currently pregnant and eligible and linked to PPTCT services.

6. HIV status of children/siblings: The adjacent table documents important information on siblings including names, ages, HIV status (positive, negative, untested) and whether linked to care is documented. HIV status of half-sibling status should also be documented.

7. Personal History: this portion includes various sub-components:

    a. Education: this indicator is designed for adult patients. Physicians taking care of children sometimes mark parental education here and sometimes 'illiterate' to denote 'not enrolled in school' for children 7 years and above.

Recommendation: please mark primary/secondary/college if applicable to the patient or 'illiterate' to denote 'not enrolled in school' for every child who is 7 years and above until this glitch is amended.

    b. Work: this indicator is designed for adult patients. Physicians taking care of children sometimes mark parental occupation over here.

Recommendation: leave blank for children unless employed.

c. HIV Exposure: this indicator is for all ages. Options are predominantly relevant to adults (sex with male partner, sex with female partner, sex with positive spouse, sex with male sex worker, sex with female sex worker, sex with hijra sex worker, people who inject drugs, blood or blood products, occupational exposure). Options for children are limited (blood/ blood products, mother to child transmission) with no open options to document repeated injection or infusion use or other causes. Unknown/unclear (no evident risky exposures) and how it can be teased apart from 'denial' is again an ambiguous entry.

Recommendation: The physician may end up marking unknown/unclear in the case of children with negative mothers and no history of blood transfusions.

d. Risk Category: Options include General population or Key Population (MSM, MSW, FSW, PWID, TG, HSW). The option 'Vulnerable Population' is classically applied to street children and networks of Key Populations.

Recommendation: All women of reproductive age (WRA) and all children in high prevalence districts are 'vulnerable' and should be marked as such.

e. Substance Abuse: This indicator is for adult patients. Physicians taking care of children mark 'None' here. Other options are cigarette, alcohol, injecting drugs, chars/bhang, others

f. History of STDs: This indicator is for adult patients however should be explored after a discrete sexual exposure history for children, especially unsupervised adolescents. The options are a generic yes and no with additional options if answer is yes (gonorrhea, syphilis, chlamydia, herpes simplex, genital warts, others). Children without a sexual history may present with genital warts with advanced disease.

g. Co-infections/ non-communicable diseases

This section deals with a checklist of co-morbid the status of which is already known and if not, needs to be explored and ruled out.

Infection-related: Pulmonary TB, Extra-pulmonary TB, HBV, HCV, MAC, PCP, Meningitis, Herpes Zoster, Candidiasis, CMV Retinitis

Non-communicable conditions: these mainly address non-communicable conditions peculiar to adults alone (Kaposi Sarcoma, Lymphoma, Ischemic Heart Disease, Stroke, Diabetes, and Hypertension).

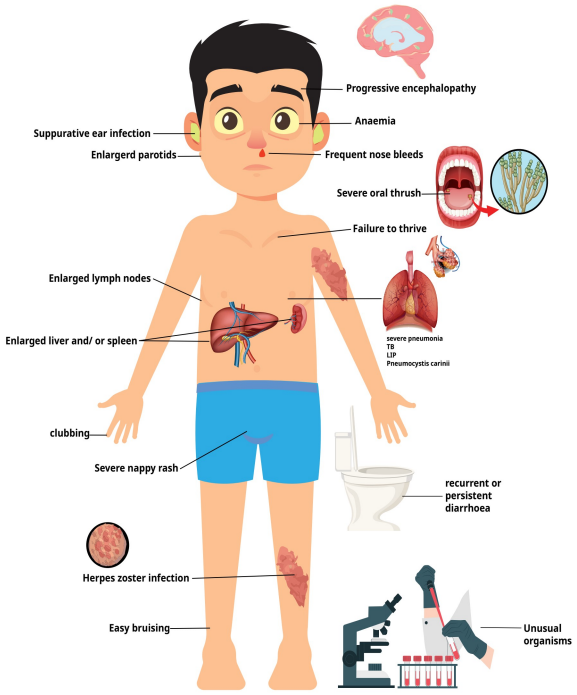
Perinatally-infected adolescents may be at increased risk of non-infectious co-morbidities later in life. These include atherosclerotic vascular disease (AVD), chronic bone disease (CBD), chronic kidney disease (CKD) and chronic lung disease (CLD).

Presenting complaints:

This portion gives closed options and one open option labelled 'Other'.

The patient may have many symptoms. An attempt must be made to decide which symptom prompted patient to seek help and further effort made to find out which complaint is relevant to the physician. Your idea of what is worrying may be different from what bothers the patient the most. For example the parents may be worried about cough during the night but you may find severe acute malnutrition which is not on the parent's radar. Always address what bothers them most else they will go away un-satisfied with visit.

Figure 8 Clinical Features of HIV Infection



In each chief complaint, ask yourself the following questions:

- where is the problem (anatomical site) (barking cough: upper respiratory tract)
- what is the problem (pathological diagnosis) (laryngotracheobronchitis)
- how is it affecting person (physiological and functional diagnosis) (difficulty in breathing, inspiratory sound)
- what caused it (viral (RSV? Adenovirus?)

At this point, the physician should digress from Program Booklet and refer to Table 5 and 6 for further relevant details in history.

Table 5 History-taking sequence

Presenting symptom (PS)
History of the presenting illness (HPI): Details of current illnesses Details of previous similar episodes Extent of functional disability Effect of the illness
Durg and treatment history: Current treatment Drug history (dose, duration, indication, side effects, prescription, over the counter and alternative therapies) Past Treatments Drug allergies or reactions
Past History (PH): Past illnesses Surgical operations (dates, indication, procedure) Menstrual and reproductive history for women Immunizations Blood transfusions (and dates)
Social History (SH): Upbringing and education level Marital status, social support, living conditions, financial conditions Diet and exercise Occupation and hobbies Overseas travel (where and when) Smoking and alcohol use Analgesic and iilicit (street) drug use Mood and sexual history
Family History (FH)
Systems Review (SR)

Table 6 Systems Review in a child with HIV with targeted questions

The Systemic Review	Questions specific to HIV related conditions
Cardiovascular system	Exercise intolerance, excessive sweating, blueness lips or hands
Respiratory system	Shortness of breath, recurrent chest infections, severe pneumonias with oxygen dependence, history of exposure to adult with Pulmonary TB
Genitourinary system	Recurrent dysuria or frequency of urination, history of vaginal or urethral discharge
Hematological Review	Pallor, petechiae (low Hb or white count or platelets on CBC), splenomegaly
Musculoskeletal system	Joint swelling or pain, painful limp, prolonged or intermittent fever
Endocrine system	Tanner staging and onset of puberty, increased thirst and urination, bone pains, history of lipodystrophy
Neurological and mental state	Seizures, motor and cognitive milestone achievement, gait

TB Evaluation

This is a mandatory check on every visit and requires the physician to use a clinical algorithm (incorporating history questions, examination findings and laboratory and radiology tests) to distinguish Tuberculosis disease from TB infection (exposure).

Table 7 Pakistan Pediatric Association Clinical Scoring

Score	1	2	3	4	5
Age	<5				
Close Contact	TB Suggestive	Smear – Clinical TB	Smear + Bacteriologic+		
PEM/SAM	Yes	Not responding to nutritional rehab for 2 months			
Measles Pertussis	3-6 months	<3 months			
HIV		Yes			
Immune compromise	Yes				
Clinical		Suggestive			
Radiological	Non-specific	Suggestive of TB	Strongly suggestive		

Score	1	2	3	4	5
TST	5-10mm		>10mm		
Xpert					+
Granuloma	Non-specific				+ for TB
Score	Interpretation	Suggested Actions			
0-2	Unlikely TB	Investigate other causes			
3-4	Possible TB	Do not treat for TB Manage the presenting symptoms			
5-6	Possible TB	Investigate and exclude other causes of illness Investigation may justify therapy			
7 or more	Probable TB	Confirm (if possible)			

Treatment History

ART: The Medical file now directs the physician from examination towards treatment history where prior ART and its choice and duration are documented. Baseline CD4 is also written down. Questions about current ART include has it been started (yes/no), names of drugs, same as previous regimen or changed, reason for stopping/substituting or switching regimens (toxicity, treatment failure, poor adherence, illness/hospitalization, new drugs available, pregnancy, clinical/immunological/virological failure).

TB Treatment: Categorize child as Pulmonary or Extrapulmonary TB (potential site) and the regimen started. Children are generally non-DOTS. Document where the child is registered (health center, district) TB No if available) start date of treatment and if MDR is suspected or confirmed. Treatment Outcome is documented at the end of therapy as cure, treatment completed, treatment failure, death default and transfer out.

OCPs This applies to adult men and women of reproductive age (15-45 years). The modes used are documented and include condom, OCPs, IUCD, implant, tubal ligation, vasectomy and others.

Gynecological History

For a pediatric patient, this portion is only partially relevant if the baby is an HIV-exposed baby sent for prophylaxis (PPTCT). In this case mark Yes to Referred to PPTCT. Remaining information is not valid for a child.

Growth Assessment of child with HIV

Growth delays are expected in children with HIV. Almost 40% of under 18 months are developmentally delayed. 1/3rd die in first year, 60% in first three years. These children require increased energy, protein

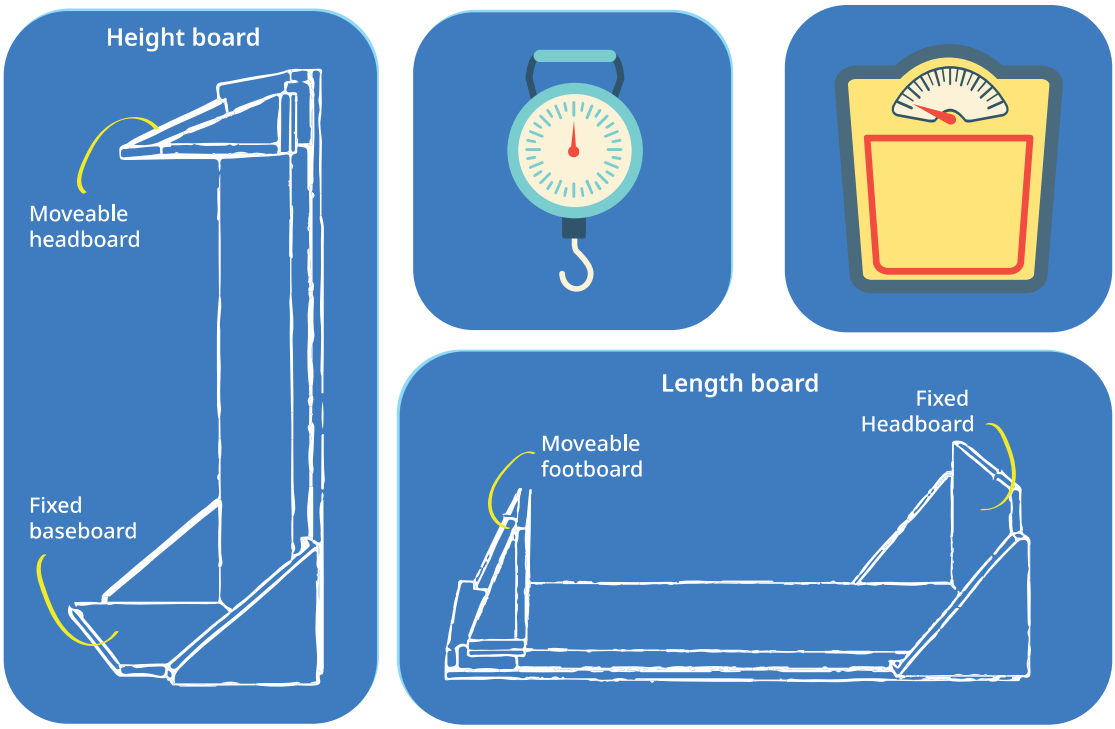
and other micronutrients.

Components of care for children with HIV at each clinical visit include:

- Growth Measurements (Anthropometry):

All children should undergo weight, height, OFC, MUAC assessments at each visit. Tools for measurement include a simple weighting machine, a stadiometer or measuring tape, a arms circumference tape

Figure 9 Anthropometric Tools



- Growth monitoring and documentation

Growth measurements should be plotted appropriately in the growth charts (See end chapter)

- Determining Nutritional Status

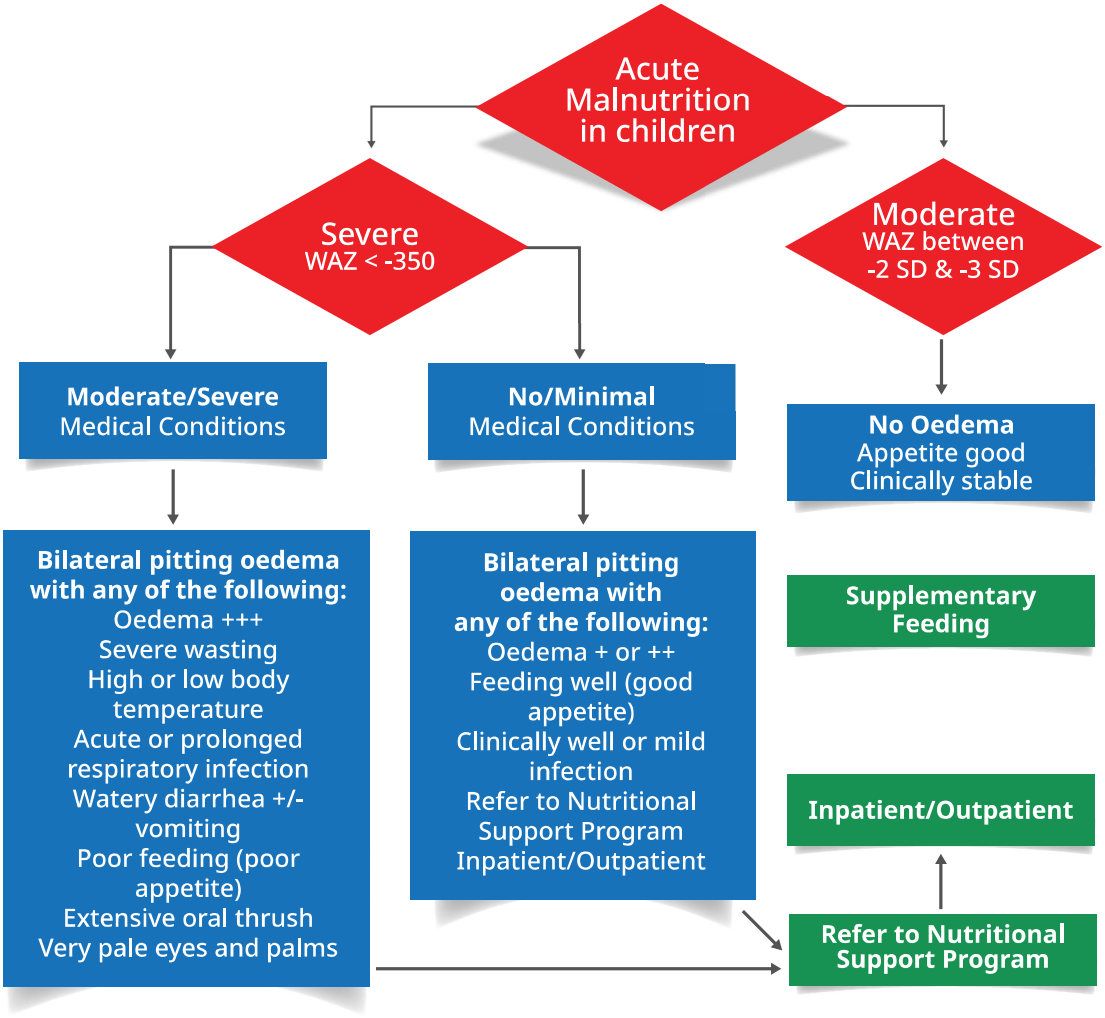
The WHO Classification is used to categorize children with Severe Acute Malnutrition (SAM), Moderate Acute Malnutrition (MAM) or No Malnutrition.

All program physicians should evaluate nutrition as per WHO Classification (Table 8, Fig 10) and assign care plans as suggested by WHO Guideline (Updates on the management of severe acute malnutrition in infants and children. Geneva: World Health Organization; 2013)

Table 8 Malnutrition by WHO Classification (using wasting as a measure)

Assess	Classify	Care Plan
Weight for Age Z score (WAZ) or Weight for Height Z score (WHZ) <-3SD or bilateral pitting oedema or MUAC <115mm(6m-5y) <129mm (5-9y) <160mm (10-14y)	Severe Acute Malnutrition (Wasting)	C
Weight for Age Z score (WAZ) or Weight for Height Z score (WHZ) ≤-2 SD and ≥-3 SD or MUAC ≥115 mm and <125 mm or Reported weight loss or Confirmed weight loss (>5%) since the last visit or Growth curve flattening or Any co-infection or OI	Moderate Acute Malnutrition (Poor weight gain)	B
Weight for Age Z score (WHZ) >-2SD	No Malnutrition	A

Figure 10 Nutritional Assessment of children with HIV



If a child is <5 years and has Severe Acute Malnutrition (weight for age Z score <-3SD or MUAC <110mm) and more than 1 sign of severe illness (pitting edema, wasting, fever, recurrent respiratory of diarrheal infections, extensive oral thrush, poor feeding or severe pallor), **inpatient nutritional rehabilitation** is needed. The physician must refer to the nearest Nutritional Support Program Unit.

If a child is <5 years and qualifies as SAM (weight for age Z score <-3SD or MUAC <110mm) and none or 1 sign of severe illness given above, outpatient nutritional rehabilitation with RUTF is required. Refer to the nearest NSP unit for SAM management at home (Care Plan C).

For children under 5 with MAM (WAZ -2 to -1 SD or MUAC 110-125mm) and no edema (clinically stable, good appetite), counsel on supplementary feeding with Vitamin D, iron supplementation and deworming advice as per Care Plan B. (See Technical note: supplementary foods for the management of moderate acute malnutrition in infants and children 6–59 months of age. WHO 2012)

Nutritional Assessment of Adolescent (10-19 years) with HIV

Weight-for-age reference data are not available beyond age 10 because this indicator does not distinguish between height and body mass in an age period where many children are experiencing

the pubertal growth spurt and may appear as having excess weight (by weight-for-age) when in fact they are just tall. Height-for-age reference data is available in this age. Though BMI is not validated as a true depiction of appropriate growth in South Asian adolescents, it can allow a gross interpretation of overall growth in Children Living with HIV and between 10-19 years.

To calculate BMI use formula: weight in kilograms (kg) divided by height in meters (m) squared (kg/m2)

Obesity: >+2SD (BMI ≥ 30 kg/m2 at 19 years)

Overweight: >+1SD (BMI 25-29.9 kg/m2 at 19 years)
Thinness: <-2SD> (BMI < 18.5 kg/m2 at 19 years)

Severe thinness: <-3SD

Assess Vaccination Gaps:

Use the following immunization schedule to recheck if your patient is up to par with his vaccinations.

Table 9 Schedule of Vaccination for Children Living with HIV (CLHIV)

Visit	Age	EPI Vaccines	Private Company Vaccines
1	At birth	Polio +BCG*	
		*exposed infants BCG if mother is known positive and virally suppressed BCG if mother status is unknown or negative BCG deferred (if mother status is positive and not virally suppressed)	
2	6 weeks	Diphtheria-Pertussis-Tetanus-Hepatitis B-Hemophilus Influenza	Diphtheria-acellular Pertussis-Tetanus-Hepatitis B-Hemophilus Influenza-Inactivated polio
		Pneumococcal Conjugate Vaccine 10	Pneumococcal Conjugate Vaccine 13
		Oral Polio Vaccine	
		Oral Rota Virus Vaccine*	
			Meningococcal Conjugate Vaccine
3	10 weeks	Diphtheria-Pertussis-Tetanus-Hepatitis B-Hemophilus Influenza	Diphtheria-acellular Pertussis-Tetanus-Hepatitis B-Hemophilus Influenza-Inactivated polio
		Pneumococcal Conjugate Vaccine	Pneumococcal Conjugate Vaccine 13
		Oral Polio Vaccine	
		Oral Rota Virus Vaccine*	
4	14 weeks	Diphtheria-Pertussis-Tetanus-Hepatitis B-Hemophilus Influenza	Diphtheria-acellular Pertussis-Tetanus-Hepatitis B-Hemophilus Influenza-Inactivated polio
		Pneumococcal Conjugate Vaccine	Pneumococcal Conjugate Vaccine 13

Visit	Age	EPI Vaccines	Private Company Vaccines
		Oral Polio Vaccine	
		Oral Rota Virus Vaccine*	
		Inactivated Polio Vaccine	Meningococcal Conjugate Vaccine*
5	6 months		Annual Flu vaccine
6	9 months	Measles*	Measles/Mumps/Rubella*
		Typhoid Conjugate Vaccine	
7	12 months	Measles	Measles/Mumps/Rubella*
			Hepatitis A
			Meningococcal Conjugate Vaccine
8	15 months	Pneumococcal Conjugate Vaccine 10	Pneumococcal Conjugate Vaccine 13
			Varicella*
9	18 months	Diphtheria-Pertussis-Tetanus-Hepatitis B-Hemophilus Influenza	Diphtheria-acellular Pertussis-Tetanus-Hepatitis B-Hemophilus Influenza-Inactivated polio
			Hepatitis A
10	>2 years		Typhoid Conjugate Vaccine
11	4-5 years	Diphtheria-Pertussis-Tetanus-Hepatitis B-Hemophilus Influenza	Diphtheria-acellular Pertussis-Tetanus-Hepatitis B-Hemophilus Influenza-Inactivated polio
		Measles*	Measles/Mumps/Rubella*
			Varicella*
		Oral Polio Vaccine	
12	9 years		Human Papilloma Virus Vaccine
	9 years 6 months		Human Papilloma Virus
14	10 years	Tetanus Toxoid	Tdap

*subject to CD4>200cells/mm^3

Clinical Staging Caveat:

All children at each visit should undergo clinical staging **(Table 10)** along with TB screening using the PPA chart score. ART should preferably be deferred for children with a PPA score ≥7 and ATT started. For a PPA score <5, ART can be started and the child followed regularly.

Where available, a CD4 count should be done at the first visit to assess the level of immune suppression. Decisions on the need for prophylaxis (TPT, CPT, infant prophylaxis etc.) can be made during these visits based on clinical and CD4 staging.

Table 10 WHO Staging of HIV Disease in adolescents and children

Clinical Stage 1 Child	Caveat	Clinical Stage 1 Adolescent	Caveat
Asymptomatic		Asymptomatic	
Persistent generalized lymphadenopathy	enlarged lymph nodes in two or more extra-inguinal regions with no apparent underlying cause	Persistent generalized lymphadenopathy	enlarged lymph nodes in two or more extra-inguinal regions with no apparent underlying cause
Clinical Stage 2 Child	**Caveat**	**Clinical Stage 2 Adolescent**	**Caveat**
Unexplained hepatosplenomegaly	examine liver and spleen span (eg in absence of CMV)		
Papular pruritic eruptions		Papular pruritic eruptions	
Seborrhoeic dermatitis		Seborrheic dermatitis	
Fungal nail infections		Fungal nail infections	
Angular cheilitis		Angular cheilitis	
Linear gingival erythema			
Extensive human papillomavirus infection or molluscum infection	Warts or umbilicated lesions (>5 % of BSA)		
Recurrent oral ulcerations	two or more episodes in 6 months	Recurrent oral ulcerations	
Unexplained persistent Parotid enlargement	unilateral or bilateral parotid swelling (just in front of the ear) for ≥ 14 days, with or without associated pain or fever		
Herpes zoster	painful rash with blisters confined to one dermatome on one side	Herpes zoster	

Recurrent or chronic upper respiratory tract infection (otitis media, otorrhoea, sinusitis)	two or more episodes in any 6-month period	*Recurrent respiratory tract infections (sinusitis., tonsillitis, otitis media, pharyngitis)	*3 or more severe episodes in past 12 months
		Moderate unexplained weight loss (<10% of presumed or measured body weight)	*Weight for height z score btw -2 and -3
Clinical Stage 3 Child	**Caveat**	**Clinical Stage 3 Adolescent**	**Caveat**
Unexplained moderate malnutrition not adequately responding to standard therapy	WHZ btw -2 and -3 not responding to Plan B	Unexplained severe weight loss (>10% of presumed or measured body weight)	
Unexplained persistent diarrhea	For 14 days or more	Unexplained chronic diarrhea	for longer than 1 month
Unexplained persistent fever	above 37.5C, intermittent or constant, for longer than 1 month	Unexplained persistent fever	above 37.5C, intermittent or constant, for longer than 1 month
Persistent oral candidiasis	after first 6 months of life	Persistent oral candidiasis	after first 6 months of life
Oral hairy leukoplakia		Oral hairy leukoplakia	
Pulmonary tuberculosis Lymph Node Tuberculosis		Pulmonary Tuberculosis	
Acute necrotizing ulcerative gingivitis or periodontitis		Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis	
Severe recurrent bacterial pneumonia	2 or more episodes in 6 months		
Symptomatic lymphoid interstitial pneumonitis			
Chronic HIV-associated lung disease, including bronchiectasis			
HIV-related cardiomyopathy			
HIV-related nephropathy			

		Recurrent severe presumed bacterial infections (such as empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)	
Unexplained anemia (<8gm/dl), neutropenia (<0.5 x 10^9/l) and/or chronic thrombocytopenia (<50 x 10^9/l)	For more than 1 month	Unexplained anemia (<8gm/dl), neutropenia (<0.5 x 10^9/l) and/or chronic thrombocytopenia (<50 x 10^9/l)	
Clinical Stage 4 Child	**Caveat**	**Clinical Stage 4 Adolescent**	**Caveat**
Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy	WHZ <-3 SD and not responding to Plan A	HIV wasting syndrome	
Pneumocystis (jirovecii) pneumonia	Pneumonia marked by severe dyspnea and hypoxemia	Pneumocystis (jirovecii) pneumonia	
Recurrent severe presumed bacterial infections (such as empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)	2 or more episodes within 1 year	Recurrent severe bacterial pneumonia	
Chronic herpes simplex infection (orolabial, genital or anorectal or cutaneous)	more than 1 month duration	Chronic herpes simplex infection (orolabial, genital or anorectal or cutaneous)	more than 1 month duration
Disseminated or extrapulmonary TB (excluding lymph node)		Extrapulmonary tuberculosis	
Kaposi sarcoma		Kaposi sarcoma	
Oesophageal candidiasis		Esophageal candidiasis (or candidiasis of trachea, bronchi or lungs)	

Symptomatic HIV seropositive infant < 18 months with two or more of the following: oral thrush, severe pneumonia, failure to thrive, severe sepsis[b]	Presumptive diagnosis of stage 4 in seropositive child <18 months must be confirmed with viral load	
Cytomegalovirus retinitis		Cytomegalovirus infection (retinitis or infection of other organs)
Central nervous system toxoplasmosis	After neonatal period	Central nervous system toxoplasmosis
Any disseminated endemic mycosis, including cryptococcal meningitis (e.g. extrapulmonary cryptococcosis, histoplasmosis, coccidiomycosis, penicilliosis)		Extrapulmonary cryptococcosis, including meningitis Chronic isosporiasis Disseminated mycosis (extrapulmonary histoplasmosis, coccidioidomycosis)
Cryptosporidiosis or isosporiasis	with diarrhoea lasting > 1 month	Chronic cryptosporidiosis
Cytomegalovirus infection	onset at age > 1 month in an organ other than liver, spleen or lymph nodes	Cytomegalovirus infection (retinitis or infection of other organs)
Disseminated mycobacterial disease other than TB (MOTT/ NTM)		Disseminated nontuberculous mycobacterial infection
Candida of trachea, bronchi or lungs		Esophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
Acquired HIV-related rectovesical fistula		
Cerebral or B cell non-Hodgkin lymphoma		Lymphoma (cerebral or B-cell non-Hodgkin) Symptomatic HIV-associated nephropathy or cardiomyopathy

		Invasive cervical carcinoma
Progressive multifocal leukoencephalopathy	progressive neurological impairment, microcephaly, delay in achieving developmental milestones, hypertonia or mental confusion	Progressive multifocal leukoencephalopathy
HIV encephalopathy		HIV encephalopathy
Recurrent septicemia (including nontyphoidal Salmonella)		Recurrent septicemia (including nontyphoidal Salmonella)
		Atypical disseminated leishmaniasis

General Physical Examination

This includes vital signs such as BP (mmHg), pulse (b/min) and Temp (□ C). Even though a thorough examination may not be possible in a busy clinic setting, it should be practiced where possible to minimize missing signs which are important.

Skin, Mucous Membranes and Nails:

In addition we should document jaundice (sclera above eyeballs), pallor (palmar and conjunctival), lymph node enlargement, thrush, thyroid enlargement, edema, hydration status (sunken orbits, dry mucus membranes, reduced skin turgor, history of decreased urine), cyanosis, and clubbing (may hint at chronic lung infections or HIV itself).

Systemic Examination

In the Program Booklet, this is an open-ended component with space given for positive findings on examination of systems followed by a box for documenting Clinical Stage.

Opportunistic Infections, Treatment and Prophylaxis

By this time, you will have completed a detailed history, growth assessment, nutritional assessment, vaccination assessment, TB evaluation, general and physical examination and clinical staging. You will need to order tests and rule out opportunistic infections if advanced clinical stage 3-4 or severe immune-suppression (baseline CD4<100).

Refer to chapter on OIs for treatment and three common prophylaxis regimens deployed:

1. Cotrimoxazole Prophylaxis
2. TB Preventive Therapy
3. MAC Prophylaxis

Investigations:

The physician should now organize a baseline set of laboratory and radiology tests before initiation of ART.

Table 11 Routine testing in PLHIV in relation to ART

Who	How often	Test / Evaluation
Baseline before starting ART		
All patients	Once	Mandatory: HIV serology or HIV RNA or DNA (age<2years), HbsAg, HCV Ab, CBC, BUN/Creatinine, LFTs/ALT, CD4, CXR, Mantoux, urine dipstick Optional but preferred: HBsAb

*eGFR can be calculated for children as follows: (0.41 × Height in cm) / Creatinine in mg/dL

Treatment Plan:

The Physician should now collate salient points in history, exam and laboratory and radiology work up which needs to be addressed in the treatment plan.

Definitive Treatment:

ART Regimen should follow principles laid out in Chapter 4.

Supportive Treatment:

Prophylaxis (cotrimoxazole preventive therapy (CPT), MAC Prophylaxis, TB Preventive Therapy (TPT) as per Consolidated Guidelines for HIV Prevention and Treatment in Pakistan 2023

Macronutrient Supplements (if Severe or Moderate Acute Malnutrition)

Micronutrient Supplements (Iron, Vitamin D)

Treatment of acute common childhood infections (See Chapter 6)

Treatment of uncommon opportunistic infections (Chapter 7) and co-infections (See Chapter 5)

School and Home Plan (See Chapter 10)

Referrals to higher specialized centre for suspected advanced disease: motor delays etc)

Family Care: recommend family testing (mother, father, siblings, extended family in same household) and check for compliance on every visit till complete

Table 12 Interpretation of History and Exam and managing Care Plan

Objective1 (History)	Interpretation	Objective 2 (Investigate)	Objective 3 (Treatment Plan)
family testing status	Is HIV status of everyone in the family of index case known? (active case finding using index based testing as strategy)	Offer facility-based testing for untested family members	Link family members to care if positive
likely mode of transmission	If blood disorder requiring repeat transfusions (mitigate future risk for patient)	Send HBsAg & HBsAb and HCV Ab of patient at baseline and repeat HBsAg & HCV Ab every 6 months	Treat Co-I as per guidelines Vaccinate for HBV and HAV
	If history of repeated injections (mitigate future risk for patient but also family members using same healthcare provider)	Offer facility-based testing for all untested (RDTs) as possibility of similar exposure to common source of spread (HCP)	Link family members to care if positive
	If mother is positive or status unknown (mitigate risk of future MTCT)	Test her immediately	Link family members to care if positive
Growth and Nutrition	WHZ and BMIZ are related to malnutrition (poor food quantity and quality) AND advanced HIV disease	Investigate for severe immune-suppression and rule out OIs	ART as per Program Prophylaxis (cotrimoxazole preventive therapy (CPT), MAC Prophylaxis, TB Preventive Therapy (TPT)) as per Program Macronutrient Supplements (if Severe Acute Malnutrition Micronutrient Supplements (Iron, Vitamin D) Treatment of acute common childhood infections Treatment of uncommon opportunistic infections and co-infections School and Home Plan (Psychosocial Support) Other needs (motor delays etc)
Vaccination status	Check age-appropriate coverage AND avoid vaccine-preventable infections	Check CD4 to ensure live vaccines can be given safely	
Co-infections	Screen for TB/HCV/ HBV/STIs	Investigate as per guidelines	
Opportunistic Infections	Screen for relevant OIs	Investigate as per guidelines	
Clinical Staging	Label as 'Advanced Disease' (Clinical Stage 3-4) or relatively 'Early/ Stable disease' (Clinical Stage 1-2)		

Caveats in Care:

Feeding in HIV-exposed or HIV-infected infants:

For infants born to HIV-positive mothers, breastfeeding is recommended for at least 12 months and may continue for up to 24 months or longer, provided the mother adheres to antiretroviral therapy (ART). HIV-positive mothers should exclusively breastfeed for the first six months, introducing complementary foods afterward while continuing breastfeeding. Breastfeeding should only be stopped when a nutritionally adequate and safe alternative is available. Mixed feeding, while not ideal, is not a reason to discontinue breastfeeding if ART is maintained. Alternatives to breastfeeding for infants under six months include commercial infant formula or expressed, heat-treated breast milk. For older infants, alternatives include commercial formula or boiled animal milk, provided alongside a balanced diet. Formula feeding should only be considered when specific conditions are met, including access to safe water, reliable supply, clean preparation, and support from the family and healthcare providers. These criteria ensure that formula feeding is safe, sustainable, and minimizes the risks of malnutrition and diarrheal disease.

Neuro-developmental assessment:

Children with HIV, particularly those diagnosed within the first two years of life, may experience developmental delays, affecting motor and cognitive milestones. It is crucial to assess both motor skills (gross and fine) and cognitive abilities (including vocabulary, speech, and non-verbal skills) at key intervals: 3 months, 6 months, 9 months, and 18 months. If delays are observed, appropriate referrals should be made. The milestone chart at the end of the chapter should be used as a guide for these assessments (Fig 3.17).

Children with Thalassemia Major (TM):

Children with TM and HIV face complex medical challenges. Nearly one-third of pediatric HIV cases in Pakistan are transfusion-related, with key populations including children with TM and bleeding disorders like hemophilia. Managing HIV in these children is difficult due to complications from iron overload and liver dysfunction caused by chronic transfusions, which can exacerbate the toxicities of antiretroviral therapy (ART). Effective management requires collaboration with an infectious disease specialist.

Iron overload in TM leads to multi-organ damage including liver, cardiac, endocrine, and pulmonary dysfunctions. Chelation therapy is critical but must be carefully managed due to its side effects, such as hearing loss and renal dysfunction, which require a multidisciplinary approach. Additionally, iron overload can accelerate HIV progression, making optimal chelation crucial.

Infections are another significant risk for TM patients. Hepatitis B and C are a constant risk with each transfusion. Hepatitis B vaccinations must be optimized and regular screening continued. Those who have undergone splenectomy are particularly vulnerable to severe infections from encapsulated bacteria and other pathogens. Blood-borne infections, such as CMV and Yersinia, pose unique risks in HIV-infected TM patients, necessitating specific preventive measures and treatments. Managing these patients requires vigilance and comprehensive care to address the dual challenges of HIV and Thalassemia Major.

Program Deliverables:

The Program provides the following indicators to Global Fund reflecting Service Delivery for Children with HIV. Center physicians must be mindful of these indicators reflecting each individual patient's care and collectively as a unit's performance.

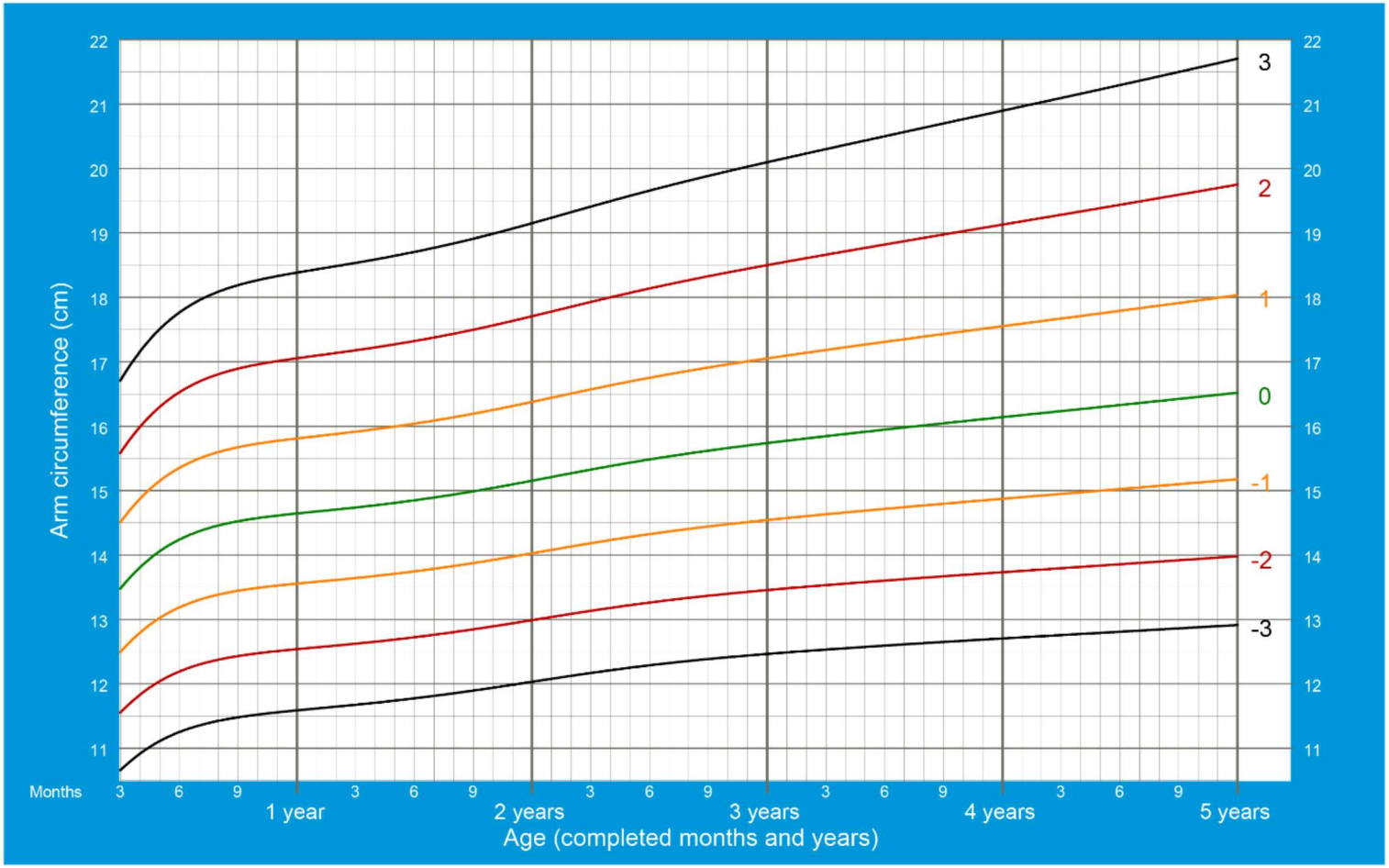
Table 13 Program Indicators reflecting Service Delivery for children with HIV

No	Indicator definition	Indicator for Pediatric ART
1	Identified HIV +ve children	a. Total number of HIV +ve children ever registered in Pediatric ART clinic till beginning of the current month.
		b. Total number alive HIV +ve children ever registered in Pediatric ART clinic till beginning of current month
		c. Total number of new HIV +ve children registered in Pediatric ART clinic in current month
2	Registered HIV+ve children on ART Definition: Children initiated on ART as soon as possible after diagnosis (should be >90%)	a. Total number of alive HIV +ve children ever registered in Pediatric ART clinic till beginning of the current month and on ART
		b. Total number of new HIV +ve children registered in Pediatric ART in current month initiated on ART in current month
3	Registered HIV +ve children on ART and tested for VL at least once in 12 month. Definition: Children initiated on ART should be tested for VL at 3mo, 6mo, 12 mo in first year of ART and minimum once a year while on ART (should be >90%)	a. Total number of alive HIV +ve children ever registered in Pediatric ART clinic till end of the current month and, on ART and, tested for viral load at least once in last 12 months
		b. Total number of alive HIV +ve children ever registered in Pediatric ART and continuing treatment in current month or quarter (depending on quantity of medicine given at each visit)
4	Registered HIV +ve children on ART and tested for VL at least once in 12 month, and virally suppressed (<1000) Definition: Children initiated on ART should be tested for VL at least once a year (guideline says twice a year plus whenever clinical deterioration occurs) and VL should be <1000 (Guideline says undetectable or <20) (should be >90%)	Total number of alive HIV +ve children ever registered in Pediatric ART clinic till end of the current month and, on ART and, tested for viral load once in last 12 months and, VL<1000

Arm circumference-for-age BOYS

3 months to 5 years (z-scores)

World Health Organization

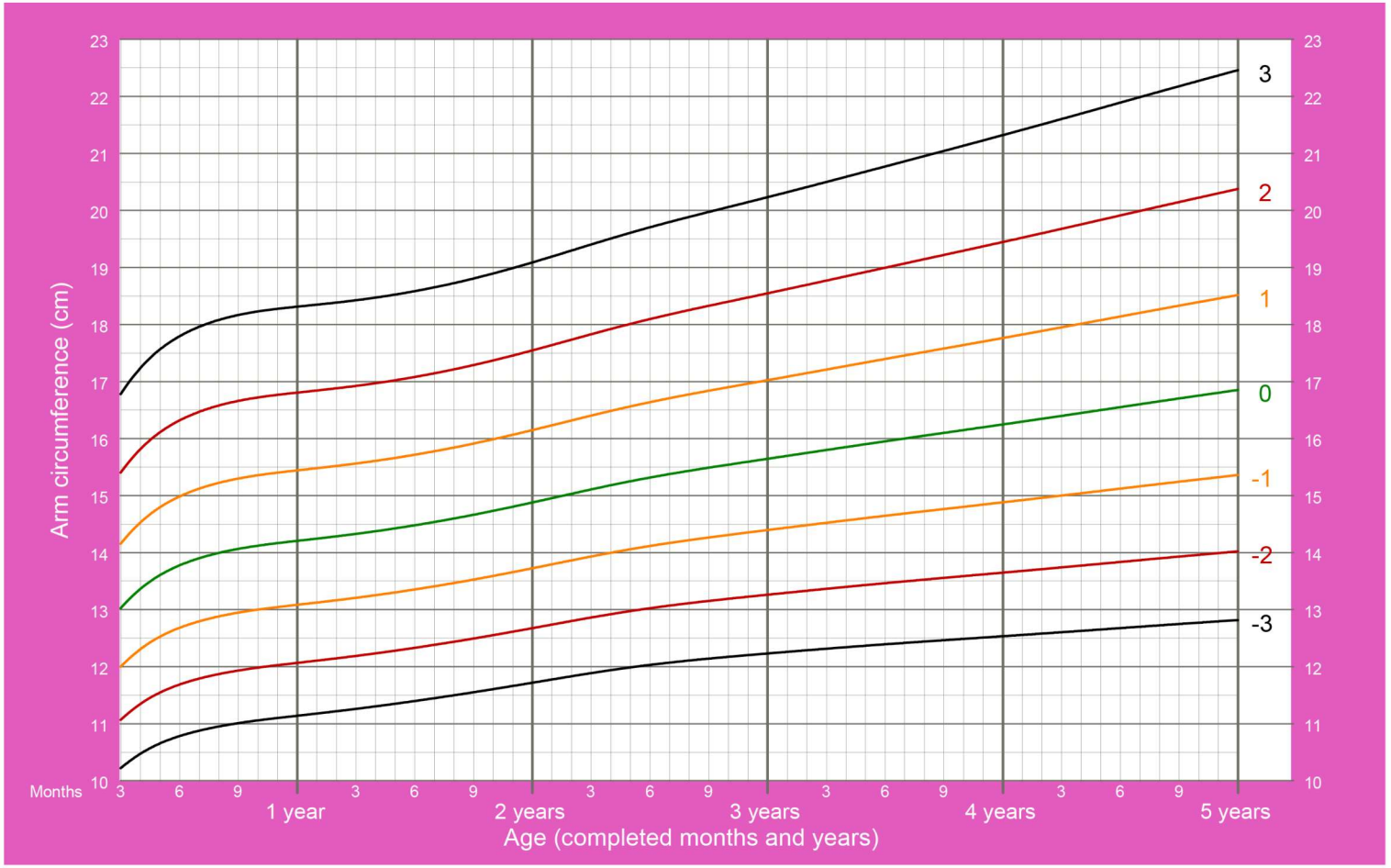


WHO Child Growth Standards

Arm circumference-for-age GIRLS

3 months to 5 years (z-scores)

World Health Organization

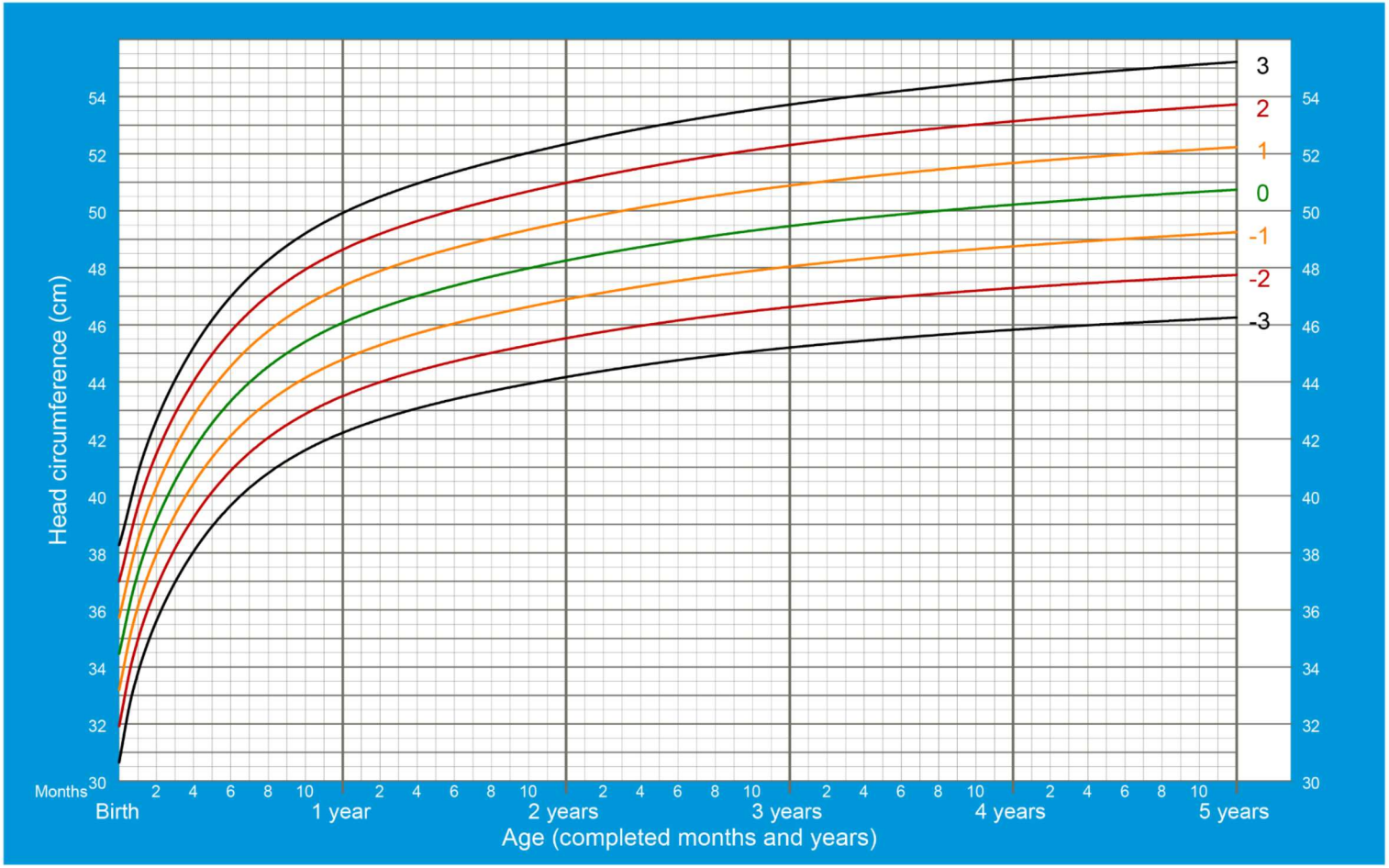


WHO Child Growth Standards

Head circumference-for-age BOYS

Birth to 5 years (z-scores)

World Health Organization

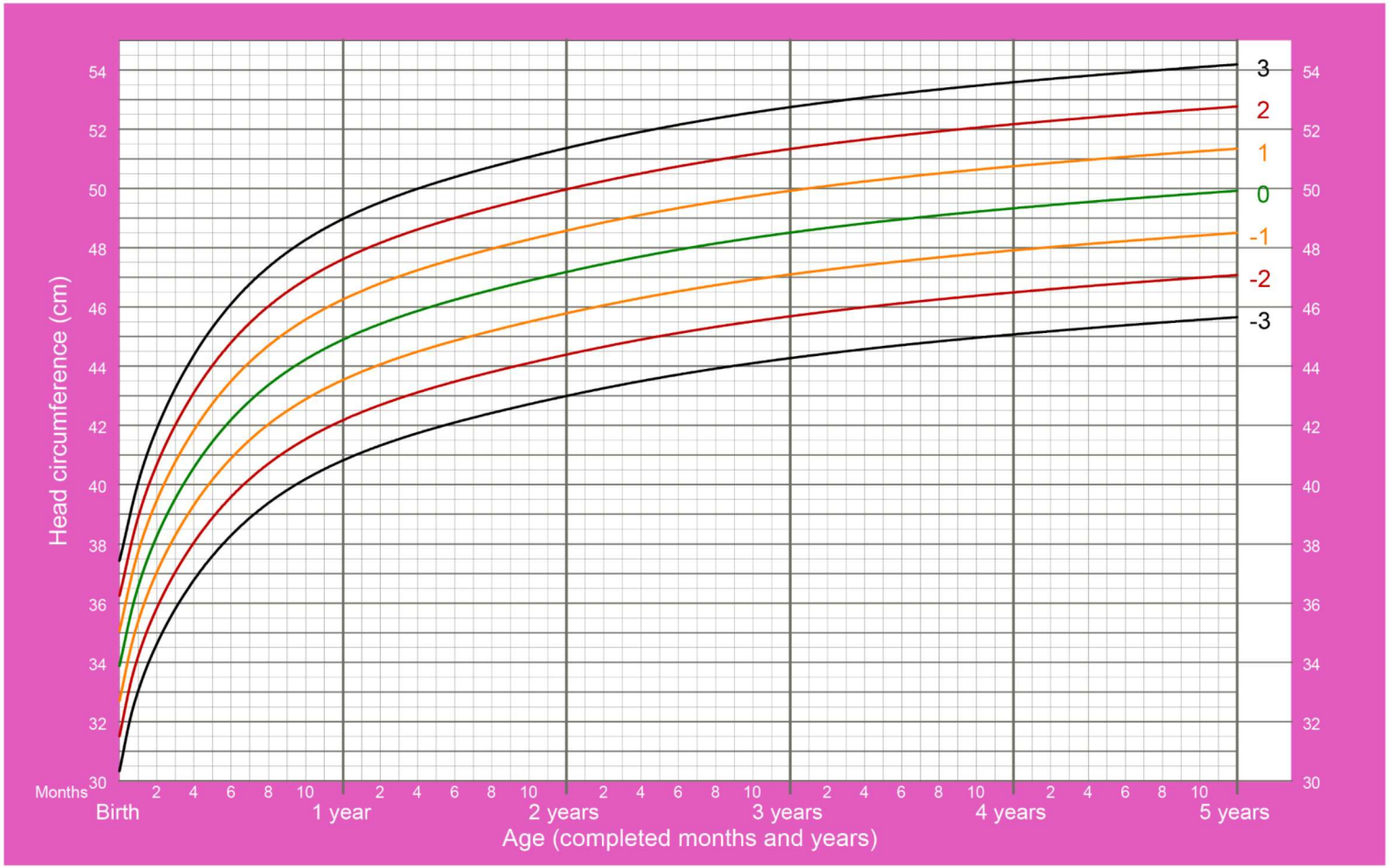


WHO Child Growth Standards

Head circumference-for-age GIRLS

World Health Organization

Birth to 5 years (z-scores)

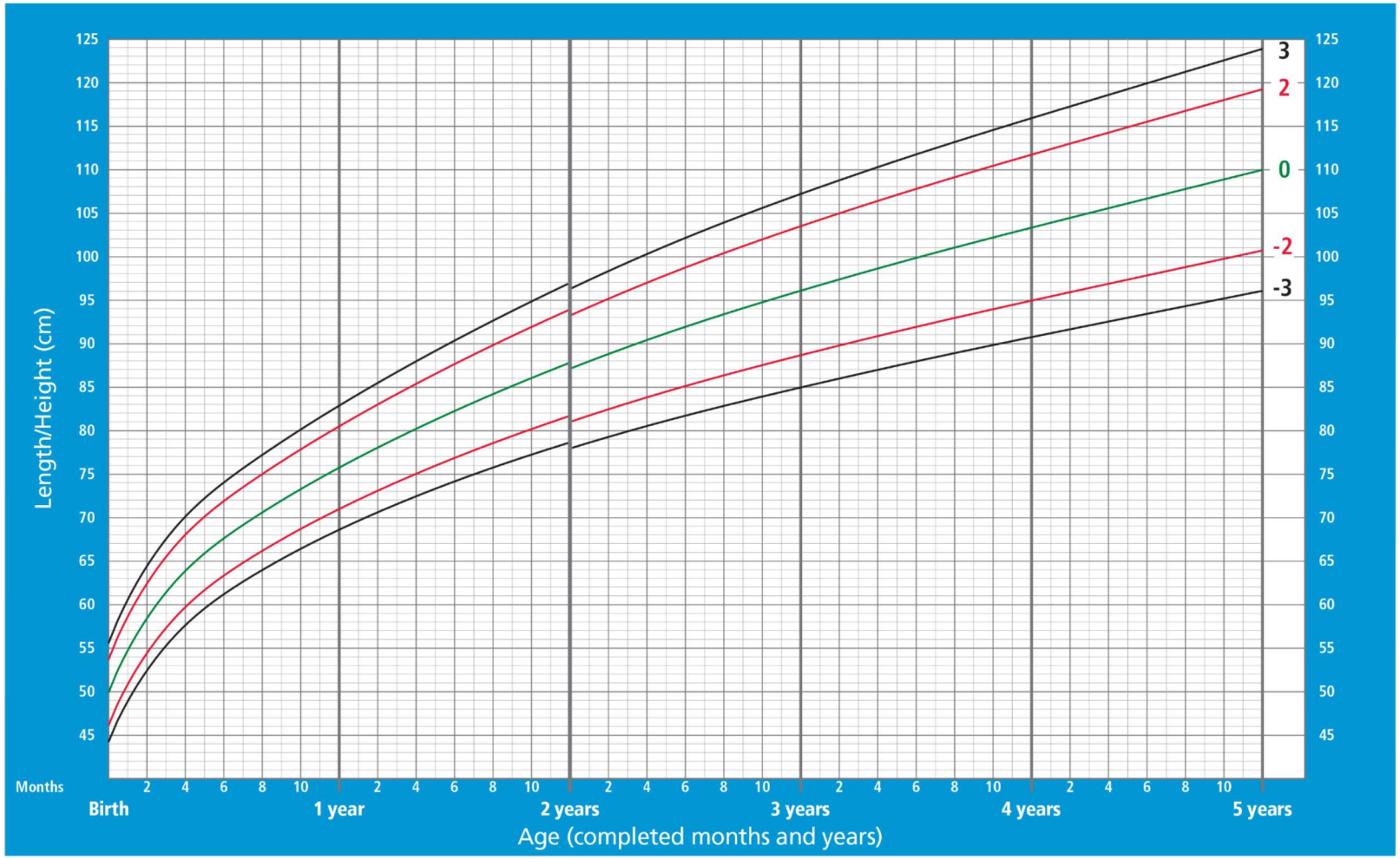


WHO Child Growth Standards

Length/height-for-age BOYS

Birth to 5 years (z-scores)

World Health Organization

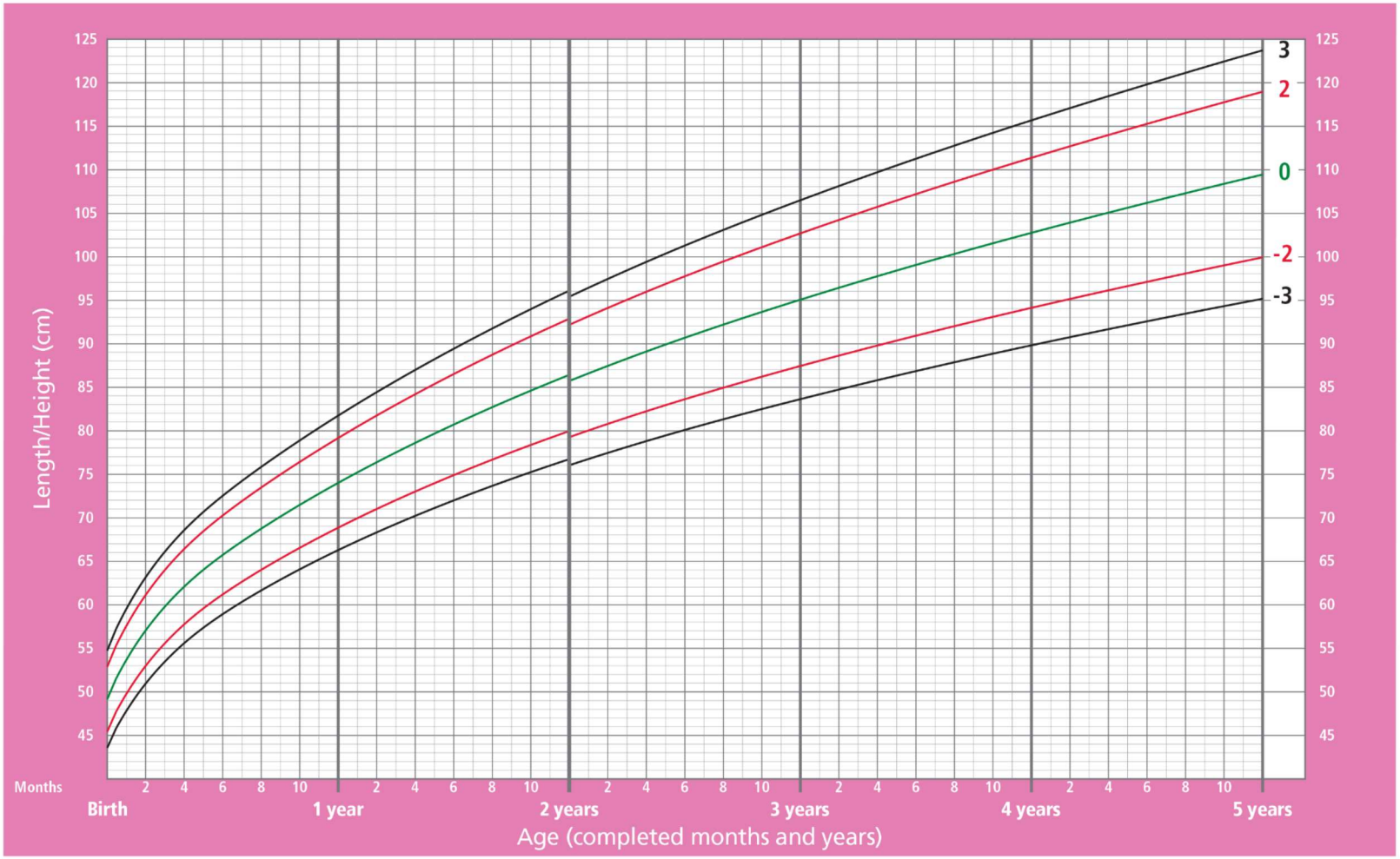


WHO Child Growth Standards

Length/height-for-age GIRLS

Birth to 5 years (z-scores)

World Health Organization

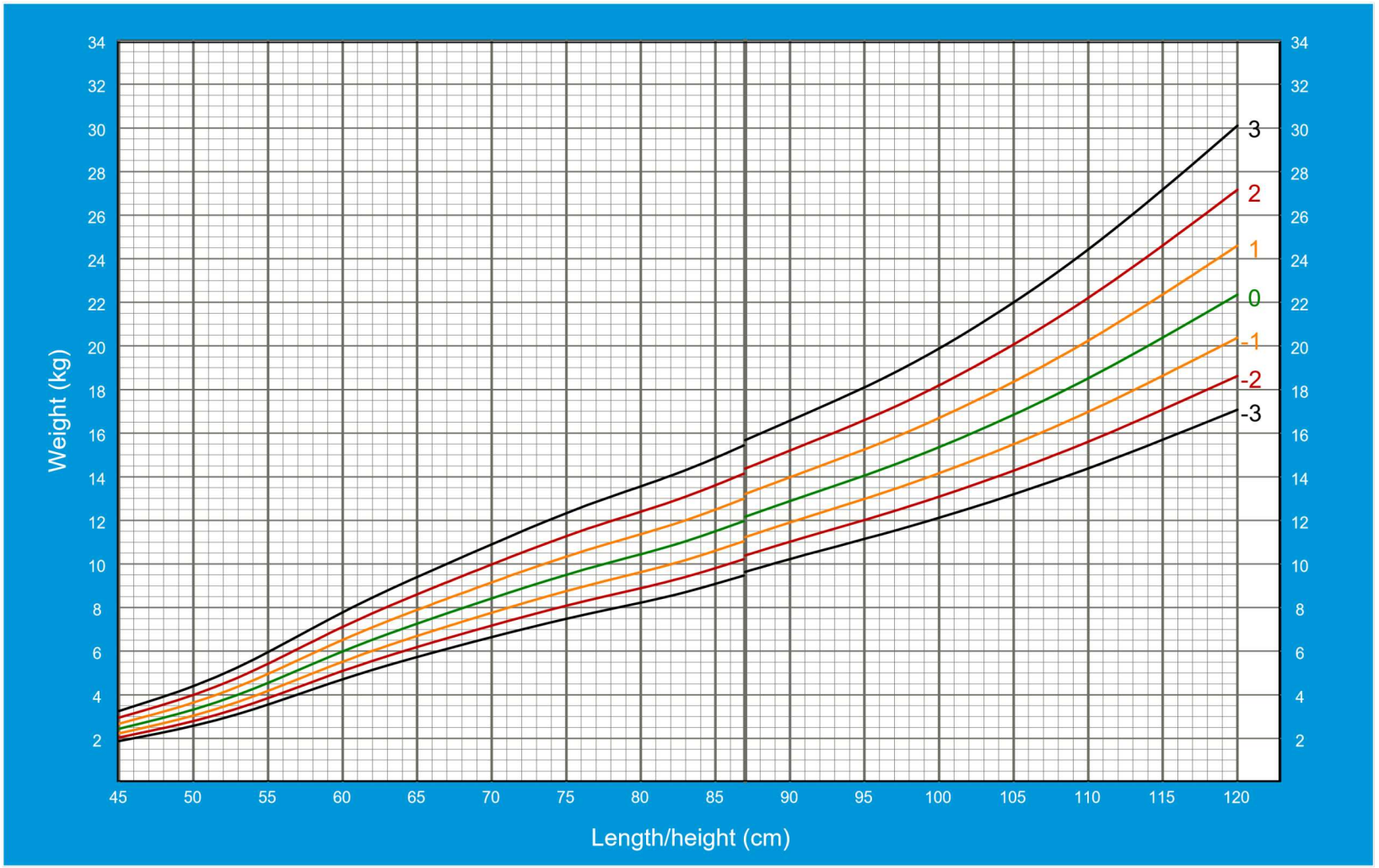


WHO Child Growth Standards

Weight-for-length/height BOYS

Birth to 5 years (z-scores)

World Health Organization



WHO Child Growth Standards

Weight-for-length/height GIRLS

Birth to 5 years (z-scores)

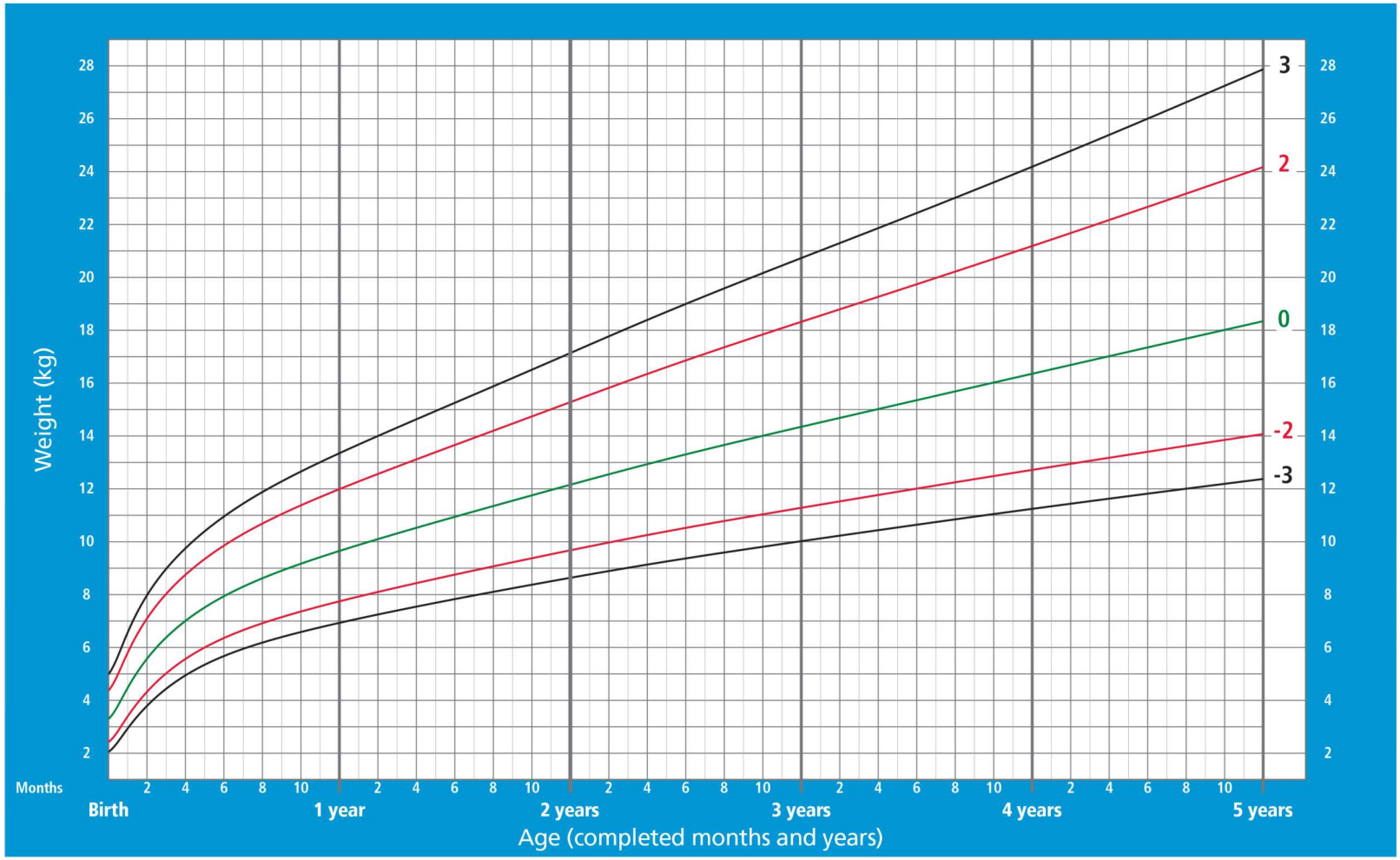
World Health Organization

WHO Child Growth Standards

Weight-for-age BOYS

Birth to 5 years (z-scores)

World Health Organization

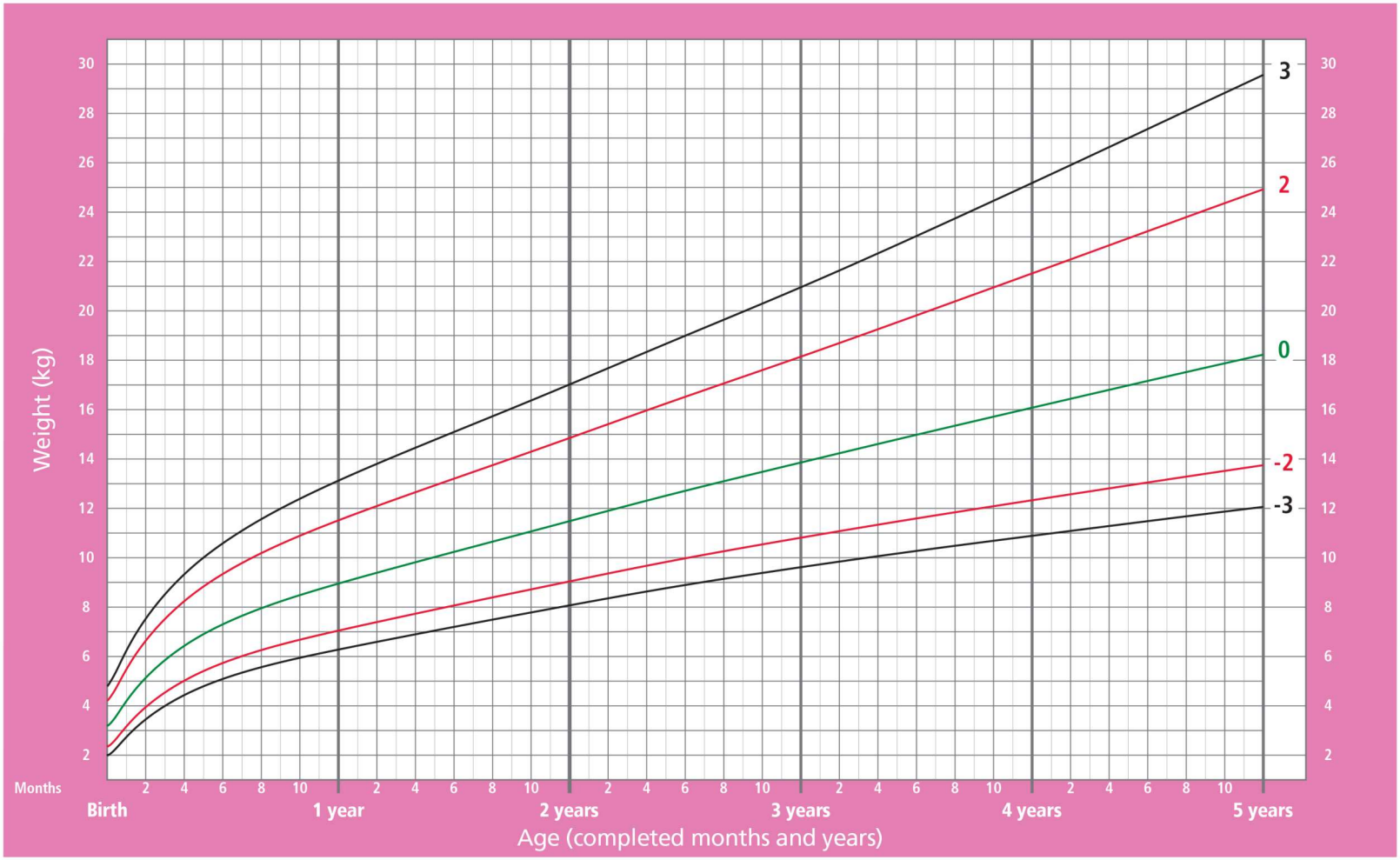


WHO Child Growth Standards

Weight-for-age GIRLS

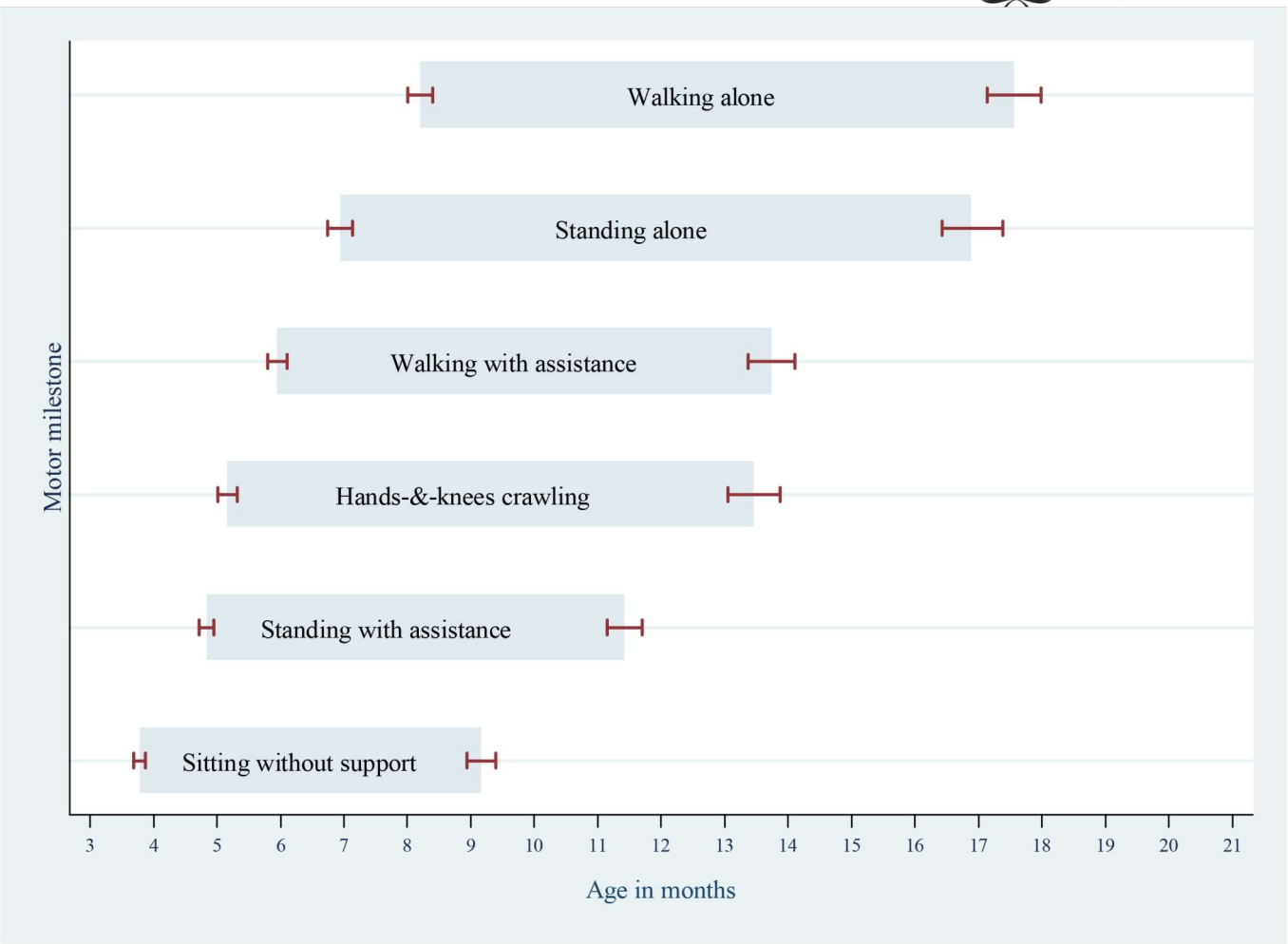
Birth to 5 years (z-scores)

World Health Organization



WHO Child Growth Standards

Windows of achievement for six gross motor milestones



Reference: WHO Multicentre Growth Reference Study Group. WHO Motor Development Study: Windows of achievement for six gross motor development milestones. Acta Paediatrica Supplement 2006;450:86-95.

Chapter 04

Antiretroviral therapy (ART)

Learning Objectives:

The learner should be able to:

1. List ART Classes
2. Construct an ART regimen for a treatment naïve child with HIV
3. Recognize common HIV Drug Resistance Mutations (DRMs)
4. Appraise for Treatment Failure
5. Construct a second line ART regimen when child fails first line regimen

Appropriate and timely initiation of ART has the potential to prolong survival in children with HIV.

When to start Medicines

- Goal: Rapid ART Initiation
  - Start HIV Medicines as soon as possible after diagnosis
  - If caregiver is not ready, monitor the virologic, immunologic, and clinical status at least every 3 to 4 months
- What conditions make it especially important to start HIV medicines right away?
  - Pregnancy
  - Age less than 2 years
  - Early HIV Infection
  - AIDS-defining conditions (See Table 3.4)
- Once a person starts taking HIV medicines, medication adherence is key
  - to maintaining an undetectable viral load
    - which reduces the risk of HIV transmission (U=U)

What to Start

Classes

HIV Medicines are grouped into seven drug classes according to how they fight the HIV virus (examples in brackets)

1. Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs): Efavirenz, Nevirapine
2. Nucleoside Reverse Transcriptase Inhibitors (NRTIs): Abacavir, Emtricitabine, Tenofovir, Lamivudine, Zidovudine
3. Protease Inhibitors (PIs): Atazanavir, Darunavir, Fosamprenavir, Ritonavir, lopinavir
4. Fusion Inhibitors (FI): efuvirtide, maraviroc
5. CCR5/CXCR4 Antagonists: maraviroc, aplaviroc, vicriviroc/AMD3100, AMD3465

6. Integrase Strand Transfer Inhibitors (INSTIs): raltegravir, dolutegravir
7. Post-attachment Inhibitors (PA-I): Ibalizumab-uiyk (IBA), Rukobia (fostemsavir)

Rationale for combination therapy in HIV

1. Synergistic killing through attack through multiple pathways
2. Prevention of emergence of virus resistance

How do we choose an HIV regimen

- Convenience (Fixed Drug Combinations)
  - Standard regimens for region or country (eg: Dolutegravir (DTG) based regimens in Pakistan)
  - Country-wide transitioning from NVP based regimens and LPV-r based regimens to DTG-regimens based on local guidelines
- Possible side-effects
- Pre-existing conditions
- Potential interactions

Examples of regimens from 2006-2024:

The National AIDS Control Program of Pakistan (NACP) started Classic NNRTI-based at time of program inception in 2006.

Table 14 NNRTI-based Regimen at the time of program inception (2006).

Nucleoside Analogue Reverse Transcriptase Inhibitors (NRTIs)	Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)	Protease Inhibitors (PIs)
Zidovudine	Nevirapine	Nelfinavir
Stavudine	Efavirenz	Lopinavir Ritonavir
Didanosine		Atazanavir
Abacavir		
Emtricitabine		
Lamivudine		

By 2015, PI-based regimens were recommended (2NRTIs + 1PI) due to rising nevirapine and efavirenz resistance.

Table 15 PI-based Regimen

Nucleoside Analogue Reverse Transcriptase Inhibitors (NRTIs)	Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)	Protease Inhibitors (Pis)	Integrase Strand Transfer Inhibitors (INSTIs)
Zidovudine (ZDV) Stavudine (d4T) Didanosine (ddI) Abacavir (ABC) Emtricitabine (FTC) Lamivudine (3TC) Tenofovir (TDF)	Nevirapine (NVP) Efavirenz (EFV)	Nelfinavir (NFV) Lopinavir (LPV) Ritonavir (r) Atazanavir (ATV)	Dolutegravir (DTG)

By 2019, PI resistance was being increasingly encountered and INSTI-based regimens (2NRTIs+1INSTI) were recommended.

Table 16 Integrase Inhibitors (INSTI)-based Regimen

Nucleoside Analogue Reverse Transcriptase Inhibitors (NRTIs)	Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)	Protease Inhibitors	Integrase Strand Transfer Inhibitors
Zidovudine (ZDV) Stavudine (d4T) Didanosine (ddI) Abacavir/Lamivudine (ABC/3TC) Emtricitabine (FTC) Tenofovir (TDF) Lamivudine (3TC)	Nevirapine (NVP) Efavirenz (EFV)	Nelfinavir (NFV) Lopinavir (LPV) Ritonavir (r) Atazanavir (ATV)	Dolutegravir (DTG)

First line ART in adolescents:

Preferred regimen:

For most **new** patients who are adolescents, the first-line ART is similar to that recommended in adults and consists of a backbone of two NRTIs (always including 3TC) with one INSTI (DTG). While various combinations are possible, the preferred regimen is: **TDF + 3TC + DTG**

This regimen is preferred over the others due to its improved efficacy and favorable side effect profile. They also preserve second-line regimens in cases of treatment failure if therapy is started earlier.

Table 17 First line regimen for Adults (including pregnant women) and Adolescents (10-19 years)

Preferred regimen NRTI+NRTI+INSTI	Alternative NRTI+NRTI+NNRTI/PI-r	Special circumstances
TDF+3TC+DTG (TLD)	TDF+3TC+EFV400[a] TDF + 3TC (or FTC) + PI/r[a]	TDF + 3TC (or FTC) + EFV600[a] AZT + 3TC + EFV600[a] TDF + 3TC (or FTC) + RAL TAF[b] + 3TC(or FTC) + DTG ABC + 3TC + DTG TDF + 3TC (or FTC) + PI/r[a]

[a]EFV-based ART should not be used in settings with 10% or higher national estimates of pretreatment resistance to EFV. In settings with high HIV drug resistance prevalence and where DTG is unavailable or unsuitable due to toxicity, a boosted PI-based regimen should be used. The choice of PI/r will depend on programmatic characteristics. Alternatively, HIV drug resistance testing should be considered, where feasible, to guide first-line regimen selection

[b]TAF may be considered for people with established osteoporosis and/or impaired kidney function

First Line ART in children less than 10 years

Dolutegravir (DTG) has been proven safe, tolerable, and effective for infants and children aged four weeks to 12 years and is approved in the US and Europe. WHO recommends DTG as the preferred first-line regimen for children with an approved dosing. Despite limited experience with DTG in children, WHO advises regular active toxicity monitoring but encourages scaling up DTG use without delay. DTG dispersible tablets should ideally be dispersed in water or swallowed whole, though mixing with food or liquids is acceptable if the full dose is consumed.

Table 18 First Line regimen for Neonates and Older children

Preferred regimen NRTI+NRTI+INSTI	Alternative NRTI+NRTI+NNRTI/PI-r	Special circumstances
ABC + 3TC + DTG[c]	ABC + 3TC + LPV/r TAF + 3TC (or FTC) + DTG	ABC + 3TC + EFV (or NVP) ABC + 3TC + RAL[e] AZT + 3TC + EFV[f] (or NVP) AZT + 3TC + LPV/r (or RAL)
Preferred first-line regimens (Neonates) NRTI+NRTI+INSTI	Alternative first-line regimens NRTI+NRTI+NNRTI	Special Circumstances NRTI+NRTI+PI
AZT (or ABC) + 3TC + RAL[g]	AZT + 3TC + NVP	AZT + 3TC + LPV/r[h]
ABC + 3TC + DTG	ABC + 3TC + LPV/r TAF + 3TC (or FTC) + DTG	ABC + 3TC + EFV (or NVP) ABC + 3TC + RAL AZT + 3TC + EFV (or NVP) AZT + 3TC + LPV/r (or RAL) AZT + 3TC + EFV (or NVP) AZT + 3TC + LPV/r (or RAL)

[c]For age and weight groups with approved DTG dosing, from four weeks and 3 kg

[d]For age and weight groups with approved TAF dosing

[e]RAL can be used as an alternative regimen only if LPV/r solid formulations are not available.

[f]EFV should not be used for children younger than three years of age

[g]Neonates starting ART with a RAL-based regimen should transition to DTG as soon as possible (see Annexure 6 for dosing).

[h]LPV/r syrup or granules can be used if starting after two weeks of age.

Use dosages as laid out in Table 12.4 (Dosing chart for ART for infants, children and adolescents with HIV (including ART Presumptive Therapy)

Transition to optimal ARV drug regimens for children

NNRTI-based regimens are discouraged now that alternatives are available because they provide lower viral load suppression, as demonstrated by growing programmatic and observational data. DTG-based regimens offer a more effective and well-tolerated alternative that overcomes potential NNRTI resistance and gives the chance to completely synchronize regimens between children and adults. Therefore all infants and children (older than four weeks and weighing at least 3 kg) who are established on first-line ART should be transitioned to a DTG-based regimen, regardless of their current regimen. At the time of transition, viral load testing should be performed, however, if not available, this should not delay the transition.

Table 19 Transitioning to optimal ART regimens for children established on ART

Current Regimen	Weight	Optimal regimen for transition	Considerations
AZT + 3TC + NVP AZT + 3TC + EFV ABC + 3TC + NVP	<20kg	ABC + 3TC + DTG	With DTG 10mg available, earlier transition to DTG is possible
	20-30	ABC + 3TC + DTG	If stable, children can transition to TDF+3TC (or FTC) + DTG when they reach 30 kg or earlier if an appropriate formulation
	>30kg	TDF + 3TC + DTG	—
ABC + 3TC + EFV	<20kg	ABC +3TC + DTG	If stable, children can transition to DTG when they reach 20 kg or earlier if appropriate formulation
	20-30	ABC + 3TC + DTG	If stable, children can be transitioned to TDF+3TC (or FTC)+DTG when they reach 30 kg or earlier if appropriate formulation
	>30kg	TDF + 3TC (or FTC) + DTG	—
ABC + 3TC + LPV/r AZT + 3TC + LPV/r	<20kg	Can continue until finite supply of LPV/r used up or transition to ABC + 3TC + DTG	Ensure the use of FDCs (ABC/3TC) to reduce pill burden. Transition to DTG as soon as appropriate formulation (10mg DT) available
	20-30	ABC + 3TC + DTG	If stable, children can be transitioned to TDF+3TC (or FTC)+DTG when they reach 30 kg
	>30kg	TDF + 3TC (or FTC) + DTG	—

Monitoring ART

Before initiation of ART

On their first visit to the ART center, all patients should undergo an HIV test (HIV serology or viral load if less than 2 years) for confirmation. Following this, all patients should have a CD4 count done at baseline. Patients should also be screened once for hepatitis B (by HBsAg), HCV (anti-HCV) and syphilis (by RPR or syphilis antibodies if vertical transmission suspected).

At the time of initiation of ART

Once a decision to start ART has been made, certain baseline tests need to be sent to assess the safety of the regimen chosen, as well as to monitor future side-effects. However, as ART may be initiated on the first visit, this should not be delayed while awaiting the above results.

Baseline tests include:

a) Hemoglobin before starting AZT

b) Kidney function tests including urine DR, creatinine and estimated GFR (eGFR) before starting TDF

After initiation of ART

After starting ART, patients should be called back within 1 to 2 weeks to check for any early adverse effects with the ART, to assess if the medications are being taken correctly (the same time each day with a maximum of an hour difference) and to address any other concerns the patient may have had since the last visit. If the ART was started on the first visit, the second clinic visit provides an opportunity to review the CD4 cell counts and start CPT if required (age less than 5 years or CD4< 350/mm^3). Similarly, TPT may be initiated if not done so on the first visit, after ruling out active TB. For the first 3 months, additional follow-ups may be scheduled depending on the patient's and physician's comfort, ongoing medical issues and social situation.

The goal of ARTs is an undetectable VL. The threshold for virological failure is over a VL of over 1000 copies/ml (done twice, 3 months apart with adherence counselling). Low level viremia (between 50 copies/ml and 1000 copies/ml) may be predictive of failure and such patients may need to be followed more closely. On the other hand, those with a VL of 50 copies/ml, who are stable may require less frequent follow-ups.

Therefore VL may be conducted 3 months after the ART is started if logistically possible. However, if the viral load is high, treatment should **not** be modified based on a single VL finding and must be rechecked in 3 months after adherence counselling. A VL must be checked 6 months after ART initiation.

For patients who are undetectable (defined as VL <50 copies/ml) repeat VL can be done every 6 months to once a year if there are no ongoing concerns regarding adherence. For patients with suppressed viral loads (defined as VL between 50 copies/ml and 1000 copies/ml), VL should be repeated in 3 months, after adherence counselling. If despite counselling the VL remain in this level, VL should be done every 3 months without changing the regimen. On the other hand, if the VL increases to >1000 copies/ml (not suppressed), viral loads must be checked 3 months later or earlier

and if still elevated on the second result, 3 months apart, despite adherence counselling, the regimen should be changed.

In certain instances, there may be a need for additional VL testing. For example, VL should be checked earlier if therapy is changed (for reasons other than virological failure), e.g. in children on a triple NRTI regimen due to concurrent Anti-TB Therapy.

CD4 count should be checked with the VL till the patient is documented as stable on ART (PLHIV receiving ART for at least 12 months, no adverse drug reactions requiring regular monitoring, no current illnesses, and good understanding of adherence and evidence of treatment success including two consecutive undetectable viral load measures). Indications to continue monitoring CD4 counts despite virologic suppression include a CD4 below 350 cell/mm (to decide on holding prophylaxis) or clinical failure despite undetectable viral load (like in cases of HIV-2).

Moreover, patients on certain ART drugs should be tested periodically (every 3 to 6 months) to detect side effects. These include checking hemoglobin if, on AZT, urine dipstick or Detailed Report (urine DR) and creatinine and eGFR if on TDF.

Table 20 Routine testing in PLHIV in relation to ART

Who	How often	Test / Evaluation
Baseline		
All patients	Once	Mandatory: HIV serology, HbsAg, HCV Ab, Syphilis testing, random blood sugar, CXR, Creatinine, CD4 Optional but preferred: HBsAb, Mantoux, CBC, BUN ALT, urine dipstick
Before starting ART		
All patients	At every visit	Clinical examination and staging, nutritional assessment, verbal screening for TB
	Every 6 months	CD4 count
PWID/Blood Transfusion recipients	Every year	HCV Ab and HepBs Ag (if previously negative and unvaccinated)
MSM, SW and TG	Every year	Syphilis and clinical screening for STIs
At the time of initiation		
In all patients	Once	Pregnancy test, clinical examination
If starting AZT	Once	Hemoglobin

Who	How often	Test / Evaluation
If starting TDF	Once	Urine dipstick DR, creatinine/eGFR*
After initiation		
All patients	3 months after initiation and then every 6 to 12 months	Clinical examination, nutritional assessment, reinforcement of adherence
All patients	Serial VL	If <50 copies/ml (undetectable): 6 months to yearly If >50 copies/ml (suppressed): 3 monthly If >1000 copies twice: Failure
If CD4 less than 350 cells/mm3 at the time of starting ART	Every 6 months	CD4 counts (till CD4 over 350 for 2 consecutive tests)
Suspected failure	Immediately	VL, and HIV resistance testing (if available)
If on AZT	Every 3 months	Hemoglobin
If on TDF	Every 3 months for the first year then 6 monthly	Urine dipstick DR, creatinine/eGFR*
If pregnant	At the time of the establishment of pregnancy and 36 weeks of gestation	VL
PWID	Every year	HCV and HepBsAg (if previously negative and unvaccinated)
Thalassemia/ Disorders requiring regular blood product transfusions	Every year	HCV Ab, HepBsAg Liver (ALT/Bilirubin) and Kidney (BUN/Cr) function Basic thyroid (TSH/fT4) and parathyroid function (Ca/ Ph/Mg/PTH/Vit D) after age 5 years Cardiac assessment after age 8 years

*eGFR can be calculated for adults as follows: (age-140) X weight (multiply by 0.85 if female)

72 X creatinine

*eGFR can be calculated for children as follows: (0.41 × Height in cm) / Creatinine in mg/dL

Response and failure to ART

Monitoring individuals receiving ART is important to ensure successful treatment, identify adherence problems and determine whether ART regimens should be switched in case of treatment failure. Detecting failure earlier is essential if this is due to poor adherence so that interventions may be put in place quickly to improve adherence before the virus becomes resistant. Similarly, if resistant mutations do develop, switching therapy early will preserve future options. This is especially true for resistance in TDF-based regimens, where if stopped early, AZT susceptibility is maintained. The response to ART may be assessed using virological criteria (VL measurement), immunologic criteria (CD4 counts) or clinical criteria (clinical signs and symptoms). Of these, the preferred and earliest means of assessing response and failure is using VL.

Clinical failure

Using clinical signs and symptoms is an inexpensive means and delayed signal of assessing if a patient has responded or is failing ART. However, this is extremely insensitive and non-specific and patients may often present very late or may appear to be failing but the change in condition is part of their clinical course (such as IRIS). Patients should therefore not be monitored solely based on clinical response (or failure), though the following definitions may trigger earlier assessment for failure. Second-line ART should never be started based on clinical failure alone.

Clinical failure is defined as:

a) Adults and adolescents

New or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4 conditions) after 6 months of effective treatment

b) Children

New or recurrent clinical event indicating advanced or severe immunodeficiency (WHO clinical stage 3 and 4 conditions except for TB) after 6 months of effective treatment

Immunologic failure

Immunologic monitoring of patients using CD4 counts is a more accurate means of assessing failure as compared to clinical monitoring. However, using immunologic monitoring alone does pose certain difficulties. Firstly, CD4 counts tend to rise and fall more slowly compared to VL which leads to delays in the detection of ART failure as well as difficulty in assessing if improving compliance has made an effect. Moreover, CD4 counts have lower sensitivity and positive predictive values for detecting failure compared to VL in both adults and children and, are now not available easily.

This means that many cases of immunological failure may have adequate virological suppression and are therefore at risk of being misclassified as having treatment failure and switched unnecessarily to second-line therapy. However, just as in clinical monitoring, immunologic monitoring may be used as a trigger to detect early virological failure. CD4 counts should, therefore, be checked twice yearly in all patients on ART. Finally, in all cases of suspected immunologic failure, a concomitant infection must be ruled out, as this may decrease the CD4 counts.

Immunologic failure is defined as

a) Adults and adolescents

CD4 count at or below 250 cells/mm^3 following clinical failure or persistent CD4 level below 100 cells/mm^3

b) Children younger than 5 years

Persistent CD4 levels below 200 cells/mm^3 OR CD4 <10%

c) Children older than 5 years

Persistent CD4 levels below 100 cells/mm3

Virological failure

Virological monitoring is the method of choice to assess response to ART. When compared with immunological and clinical monitoring, VL monitoring provides an early and more accurate indication of treatment failure and the need to switch to second-line drugs. This reduces the accumulation of drug-resistance mutations and improves clinical outcomes. VL measurement can also serve as a proxy for the risk of transmission at the individual and population levels. Hence VL should be initially checked 3 months after starting (or changing ART) twice and then depending on the VL every 6 monthly to yearly (for undetectable) or 3 monthly (for suppressed). A baseline VL, at the time of starting the therapy, is not required.

A VL over 1000 copies/ml may indicate virological failure. In such cases, adherence must be reassessed and stressed (see section 5.2) and the VL rechecked 3 months later. If the VL remains over 1000 copies/ml, the patient should be labeled as virological failure and second-line ART initiated. Resistance testing should be performed in such cases if available however is not mandatory and second line therapy can be started as in section 3.11.

It should also be noted, that "blips" or minor and transient fluctuations in VL do occur on therapy and these are not associated with failure, development of resistance or with increased risk of transmission. A blip is defined as a VL of up to (but not more than) 1000 copies/ml in a previously suppressed patient followed by subsequent VLs of less than 50 copies/ml. Therefore, care must be taken to label a patient as virological failure only after 2 *consecutive* readings are over 1000 copies/ml (after correcting for adherence).

The definition for virological failure is therefore

Plasma VL above 1000 copies/ml (based on two consecutive viral load measurements in a 3 - month interval, with adherence support following the first viral load test, after at least six months of starting a new ARV regimen.

Table 21 How to monitor Treatment Failure

Criteria	Virologic	Immunologic	Clinical
Children < 5 years	Plasma viral load above 1000 copies/ml • based on two consecutive viral loads within 3mo with adherence support • after at least six months of using ARV drugs	Persistent CD4 levels below 200 cells/mm^3	New or recurrent clinical event indicating severe immunodeficiency (WHO Stage 3 or 4) after 6 months of effective treatment
Children ≥ 5 years		Persistent CD4 levels below 100 cells/mm^3	
Adolescents		CD4 count falls to the baseline (or below) OR Persistent CD4 level below 100 cells/mm^3	New or recurrent clinical event indicating severe immunodeficiency (WHO Stage 4) after 6 months of effective treatment

Drug Resistance testing and genotyping

Drug resistance in HIV is associated with various mutations, and therefore presence or absence of these mutations can help predict response. These mutations are detected using a process called genotyping. Currently, the technology to perform genotyping is limited but may be expanded soon. If genotyping is available, this should be performed in all cases of treatment failure, especially those failing second-line therapy.

It should be noted that on stopping a failing regimen, the resistant (mutant) virus levels in the blood will decline over the next 2 weeks, to be replaced with the sensitive (or wild-type) virus. Therefore genotyping must be done while the patient is still on the failing regimen. Similarly, if a genotype is done after failing a second-line regimen, the viruses resistant to the first regimen may not be detected, though it will re-emerge if the first-line therapy is restarted. Therefore it is important to interpret genotype results carefully and to seek expert advice before switching therapy based on this.

How to test for HIV-DR

Genotypic Testing

a. Determines presence of mutations that are known to confer decreased drug susceptibility
    i. RT and Protease genes
    ii. INSTI gene
b. Done when
    i. Acute HIV infection (before ART)
    ii. Chronic HIV Infection (VL>1000)

Phenotypic Testing (PT)

c. Measures drug susceptibility of the virus by determining the concentration of drug that inhibits viral replication in tissue culture

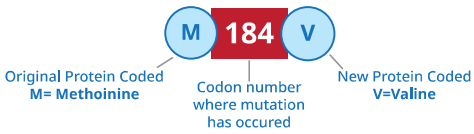
d. Done in addition to GT when

   i. Complex resistance mutation patterns detected e.g. PI resistance

How are mutations reported?

HIV drug resistance is caused by changes in the genetic structure of HIV that affect the ability of medicines to block the replication of the virus. All antiretroviral drugs, including those from newer drug classes, are at risk of becoming partially or fully inactive due to the emergence of drug-resistant virus.

Figure 11 Reporting Convention of HIV Gene Mutation



Mutations are generally reported as a number (codon number where mutation has occurred) flanked by two alphabets representing original protein coded and new protein coded.

Table 22 Code letters for Amino Acid placement in HIV genome

Code letter	AA	Code letter	AA
A (Ala)	Alanine	M (Met)	Methionine
C (Cys)	Cytosine	N (Asp)	Asparagine
D (Asp)	AsparticA	P (Pro)	Proline
E (Glu)	GlutamicA	Q (Glu)	Glutamine
F (Phe)	PhenylA	R (Arg)	Arginine
G (Gly)	Glycine	S (Ser)	Serine
H (His)	Histidine	T (Thr)	Threonine
I (Ile)	Isoleucine	V (Val)	Valine
K (Lys)	Lysine	W (Trp)	Tryptophan
L (Leu)	Leucine	Y (Tyr)	Tryosine

Table 23 Selected genotype mutations which result in resistance to NRTIs/NNRTIs

Mutation	Selected by	Mechanism	Effects on other NRTIs	Comment
M184V	3TC FTC ABC	Impairs drug incorporation	↓Suscep to 3TC&FTC ↑Suscep to ZDV, D4T & TDF	Presence delays appearance of TAMs. TAMs+M184V↓ response to ABC
TAMs 1: M41L, L210W, T215Y/F 2: D67N, K70R, K219Q/E	ZDV D4T	Mutation leads to excision of drug from DNA chain terminus	↓Suscep to all NRTIs; The more TAMs, the more resistance	TAM acquisition slowed by presence of m184v; TAMs↑ suscep to NNRTIs
151 M complex, T69 insertion	ZDV, DDI, D4T	Impairs drug incorporation	Q151: ↓Suscep to all NRTIs except minimal activity of TDF; T69 insertion: resistance to all NRTIs	
K65R	All NRTIs except ZDV (TDF)	Impairs drug incorporation	Variable↓ suscep to ABC, DDI, 3TC/FTC esp TDF	↑suscep to ZDV & D4T
L74V	ABC, DDI		↓Suscep to ABC & DDI	Presented by presence of ZDV in treatment regimen

Drug toxicity

Tenofovir (TDF)

TDF's main toxicity is nephrotoxicity, marked by proximal tubular cell dysfunction, potentially leading to acute kidney injury or chronic kidney disease. Patients at higher risk include older adults, those with underlying renal disease, low BMI, untreated diabetes, hypertension, or concurrent nephrotoxic drug use. Baseline creatinine should be checked before starting TDF, and it should not be used if eGFR is <50 ml/min. TDF may cause glucose in urine without diabetes, a sign of toxicity. Blood pressure should be monitored regularly. TDF can also reduce bone mineral density in children, requiring growth monitoring. Discontinuing TDF in HIV/HBV co-infection may trigger HBV flare-ups.

Zidovudine (AZT)

AZT can cause hematological toxicity, leading to macrocytic anemia, particularly in those with baseline anemia, neutropenia, or low CD4 counts. Hemoglobin should be checked before starting AZT, especially in vulnerable patients. AZT may also cause mitochondrial toxicity, leading to lactic acidosis or hepatomegaly, particularly in overweight patients.

Nevirapine (NVP)

NVP is being phased out now. It has a severe hepatotoxicity risk, especially in patients with hepatic disease, HBV/HCV co-infection, or high CD4 counts (≥250 in women, ≥400 in men). Monitoring hepatic enzymes is advised, particularly in high-risk groups. NVP can also cause skin rashes and, rarely, Stevens-Johnson Syndrome.

Efavirenz (EFV)

EFV's main toxicity involves central nervous system effects, usually resolving within weeks but potentially persisting. Risk factors include pre-existing depression or mental disorders. Patients should be warned about these effects, which may lead to discontinuation of ART. EFV may also cause a mild, self-limiting drug rash.

Abacavir (ABC)

ABC's main concern is a Hypersensitivity Reaction (HSR), linked to the HLA-B*-5701 allele, typically occurring within 10-14 days. Symptoms include fever, GI issues, malaise, and respiratory problems. Stopping ABC resolves symptoms, but re-challenging can trigger a fatal reaction. ABC may also increase cardiovascular risk in patients with ischemic heart disease.

Lopinavir/ritonavir (LPV/r) and Atazanavir/ritonavir (ATV/r)

LPV/r mainly causes gastrointestinal side effects, especially diarrhea and nausea/vomiting. ATV/r can cause hyperbilirubinemia. This does not represent a decrease in hepatic function and is mostly cosmetic. ATV/r does not need to be discontinued based on this unless this is causing distress in the patient. Patients should be warned of this before starting the treatment so as not to cause alarm. Moreover, as this does not represent a decrease in liver function there is no bilirubin cut-off at which ATV/r should be stopped.

Finally, all PIs have metabolic side-effects, especially hypertriglyceridemia and fat redistribution syndrome.

Dolutegravir (DTG)

DTG typically causes mild to moderate nausea, headache, and diarrhea. Serious effects include liver dysfunction, especially in HBV/HCV coinfection, and rare hypersensitivity reactions. DTG may raise serum creatinine without affecting eGFR, so minor changes should be ignored. Psychiatric side effects, including delirium, are less common but may require discontinuation. Insomnia, more common in older women, may necessitate morning dosing. DTG can cause rapid weight gain, particularly in women on DTG + FTC/TAF, warranting lifestyle advice on diet, exercise, and smoking cessation.

Management of ARV related toxicities

Table 24 side-effects and suggested the management of commonly used ARVs in Pakistan

ARV Drug	Major types of toxicity	Risk factors	Suggested management
ABC	Hypersensitivity reaction	Presence of HLA-B*5701 Gene	If ABC is being used in first-line ART, substitute with TDF or AZT. If ABC is being used in second-line ART, substitute with TDF
ATV/r	Electrocardiographic abnormalities (PR interval prolongation)	Pre-existing conduction disease Concomitant use of other drugs that may prolong the PR interval	LPV/r. If boosted PIs are contraindicated and NNRTIs have failed in first-line ART, consider integrase inhibitors (DTG)
	Indirect hyperbilirubinemia (clinical jaundice)	Underlying hepatic disease HBV and HCV co-infection Concomitant use of hepatotoxic drugs	
	Nephrolithiasis and risk of prematurity	Risk factors unknown	
AZT	Anemia, neutropenia, myopathy, lipoatrophy or lipodystrophy	Baseline anemia or neutropenia CD4 count ≤200 cells/mm^3	If AZT is being used in first-line ART, substitute with TDF or ABC If AZT is being used in second-line ART, substitute with ABC
	Lactic acidosis or severe hepatomegaly with steatosis	BMI >25 (or bodyweight >75 kg) Prolonged exposure to nucleoside analogues	
EFV	Persistent central nervous system toxicity (such as abnormal dreams, depression or mental confusion)	Depression or other mental disorder (previous or at baseline) Daytime dosing	DTG If the person cannot tolerate either INSTI (DTG), use boosted PIs
	Hepatotoxicity	Underlying hepatic disease HBV and HCV coinfection Concomitant use of hepatotoxic drug	
	Convulsions	History of seizure	
	Hypersensitivity reaction Stevens-Johnson syndrome Male gynecomastia	Risk factors unknown	

ARV Drug	Major types of toxicity	Risk factors	Suggested management
LPV/r	Electrocardiographic abnormalities (PR and QT interval prolongation, torsades de pointes)	People with pre-existing conduction system disease Concomitant use of other drugs that may prolong the PR interval	If LPV/r is used in first-line ART for children, use an age-appropriate NNRTI (NVP if available for children less than 3 years) or use an age-appropriate INSTI or EFV for children 3 years and older. ATV can be used for children older than 6 years or 15 kg If LPV/r is used in second-line ART for adults, use ATV/r or DRV/r. If boosted PIs are contraindicated and the person has failed on treatment with NNRTI in first-line ART, consider integrase inhibitors
	QT interval prolongation	Congenital long QT syndrome Hypokalemia Concomitant use of drugs that may prolong the QT interval	
	Hepatotoxicity	Underlying hepatic disease HBV and HCV coinfection Concomitant use of hepatotoxic drugs	
	Pancreatitis	Advanced HIV disease	
	Risk of prematurity, lipoatrophy or metabolic syndrome, dyslipidemia or severe diarrhea	Risk factors unknown	
NVP	Hepatotoxicity	Underlying hepatic disease HBV and HCV co-infection Concomitant use of hepatotoxic drugs CD4 >250 cells/mm^3 in women CD4 >400 cells/mm^3 for men First month of therapy (if lead-in dose is not used)	*DTG is the preferred alternative.* If the person cannot tolerate INSTI, use boosted PIs
	Severe skin rash and hypersensitivity reaction (Stevens-Johnson syndrome)	Risk factors unknown	

ARV Drug	Major types of toxicity	Risk factors	Suggested management
TDF	Tubular renal dysfunction, Fanconi syndrome	Underlying renal disease Older age BMI <18.5 (or body weight <50 kg) Untreated diabetes mellitus Untreated hypertension Concomitant use of nephrotoxic drugs or a boosted PI	If TDF is being used in first-line ART, substitute with AZT or ABC If TDF is being used in second-line ART (after AZT use in first line ART), substitute with ABC
	Decreases in bone mineral density	History of osteomalacia and pathological fracture Risk factors for osteoporosis or bone loss	
	Lactic acidosis or severe hepatomegaly with steatosis	Prolonged exposure to nucleoside analogues Obesity	
	Exacerbation of hepatitis B (hepatic flares)	Discontinuation of TDF due to toxicity	Use alternative drug for hepatitis B treatment (such as entecavir)
DTG	Hepatotoxicity Hypersensitivity reactions	Hepatitis B or C coinfection Liver disease	If DTG is used in first-line ART, and there are hypersensitivity reactions, substitute with another therapeutic class (boosted PIs or EFV).

IRIS

Immune Reconstitution Inflammatory Syndrome (IRIS) occurs in 10–30% of individuals starting ART, typically within 4–8 weeks. It manifests as paradoxical IRIS, where a previously treated infection worsens after ART begins, or unmasking IRIS, where ART reveals a previously undetected disease. Risk factors include low CD4 counts, disseminated infections, and short pre-ART treatment duration. IRIS is usually self-limiting; ART interruption is rare. Prevention involves early HIV diagnosis, timely ART initiation, thorough screening for opportunistic infections, and careful management of infections before ART.

Second and Third line ART

Adults/Adolescents (weight > 35 kg)

In patients who are failing their first-line therapy, the NRTI backbone should be modified, so that TDF (or ABC) is switched to AZT. Alternatively, if AZT was used in the initial regimen this should be changed to TDF. If ABC was used in the first regimen this should *not* be switched to TDF. In both circumstances, 3TC should be continued as it is.

On the other hand, the third drug (EFV or DTG) should be switched to a boosted PI (such as LPV/r or ATV/r) if the patient was on DTG. WHO recommends ATV/r as the preferred PI/r as the second line agent based on fewer lipids changes than other PI, good gastrointestinal tolerability, better pregnancy outcomes compared to LPV/r, once-daily dosing and low pill burden and low risk of cross-resistance with LPV/r or DRV/r when used in the first time. Note, patients failing EFV, may also be switched to DTG in the second-line regimen.

Rarely, it may not be possible to start AZT (e.g. due to profound anemia), and in such cases, a two-drug combination of DTG + LPV/r or ATV/r may be used as a second alternative, provided that DTG was not part of the initial failing regimen.

For HIV and HBV co-infected patients, both TDF and 3TC should be continued in the second-line regimen. This is to reduce the risk of hepatitis flares. However, a third NRTI should be added to the regimen (e.g. changing TDF+3TC+DTG to AZT+TDF+3TC+ATV/r).

For people with active TB disease receiving rifampicin, all boosted PIs in standard doses are contraindicated because of drug interactions and significant reductions in PI plasma concentrations. ATV/r should not be used with rifampicin because of significant drug-drug interaction. LPV/r can be used with an adjusted dose of LPV/r 800 mg/200 mg twice daily or a super-boosted dose LPV/r 800mg/800mg. However, this is associated with high levels of toxicity and requires close clinical and laboratory monitoring.

Infants and Children

Recommending potent and effective second-line regimens for infants and children is especially difficult because of the current lack of experience in resource-limited settings and the limited formulations available.

The second-line regimen used in children, therefore, depends on which initial regimen the child was on a priori.

Table 25 Second line regimens across age groups

	First-line ART regimen	Second-line ART regimen
Adults and adolescents including pregnant and breastfeeding women	TDF + 3TC+ DTG	AZT+3TC+ ATV/r (or LPV/r)
	TDF + 3TC+ EFV	AZT+3TC+DTG AZT + 3TC + ATV/r (or LPV/r)
	ABC +3TC + DTG	AZT + 3TC + ATV/r (or LPV/r)
	AZT+3TC+ EFV	TDF+3TC+DTG TDF+3TC+ ATV/r (or LPV/r)
	AZT+3TC+ NVP	TDF+3TC+DTG TDF+3TC+ ATV/r (or LPV/r)

	First-line ART regimen		Second-line ART regimen
HIV and TB	Adults and adolescents Same as above but a double dose of LPV/r or DTG Children AZT + 3TC + ABC ABC+3TC+DTG or RAL		
HIV and HBV	If AZT was used in first-line ART		Use TDF preferred over ABC
	If ABC was used in first-line ART		Use TDF
	If TDF was used in first-line ART		Continue TDF with AZT
Children and Infants	ABC used in backbone	ABC + 3TC + DTG[a]	AZT + 3TC + LPV/r (or ATV/r [b]) AZT + 3TC + DRV/r[c]
		ABC + 3TC + LPV/r	AZT + 3TC + DTG[a] AZT (or ABC) + 3TC + RAL
		ABC + 3TC + EFV	AZT + 3TC + DTGa AZT + 3TC + LPV/r (or ATV/rb)
		ABC + 3TC + NVP	AZT + 3TC + DTG[a] AZT + 3TC + LPV/r (or ATV/r[b] or DRV/r[c])
	AZT used in backbone	AZT + 3TC + LPV/r	ABC + 3TC+ DTG ABC + 3TC +ATV/r
		AZT + 3TC + EFV	ABC + 3TC + DTG ABC + 3TC + LPV/r (or ATV/r)
		AZT + 3TC + NVP	ABC + 3TC + DTG ABC + 3TC + LPV/r ABC + 3TC + ATV/r

[a]For age and weight groups with approved DTG dosing.

[b]ATV/r can be used as an alternative to LPV/r for children older than three months, but the limited availability of suitable formulations for children younger than six years, the lack of a fixed-dose formulation and the need for separate administration of the ritonavir booster should be considered when choosing this regimen.

[c]DRV should not be used for children younger than three years and should be combined with appropriate dosing of ritonavir.

Third Line Drugs

There are a very limited number of third-line drugs currently available in the country. However, choosing third-line regimens is complicated and a robust regimen must be selected by taking into account previous ART regimens the patient has been on and predicting the logical resistance mutations which may have subsequently developed. This is essential as there may be cross-resistance

between Abacavir with AZT and TDF (depending on the mutation). DRV/r is a newer generation PI that may be active in cases where there is resistance to LPV/r and if possible should be part of the salvage regimen in a patient failing second-line therapy.

Therefore whenever possible, the regimen must be guided with the help of a genotype (if available, see section 3.7.4), sent while on the failing regimen (or not more than 2 weeks after holding it). Third-line drugs must also always be selected in consultation with an expert with experience in managing treatment-experienced individuals. Plans for formalizing a referral pathway for patients requiring Drug Resistance Mutation (DRM) testing are underway.

Table 26 Suggested 3rd line options based on prior regimens

Population	First-line regimen	Second-line regimen	Third line regimen
Adult and adolescents (10-19 years)	2 NRTI +EFV	2 NRTI +ATV/r	DTG + DRV/r ± 1-2 NRTIs*
	2 NRTI + DTG	2 NRTI +ATV/r	DTG + DRV/r ± 1-2 NRTIs*
Pregnant or Breast Feeding women	2 NRTI +EFV	2 NRTI +LPV/r	DTG + DRV/r ± 1-2 NRTIs*
Infants and Children (0-10 years)	2 NRTI +LPV/r	If less than 3 years: 2 NRTI + ATV/r	DTG + DRV/r + 1-2 NRTIs*
		If more than 3 years: 2 NRTI + DTG or EFV	
	2 NRTI +EFV	2 NRTI +LPV/r	

*wherever possible consider optimization using genotyping.

When a resistance test is not available, WHO recommends recycling TDF/3TC

For PI-experienced people, the recommended DRV/r dose should be 600 mg/100 mg twice daily. For INSTI-experienced people, the recommended DTG dose should be 50 mg twice daily.

How to ensure adherence

- Strategies
  - Identify main caregiver and back-up
    - discuss at initiation and before changing regimens
      - Lifelong treatment
      - Adherence and its impact on 'wellness'
      - Administration and relation to food
      - Toxicity of drugs
      - Storage of drugs
  - Assess adherence on EVERY visit (other than VL)
- Aim
  - Once daily regimen with low pill count soon as weight allows

Where to Treat

- Designated ART Treatment Centers (CDC-Sind)
  - Karachi: AKU, CHK, LGH, TIH, JPMC, ASH
  - Larkana: CMCHL, SZCHL, THQHR
  - Hyderabad: LUMHS
  - Sukkur: GMMMCH
- Designated ART Treatment Centers (PACP)
- Designated ART Treatment Centers (KPKACP/GB/FATA)
- Designated ART Treatment Centers (BACP)
- Designated ART Treatment Centers (Federal)

Summary of Expected Drug Toxicity:

- NRTIs
  - Abacavir (ABC): ABC-HSR (HLA B5701)
  - Zidovudine (AZT): Anemia
  - Tenofovir (TDF): Renal tubular dysfunction, decreased bone density, lactic acidosis
- NNRTIs:
  - Nevirapine (NVP): Rash, Steven Johnsons Syndrome (SJS), hepatotoxicity
  - Efavirenz (EFV): CNS toxicity and teratogenicity
- INSTIs
  - Dolutegravir (DTG): Hepatotoxicity, hypersensitivity
- PIs
  - Lopinavir-ritonavir (LPV-r): hepatotoxicity, QT Interval↑, PR Interval↑

References:

Materials from HIV Physician Training Workshops for National and Provincial HIV Control Programs Pakistan (Mahmood, Mir)

Consolidated Guidelines for Prevention and Treatment of HIV and AIDS in Pakistan 2023

Table 27 Prophylactic Dosing of ARV in children

Prophylactic Regimens	Dose 0-6 weeks					Dose 6-12 weeks	
Standard Risk of Vertical Transmission (One Drug Prophylaxis)*		2 to <3 kg		3 to <4 kg		4 to <5 kg	
		AM	PM	AM	PM	AM	PM
AZT (6 weeks)	10mg/ml	1	1	1.5	1.5	2	2
	60mg DT	0.8 ml (dissolve 1 tab in 5ml water)	0.8 ml (dissolve 1 tab in 5ml water)	1.25 ml (dissolve 1 tab in 5ml water)	1.25 ml (dissolve 1 tab in 5ml water)	1.5 ml (dissolve 1 tab in 5ml water)	1.5 ml (dissolve 1 tab in 5ml water)
NVP (6 weeks)**	10mg/ml	1	0	1.5	0	2	0
	50mg DT	1ml (dissolve 1 tab in 5ml water)		1.5ml (dissolve 1 tab in 5ml water)	-	0.5	0
High Risk of Vertical Transmission (Triple Drug Presumptive ARV Therapy)***							
AZT-3TC-NVP (treatment doses)	60/30/50 (DT)	0.5 tablet twice daily		1 tablet twice daily		1 tablet twice daily	
AZT+ 3TC +RAL (treatment doses)		See Treatment Dosage in Table 12.3					
High Risk of Vertical Transmission (Dual Prophylaxis) for first 6 weeks							
AZT (6 weeks) and NVP (6 weeks)	10mg/ml 10mg/ml	1 ml twice daily and 1 ml once daily		1.5 ml twice daily and 1.5 ml once daily		2 ml twice daily and 2 ml once daily	
	60mg DT 50mg DT	See Prophylactic Doses above (One Drug Prophylaxis)					
High Risk of Vertical Transmission (Single Prophylaxis for 12 weeks)							
AZT (12 weeks) or NVP (12 weeks)	60mg DT 50mg DT	See Prophylactic doses above					

Table 28 Dosages of antiretroviral drugs for HIV-infected infants, children and adolescents <35 kg

Drug	Strength of tables (mg) or oral liquid (mg/ml)	Number of tablets by weight band morning and evening										Strength of tables (mg)	Number of tablets morning and evening			
		3-5.9 kg		6-9.9 kg		10-13.9 kg		14-19.9 kg		20-24.5 kg			25-29.9 kg		30-35 kg	
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM		AM	PM	AM	PM
Dosing for Solid Formulations (Fixed Drug Combinations) currently available through NACP for children																
AZT-3TC	60/30 (DT)	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300/150	1	1	1	1
AZT-3TC-NVP	60/30/50 (DT)	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300/150/200	1	1	1	1
ABC-3TC	60/30 (DT)	1	1	1.5	1.5	2	2	2.5	2.5	3	3	600/300	1	0	1	0
TDF-3TC-EFV	300/300/600	-	-	-	-	-	-	-	-	-	-	300/300/600	0	1	0	1
TDF-3TC-DTG	300/300/50	-	-	-	-	-	-	-	-	-	-	300/300/50	1	0	1	0
Special Formulations with limited availability or potential availability																
ABC-3TC	120/60 (DT)	1	0	1.5	0	2	0	2.5	0	3	0	600/300 (DT)	1	0	1	0
EFV	200 (scored tab)	-	-	-	-	1	0	1.5	0	1.5	0		-	-	-	-
DTG	5 (dispersible)	2	-	3	-	4	-	5	-	-	-	50	1	0	1	0
DTG	10 (dispersible)	1	-	1.5	-	2	-	2.5	-	-	-		-	-	-	-
RAL	25 (chewable)	-	-	-	-	3	3	4	4	6	6	400	1	1	-	-
	100 (chewable)	-	-	-	-	-	-	1	1	1.5	1.5	400	1	1	-	-
	100 (granule)	0.25	0.25	0.5	0.5	-	-	-	-	-	-		-	-	-	-
TDF	150 (tab)	-	-	-	-	1	0	1.5	0	1.5	0	300	1	0	1	0
ABC/3TC/ LPV-r	30/60/40/10 (capsules)	2	2	3	3	4	4	5	5	6	6		-	-	-	-
ABC	60 (DT)	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300	1	1	1	1
ATV-r	ATV (50mg) ritonavir(80mg/1ml)	Not recommended for <15 kg						ATV 200 +ritonavir 100 (15 to <25kg)				300/100	1	0	1	0
Dosing for Solid Formulation currently available for children at NACP and Provincial programs																
AZT	60 (DT)	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300	1	1	1	1
3TC	150 (tab)	-	-	-	-			0.5	0.5	1	0.5	150	1	1	1	1
NVP	50 (DT)	1	1	1.5	1.5	2	2	2.5	2.5	3	3	200	1	1	1	1
DTG	10 (DT)	0.5	-	1.5	-	2	-	2.5	-	3	-	50	1	0	1	0

Drug	Strength of tables (mg) or oral liquid (mg/ml)	Number of tablets by weight band morning and evening										Strength of tables (mg)	Number of tablets morning and evening			
		3-5.9 kg		6-9.9 kg		10-13.9 kg		14-19.9 kg		20-24.5 kg			25-29.9 kg		30-35 kg	
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM		PM	AM	PM	AM
LPV/r	100/25 (tab)	-	-	-	-	2	1	2	2	2	2	100/25	3	3	3	3
	40/10 (granules)	2	2	3	3	4	4	5	5	6	6		-	-	-	-
Dosing for Liquid Formulations for infants 4 weeks and above (available and potential availability)																
AZT	10 mg/ml	6	6	9	9	12	12	15	15	18	18					
ABC	20 mg/ml	3	3	4	4	6	6	7.5	7.5	9	9					
3TC	10 mg/ml	3	3	4	4	6	6	-	-	-	-					
NVP	10 mg/ml	5	5	8	8	10	10	12.5	12.5	15	15					
LPV/r	80/20 mg/ml	1	1	1.5	1.5	2	2	2.5	2.5	3	3					
RTV	80mg/ml	-	-	-	-	0.5	0.5	0.6	0.6	-	-					
DRV	100mg/ml	-	-	-	-	2.5	2.5	3.5	3.5			600				
RAL	10mg/ml Oral granules for suspension (100mg/sachet)	3	3	5	5	8	8	10	10	-	-					
Dosing for Liquid Formulations for neonates and infants birth to less than 4 weeks																
						2-<3kg		3-<4kg		4-<5kg						
		Gestation Age*		mg/kg		AM	PM	AM	PM	AM	PM					
AZT	10mg/ml	≥35 wks		4mg/kg BID		1	1	1.5	1.5	2	2					
		≥30 to <35wks		2mg/kg BID (birth to 2 weeks) 3mg/kg BID (2 weeks to 6-8 weeks)												
		<30wks		2mg/kg BID												
NVP	10mg/ml	34-37 wks		4mg/kg BID (first week) increasing to 6mg/kg BID thereafter												
		≥37 Weeks		6mg/kg BID		1.5	1.5	2	2	3	3					
3TC	10mg/ml	≥32 weeks GA		2mg/kg BID		0.5	0.5	0.8	0.8	1	1					
LPV-r	80/20 mg/ml	PNA 14 days onwards		16 mg/4 mg per kg BID		0.6	0.6	0.8	0.8	1	1					
RAL	10mg/ml Oral granules for suspension 100mg/sachet)	≥37wks		<1 week		0.4 ml once daily		0.5 ml once daily		0.7 ml once daily						
		>1 week		0.8		0.8	1	1	1.5	1.5						

Chapter 05

Co-infections

5.1: Hepatitis C

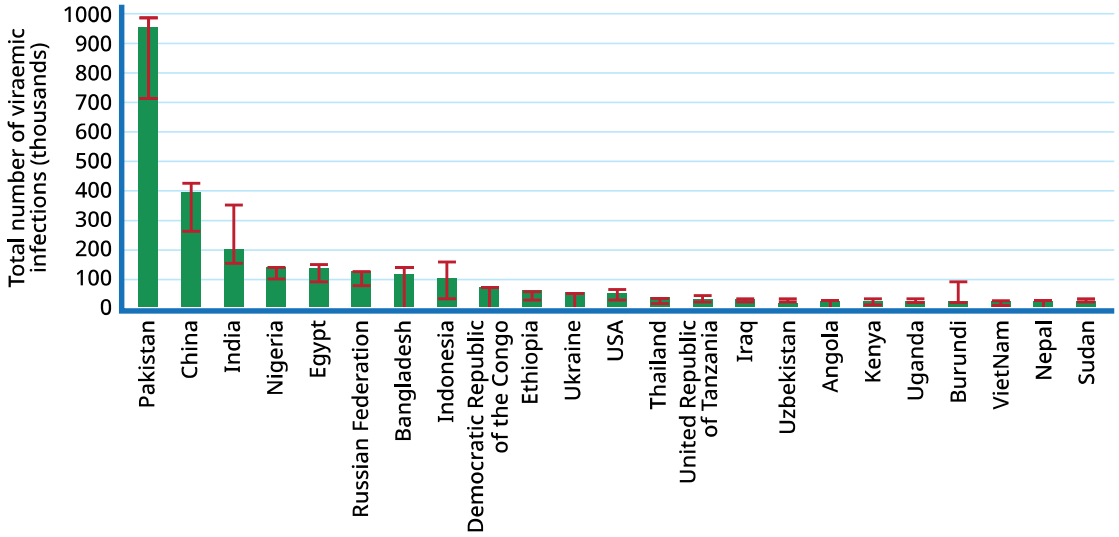
Global Burden

- Mortality & Morbidity
  - >180 million worldwide
  - CHC in >6yr decreased from 1.8% (1988 – 1994) to 1.3% (2007 – 2008)
    - Highly endemic in Pakistan – 6.8% of general population is infected
- Factors that caused decline of HCV in the western world
  - Preventive: safe sex, safe blood, safe injection practice
  - Therapeutic: IFN-a, DAA (Directly Acting Antivirals)

Twenty-three countries account for 80% of the global burden of Hepatitis C, and Pakistan, China, India and Nigeria alone account for more than 50% (Fig. 1). The predominant mode of acquisition of HCV infection in children is mother-to-child transmission. Older children and adolescents may become infected via unsafe injections and poor infection prevention and control, especially in LMICs (3).

Although most children with HCV infection have asymptomatic or minimally symptomatic liver disease (6-8), recent evidence suggests that liver disease progression may begin at a young age (9). HCV infection may also decrease the quality of life of children and adolescents, with evidence of impaired psychosocial and cognitive function, and impact on the family or caregivers (10-12). Early diagnosis and treatment in adolescents and children are key to preventing long-term morbidity related to chronic hepatitis C infection (3).

Figure 23 HCV Disease burden in twenty-three countries



Prevention of Mother to Child Transmission (PMTCT) Interventions

- Vertical transmission of HCV infection
  - 1 in 20 babies get infected
    - 40% clear infection spontaneously by 2-7y
  - C-section doesn't ↓risk of MTCT (normal vaginal delivery is recommended)
  - Breastfeeding does not ↑ risk of MTCT (breastfeeding can continue)
  - Mothers
    - Should receive Directly Acting Antivirals (DAAs)
    - Can breastfeed
  - HCV-exposed infants
    - No interventions available

The higher the viral load in the mother the higher the risk of infection. To date, interventions at birth such as C-section delivery have not been shown to alter the risk of infection at birth. The most effective treatment is DAAs as soon as the mother is diagnosed.

- Prevention of Parenteral Transmission of HCV: Interventions
  - Safe Blood
  - Safe Injection Practice
  - Early Diagnosis and Timely Treatment with Directly Acting Antivirals
  - No vaccine

Differences between adult and pediatric patients

- Mode of transmission
  - Mostly vertical transmission in children and in current climate of poor infection control, unsafe injections and blood
- Rate of clearance
  - 40% children clear by 2 years
- Progression to fibrosis
  - Vertical
    - Most have mild liver disease
      - 80% have minimal to no scarring of the liver (fibrosis) by 18 years of age
      - 20-25% can have more aggressive disease and can develop advanced scarring of the liver (cirrhosis) as early as 8 years of age
  - Parenteral
    - outcome of HCV is similar to that of adults
    - 80% will develop chronic HCV and many of those will go on to develop chronic liver disease with cirrhosis by the age of 20 – 30 years

- Duration of chronic infection (when acquired at birth)
  - HCV leading indication for liver transplantation in adults
  - Rare indication for liver transplantation in children

Diagnosis:

- HCV Antibody (IgG)
  - Inexpensive
  - Used for screening
  - Should not be used in infants < 18 mo
  - Third gen ELISA > 97% sensitive and > 98% specific
- Point of care (POC) HCV PCR testing
  - Approved by FDA in 2010
- Quantitative PCR (qPCR)

Table 29 Geographic Distribution of HCV Genotypes Worldwide:

Number	Countries
1	USA, Europe, Japan
2	Northern Italy, North America, Europe, Japan
3	India, Europe, USA
4	North Africa and the Middle East
5	South Africa
6	Hong Kong
7-9	Vietnam
10-11	Indonesia

Clinical Course (HCV)

HCV can lead to both acute and chronic disease. In some cases there can be spontaneous resolution without treatment. The disease can behave in four different ways:

- Acute hepatitis C (AHC)
  - alanine aminotransferase [ALT] > 10 normal in an individual **without** previously known liver disease or other reason for acute liver disease
  - Anti-HCV antibody detectable
  - HCV RNA detectable in serum sample

- Chronic hepatitis C (CHC)
  - Detectable HCV Ab for at least **6 months**
  - Implying ongoing liver injury
  - Detectable HCV RNA for at least 6 months
  - Positive anti-HCV differentiates between active and resolved infections
- Spontaneous resolution
  - Individuals with HCV infection who lose detectable serum HCV RNA without any treatment
  - On 2 sequential negative tests for HCV RNA at least 6 months apart
- Sustained viral response (SVR)
  - No virus detected in the blood by HCV-PCR 24 weeks after completing treatment

Aims of treatment:

- The goals of treatment in the individual patients
  - Eradicating virus infection,
  - Preventing end-stage liver disease and HCC, and
  - Removing stigma associated with HCV infection
- Overall goal
  - To decrease global burden of disease

Treatment of Hepatitis C in children

Historically, chronic Hepatitis C (CHC) in children was often managed with follow-up alone, as the disease typically progresses slowly, and severe outcomes like fibrosis are rare during childhood. This approach allowed many children to delay treatment until adulthood. However, this is no longer considered a valid option, except in a few specific cases.

Treatment options (age < 3 yrs)

- Generally should not be treated
- Why
  - HCV infection may still spontaneously resolve
  - Adverse effects of IFN-a in extremely young children are not well studied
  - Spastic diplegia has been reported in infants treated with IFN-a for hemangiomas

Treatment options (age > 3 yrs)

- PEG-IFN-α with ribavirin
  - first-line treatment for CHC in children ages 3 to 17 years
  - Superior in achieving sustained virological response (SVR) over IFN-α alone
    - PEG-IFN-α-2b (Pengintron) is 60 μg /m^2 / week given subcutaneously

- PEG-IFN-α-2a (Pegasys) is given at a dose of 180 μg/1.73m^2 weekly subcutaneously
- Ribavirin at a dose of 15mg / kg / day, PO divided twice daily

- Recommended length of therapy
  - 48 weeks of treatment for genotypes 1 or 4
  - 24 weeks of treatment for genotypes 2 or 3 in children

Hepatitis C treatment duration

- 93% kids with HCV genotype 2 or 3 treated for 24 weeks with pegylated interferon and **Ribavarin** achieved Sustained virologic response (SVR)
- 98% kids with HCV genotype 2 or 3 treated for 12 to 24 weeks with sofosbuvir plus ribavirin achieved Sustained virologic response (SVR)

New development

- In September 2019
  - FDA approved use of direct-acting antivirals in pediatric patients with Hepatitis C aged 3 years to younger than 12 years
  - Sovaldi (sofosbuvir) and Harvoni (ledipasvir/sofosbuvir)

SOF/DCV (sofosbuvir/delcatasavir), SOF/VEL (sofosbuvir/velpatasvir), G/P (Glecaprevir/Pibrentasvir), SOF/LED(ledipasvir/sofosbuvir)

Table 30 Treatment with DAAs recommended for children with chronic HCV

Age Groups	Recommended Pangenotypic DAA regimens			Non-pangenotypic DAA regimen (in settings with minimal GT3 infection)[2]
	SOF/DCV[1]	SOF/VEL[2]	G/P	SOF/LED
Adults (≥18 years)	12 weeks	12 weeks	8 weeks	12 weeks
Adolescents (12-17 years)	12 weeks	12 weeks	8 weeks	12 weeks
Older children (6-11 years)	12 weeks	12 weeks	8 weeks	12 weeks
Younger children (3-5 years)	12 weeks	12 weeks	8 weeks	12 weeks

[1]In those without cirrhosis. Treatment for 24 weeks is recommended in those who are treatment-experienced or with compensated cirrhosis. May be considered in settings where genotype 3 is known to be highly prevalent (>10%)

[2]For use in those with genotype 1,4,5 or 6 infections

Table 31 Dosing of Directly Acting Antivirals

Recommended Pangenotypic DAA regimens			Non-pangenotypic DAA regimen (in settings with minimal GT3 infection)[2]
SOF/DCV2	**SOF/VEL**	**G/P[3]**	**SOF/LED**
>26kg 400/60 mg OD (film-coated tablets)	>30kg 400/100 mg OD (FDC tablet)	>45 kg 300/120 mg OD (FDC tablet or 6 packets of oral pellets)	≥35kg 90/400 mg OD (FDC tablet)
14-25kg 200 mg/30mg[2] (as single tablets, SOF preferred as smaller, 100mg tablet)	17-29kg 200/50 mg OD (FDC tablet or granules)	30-less than 45 kg 250/100 mg OD (5 packets of oral pellets) 20- less than 30kg 200/80 mg OD (4 packets of oral pellets)	17-35kg 45/200 mg (tablet)
	<17 kg 150/37.5mg OD (coated granules)	<20 kg 150/60mg OD (3 packets of oral pellets)	<17 kg 33.75/150 mg (FDC granules packets)

FDC-Fixed Drug Combination

[1]For use in those with genotype 1,4,5, or 6 infection or where genotype 3 infection is uncommon

Monitoring during Therapy:

Table 32 Recommendation for monitoring during HCV Therapy

Laboratory Test to be monitored	Obtain test on following week of therapy
CBC with differential, absolute neutrophil count	0, 1, 2, 4, 8, 12 and every 4-8 weeks thereafter
Hepatic panel, glucose	0, 1, 2, 4, 8, 12 and every 4-8 weeks thereafter
TSH/FT4	0, 12, 24, 36, 48
Urine HCG (for WRA)	0, 24
Prothrombin time	0; only repeat if clinically indicated
Urinalysis	0; only repeat if clinically indicated
HCV RNA	0, 24, 48, 72

Cbc-complete blood count, HCG=human chorionic gonadotrophin, HCV=Hepatitis C virus, TSH=thyroid stimulating hormone

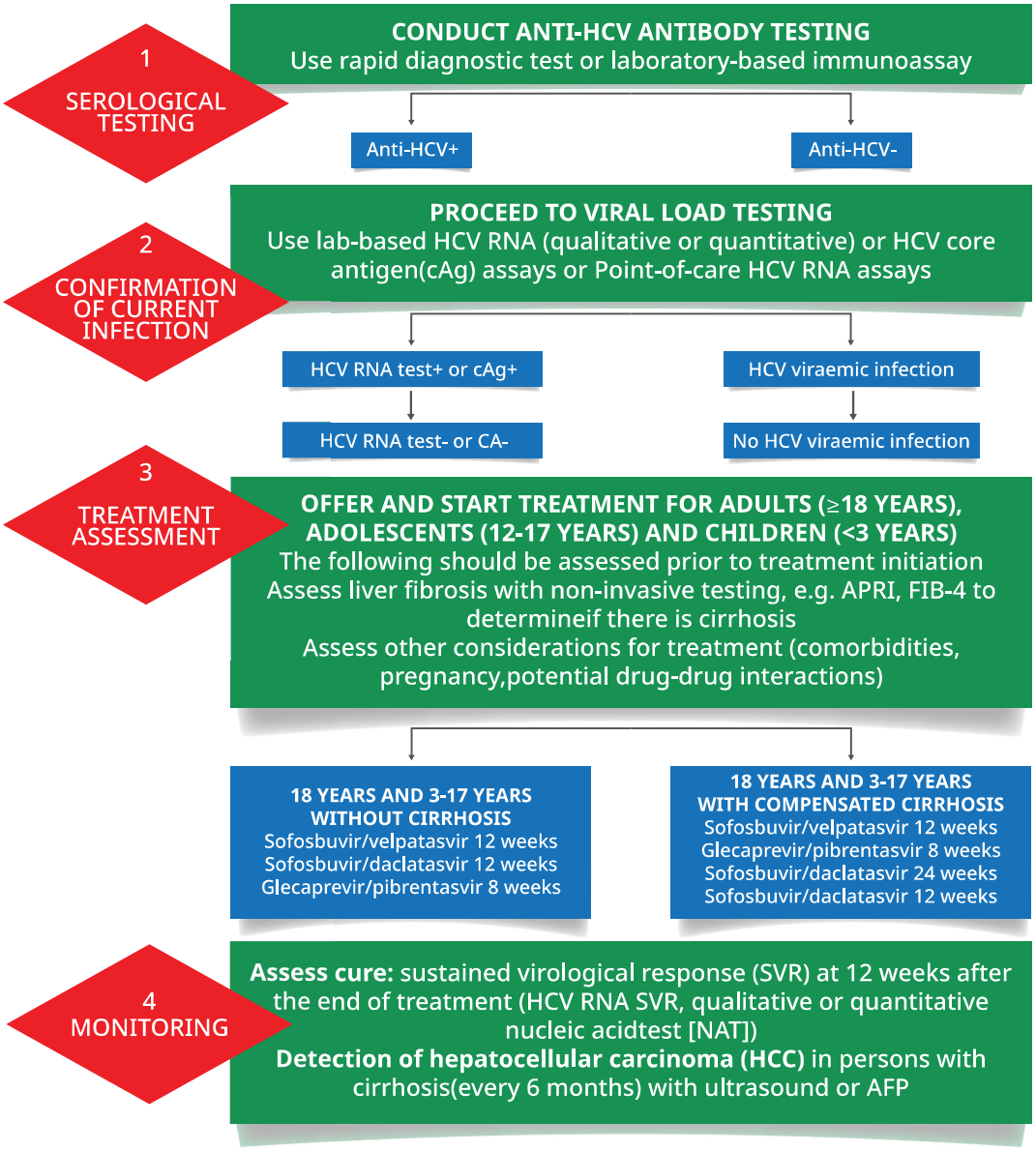
- Children with HCV should receive the hepatitis A and B vaccines
- They should also receive an annual influenza vaccine
- Families and children should be educated on the risk of HCV transmission and the techniques for avoiding blood exposure such as avoiding sharing toothbrushes, razors and nail clippers and the use of gloves to clean up blood

Table 33 : Anticipatory Guidance and screening for families with children with HCV infection

Category	No contraindication	Avoid	Routine screening
Household Contacts	Sharing food, drink, eating utensils, clothes, towels, laundry, toilet seats	Sharing toothbrushes, shaving equipment, nail clippers, tweezers, glucometers or any item likely to be contaminated with blood	Not recommended
Nonhousehold contacts	Attendign day-care, school, camps, playgrounds, paly dates, community pools, participating in contact and non-contact sports	NA	Not recommended
Casual contacts	Kissing, hugging, holding hands	NA	Not recommended
Sexual contacts	Monogamous sexual contact	Unprotected sexual activity with multiple partners	Not recommended: monogamous relationship; recommended: polygamous relationship
Other activities	NA	Tattooing, body piercing	NA

NA not applicable

Figure 24 Summary Algorithm for the diagnosis, treatment and monitoring of chronic HCV infection in adults, adolescents and children ≥3 years



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Updated recommendations on treatment of adolescents and children with chronic HCV infection. WHO Policy Brief June 2022

5.2: Hepatitis B

Global Burden

- Morbidity
  - Approximately 2 billion people infected with HBV
  - >350 million chronic HBV carriers
- Mortality 563000 deaths annually
- Epidemiology
  - After exposure, the risk of chronicity depends on the age of the child
    - Infected newborns **90% risk** of developing Chronic Hepatitis B (CHB)
    - Infants and children <5 years **25 – 30% risk** of developing Chronic Hepatitis B (CHB)
    - Adolescents or adults have a **<5% risk** of Chronic Hepatitis B (CHB)
  - Tools
    - Preventive: PPTCT (vaccine & HBIG), vaccine, safe sex, safe blood, safe injection practice
    - Therapeutic: IFN-a, Antivirals (lifelong)
- Global Strategy
  - Vaccine preventable infection with target for elimination

Prevention of Mother to Child Transmission interventions

- Mothers
  - Last trimester of pregnancy
    - Nucleoside or Nucleotide Analogues for mothers with high viremia
  - Breastfeeding
    - Does not increase the risk of transmission to the baby **PROVIDED**
      - the baby is given immuno-prophylaxis
      - The mother does not have cracked or bleeding nipples
    - Does not endanger the baby if mothers are on Nucleoside/Nucleotide Analogues
      - **Interferon** is not excreted in breast milk
      - **Lamivudine** and **Tenofovir** are excreted in breast milk
        - dose adsorbed by the infants is negligible compared to standard oral doses
      - **Entecavir** has not been studied in pregnant women as yet
        - Has been shown to be excreted in breast milk in rats and to have carcinogenic potential both in mice and rats after placental transfer
      - **Telbivudine** has no available safety data

HBV-exposed infants

- HBIG
  - Clear benefit for newborns of **HBeAg-positive mothers**
  - Unclear benefit for newborns of **HBeAg-negative mothers**
    - but reduction of the incidence of fulminant hepatitis justifies HBIG administration to all infants born of HBsAg-positive mothers, regardless of the maternal HBeAg status
- HBV Vaccine (0,1,6)
- Post vaccination HBsAb testing for high-risk populations
  - Infants born to HBsAg-positive mothers and
  - HIV-infected or other immunocompromised subjects
    - Revaccination with further 3 doses if HBsAb level is < 10 mIU/ml (non-responders)

Table 34 lists scenario and interventions when newborn requires PPTCT interventions for two vertically transmissible infections (HIV/HBV)

HBsAg+ Pregnant Woman (PW)	HIV+ Pregnant Woman
Maternal Status	
Early Catch as universal screening (ANTENATAL CARE)	Late Diagnosis as Risk-based screening (ANTENATAL CARE) Risk assessment: Test IF ≥ 1 of below • Resident in high-prevalence district • Positive spouse of sexual partner
Tests done when positive: ALT, HBeAg status, Viral Load at time of antenatal screen	Tests done when positive: VL soon as diagnosed and close to delivery
history of prior treatment: start asap	History of duration of ART by time of delivery (if < 4 weeks at this timepoint HIGH risk of transmission, else standard)
Post-exposure prophylaxis for exposed NB	
HBIG 0.5ml within 12 hours HBV Vaccine within 7 days, 1mo,6mo	Standard Risk: Single (NVP) 6 weeks High Risk: Triple (NLZ) 6 weeks
Breastfeeding Safety	
Can breastfeed AFTER administering HBIG	Can breastfeed if Mother virally suppressed Can breastfeed if formula feed not AFASS
Outcome	
HBsAg at 6 months • If negative, PPTCT success • If positive, PPTCT failure: Repeat HBsAg and HBsAb at 12-15 months (Ag-Ab+ means protection)	HIV RNA VL by age 6weeks to 2 mo (EID) • If negative, PPTCT success • If not done, PPTCT Service Failure: test as soon as possible • If positive, PPTCT intervention Failure: start on ART

Prevention of Parenteral HBV Transmission interventions:

- Vaccination
  - HBV Vaccine 1ml (20mcg) within 7 days, 1 mo and 6mo
- HBIG
  - HBIG 0.06ml/kg or 5ml within 24 hr of exposure and repeat at 1 month
- Safe Blood
- Safe Injection Practice

Table 35 Interventions in Older children requiring management of two co-infections

HBV	HIV
Conservative Management	Aggressive Management
If exposure is recent and obvious • HBIG 0.06ml/kg or 5ml within 24 hr of exposure and repeat at 1 month • HBV Vaccine 1ml (20mcg) within 7 days, 1 mo and 6mo If exposure not recent and not clear • Vaccination HBV Vaccine 1ml (20mcg) within 7 days, 1 mo and 6mo • HAV Vaccine 0.5ml 0mo,1mo Liver Status monitoring ALT q6m, HBeAg and HBeAb, HBV DNA, HBsAg Qt, HDV/HIV	Screen for HCV and TB Start ART (preferably TDF containing regimen) • DLT • ABC/**3TC** +LPV-R • Transitioning to TDF containing regimen soon as weight allows Monitoring

Table 36 Suggested Intervals of monitoring for children with chronic HBV infection

Serum HBeAg	ALT Levels	Interval of monitoring, months
Positive	Normal	6
Negative	Normal	6-12
Positive or Negative	Elevation (<2 x ULN)	3
Positive or Negative	Elevation (≥2 x ULN)	1-2

Principles of Treatment of Hepatitis B in Children (WHO Guidelines):

- Assessment of Disease Severity:
  - Evaluate liver disease severity through clinical, biochemical, and histological assessments.
  - Monitor hepatitis B virus (HBV) DNA levels, ALT (alanine aminotransferase), and HBeAg status.
- Eligibility for Treatment:
  - Prioritize treatment for children with chronic HBV infection who have evidence of liver disease, such as elevated ALT levels or significant fibrosis.
  - Consider antiviral therapy for children with cirrhosis, even if they have normal ALT levels or low HBV DNA levels.
- Antiviral Therapy Selection:
  - Preferred first-line treatments include tenofovir disoproxil fumarate (TDF) and entecavir (ETV), based on their safety and efficacy profiles in children.
  - Avoid interferon in younger children due to limited efficacy and adverse effects.
- Treatment Monitoring:
  - Regularly monitor liver function tests (LFTs), HBV DNA levels, and HBeAg status during treatment.
  - Assess for potential side effects, especially nephrotoxicity in those on tenofovir.
- Treatment Duration:
  - Continue antiviral therapy until HBeAg seroconversion (HBeAg-negative and anti-HBe positive) and undetectable HBV DNA levels are achieved, followed by an additional 12 months of treatment.
  - Consider lifelong therapy in children with cirrhosis or severe liver disease.
- Vaccination and Prevention:
  - Ensure all children receive the hepatitis B vaccine according to national immunization schedules.
  - Provide immunoglobulin and hepatitis B vaccination to newborns of HBsAg-positive mothers to prevent perinatal transmission.
- Regular Follow-Up:
  - Regular follow-up is necessary to monitor treatment response, side effects, and adherence.
  - For children not yet eligible for treatment, continue regular monitoring of HBV markers and liver health to determine if and when treatment should begin.
- Family and Patient Education:
  - Educate families and patients on the nature of chronic HBV infection, the importance of adherence to treatment, and regular follow-up visits.

Difference between Hepatitis B & C

- Transmission
  - HBV – blood & body fluids
  - HCV – blood & body fluids
- Epidemiology
  - Similar (sexual route, parenteral route)
- Natural history
  - HBV – unpredictable
  - HCV – slowly progressive
- Vaccine preventable
  - HBV – Yes
  - HCV – No
- Treatment
  - HBV – long term – no clear guidelines about stopping
  - HCV – finite – curative in overwhelming majority

References

Consolidated strategic information guidelines for viral hepatitis planning and tracking progress towards elimination: guidelines for viral hepatitis. WHO Feb 2019

5.3 Tuberculosis

Clinical Staging with HIV:

Please see Table 3.3 (WHO Staging of HIV Disease in adolescents and children).

Pulmonary Tuberculosis advances clinical stage of child with HIV to stage 3 and disseminated or extrapulmonary tuberculosis (excluding lymph node tb) to stage 4.

Lymph node tuberculosis alone is not associated with advanced HIV Disease.

Table 37 Comparative Epidemiology of HIV and TB

	HIVHIV	Tuberculosis	HIV-TB
Burden			
Mortality & Morbidity	Untreated: 52-75% Treated: 1.8 -9.4 deaths per 100 person-year	Untreated: CFR 21.9% Treated: CFR 0.9%	
Risk Factors	Age, Nutrition	Age, Nutrition, HIV infection	
Mode of Transmission	Multi-modal	Droplet	
MTCT/Blood/Sex Airborne/Droplet	Y/Y/Y -	Y/N/N Y	Y/Y/Y Y
Latent phase Symptomatic Phase	Y Y	Y Y	Y Y
Effective Vaccine	N	Y (TST)	Y (TST)
Diagnosis	Serological, Molecular	Microbiologic, Clinical Scoring	Multi-modal
Treatment	Combination Therapy Lifelong	Combination Therapy Finite	Combination therapy Interactions

Global Burden

- Leading infectious disease causing deaths
  - 10-20% of global burden is due to children
    - Under-diagnosed and under-reported
      - Paucibacillary disease
        - Microscopy negative
        - Culture negative
  - Transmission
    - Droplet

Case Definitions for National TB Program Pakistan

- Bacteriologically Confirmed TB case
  - Biological specimen is positive by smear microscopy or WHO-approved rapid diagnostics. All such cases should be notified
- Clinically diagnosed TB case
  - Does not fulfil the criteria for bacteriological confirmation but has been diagnosed with active TB by a clinician who has decided to give the patient a full course of TB treatment

Pulmonary TB:

We suspect pulmonary TB in a country with high burden of bacterial and viral pneumonia in children when we find:

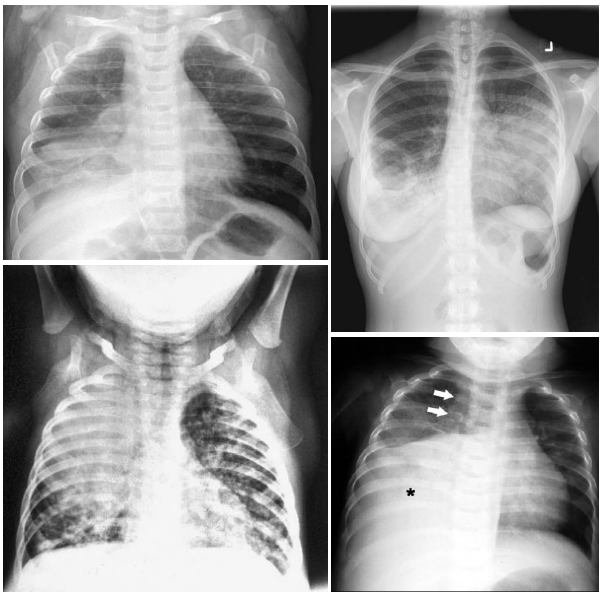
- Lobar infiltrates
- Pleural effusion
- Nodular lesions
- Miliary pattern

Extrapulmonary TB

We suspect Extrapulmonary TB when we encounter the following in clinical practice:

- Chronic lymphadenopathy (larger than 1.5cm in cervical chains, larger than 1 cm axillary and elsewhere)
- Ascitic/pleural/pericardial/CSF fluid
    - Lymphocytic pleocytosis with negative cultures
- Any condition which presents with chronic granulomatous disease on histopathology (crohn's disease, fungal infection)
- Vertebral osteomyelitis
- Monoarthritis with negative cultures
- Persistent sterile pyuria (pus in urine with negative bacterial cultures)
- Tuberculin (Mantoux) Test positive

Figure 25 a. lobar consolidation, b. consolidation and cavitating lesion, c. lobar consolidation and miliary pattern, d. lobar consolidation and effusion

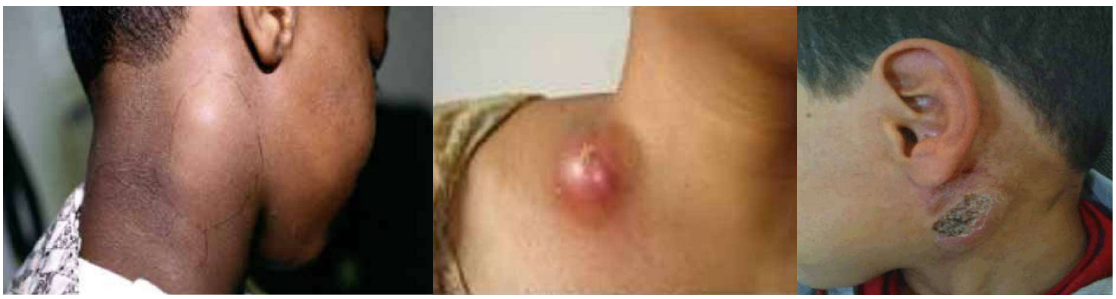


Lymph node TB:

This is the commonest manifestation of childhood tb and is difficult to diagnose as children will normally have enlarged lymph nodes due to recurrent upper respiratory infections due to pathogens other than mycobacterium tuberculosis.

Examination:

Figure 26 shows lymph node enlargement in supra-clavicular, posterior auricular and cervical chains



It is important to palpate along cervical and axillary chains.

CNS Tuberculosis:

- Most severe manifestation of extra-pulmonary tuberculosis
- Frequent within 2 years of primary infection
- Common in less than 5 years of age

TB Meningitis

- Short term mortality 20-69%
- Permanent neurological sequelae 50%

Tuberculoma

- Cerebellum
- Frontal lobe

Figure 27 shows neuroimaging findings in CNS Tuberculosis

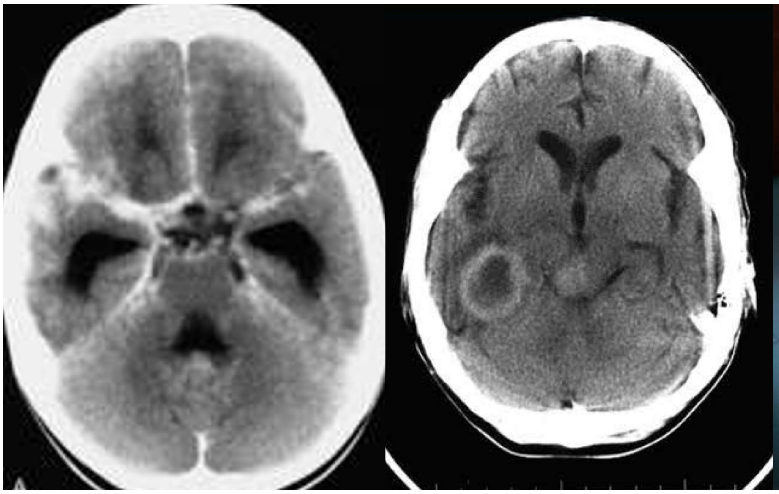
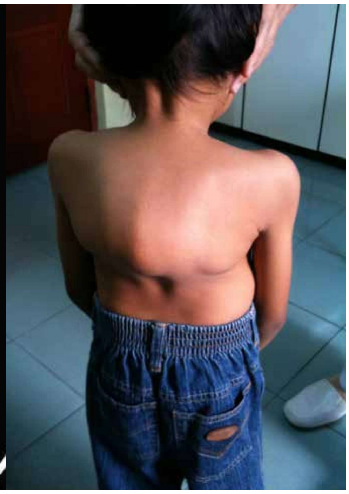


Figure 28 shows gross gibbus formation



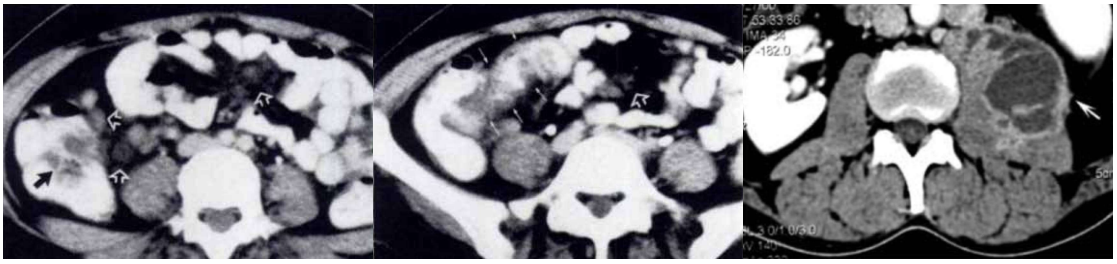
Bone Tuberculosis

- 5% of pediatric TB
- Skeletal TB
  - Osteomyelitis
  - Spondylitis
  - Arthritis
  - Ilio-psoas Abscess
- Sites
  - Dactylitis
  - Thoracic and lumber spinal (Potts disease)
    - 40% of bone TB

Abdominal Tuberculosis:

- Sites
  - GIT
  - Peritoneum
  - Mesentery
  - Ilio-psoas Abscess
  - Liver
  - Spleen
  - Pancreas
- Commonest
  - Adhesive peritonitis

Figure 29: Imaging in children with TB Enteritis and Psoas Abscess



Diagnosis:

TB Screening is a process by which one assesses if TB germs are in the patients' body. This can be by history questions or a tuberculin skin test (Mantoux Test).

Among adults and adolescents (10-19 years) living with HIV, systematic screening for TB disease should be conducted using the WHO-recommended four symptom screen including any one of fever more than 2 weeks, cough more than 2 weeks, weight loss, night sweats) or chest radiography or both.

Among children younger than 10 years who are living with HIV, systematic screening for TB disease should be conducted using a symptom screen including any one of current cough, fever, poor weight gain or close contact with a TB patient.

TB Diagnosis is a process by which one assesses if TB germs have caused disease in the patient's body. This can be by using clinical scores such as Keith Edward (Modified Pakistan Pediatric Association Score, See Table 3.3) in conjunction with laboratory and radiological tests.

Definitive tests:

These include sending respiratory or relevant tissue (pleural, lymph node, peritoneal/omental etc) for:

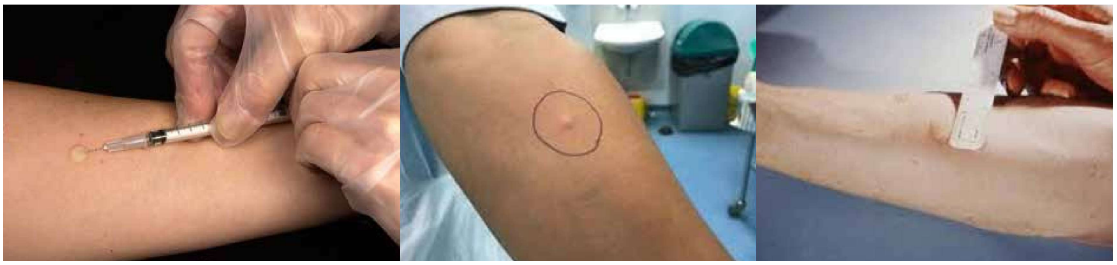
1) Microscopy using USP Method (Modified Auramine–Rhodamine Ziehl–Neelsen)
2) MTB cultures using Decontamination Method with NaOH-NALC
3) MTB PCR using Xpert MTB/RIF and Xpert Ultra

Supportive Tests:

These include

1) Mantoux test: The Mantoux test involves injecting 5 tuberculin units (TU) or 2 TU of tuberculin intradermally into the left forearm. A correctly placed injection produces a 6-10 mm pale wheal. The test is read after 48-96 hours by measuring the induration's diameter. Erythema is not measured.

Figure 30 Administering, monitoring and measuring the Mantoux Test



2) Radiology: Xray, Ultrasound, CT/MRI o suspected site of tuberculosis can suggest diagnosis even in absence of microbiological confirmation.
3) Histopathology/Body fluid cytology/biochemistry: These tests from sites of infection can also suggest the diagnosis
4) IGRA: this is a blood test which measures the body's immune response to TB Bacertia by detecting the release of interferon-gamma when T-lymphocytes are exposed to specific antigens like MTB.

Treatment: Childhood TB is treatment with combination therapy using 3-4 drugs in first two months (intensive phase) and 2 drugs in next 2-4 months (maintenance phase).

WHO gives options of shorter regimens for Non severe Pulmonary TB (Intrathoracic LN TB without obstruction, PTB confined to one lobe with no cavities and no **miliary** pattern, Uncomplicated Pleural effusion without pneumothorax or empyema):

Figure 31 below shows Treatment Options for Non-severe Pulmonary TB

REGIMAN	AGE				
	0-3 months	**3months-10 years**	**10-12 years**	**12-16 years**	**>16 years**
2HRZ(E)/4HR	Ethambutol should be added in setting with the high Background prevalence of isoniazid resistance of HIV Infection or in CLHIV.		Independent of disease severity or HIV status.		
2HRZ(E)/4HR		Non-served TB, > 3kg, add ethambutol in settings with a high background prevalence of isoniazid resistance of HIV Infection or in CALHIV.			
2HPMZ/2HPM			Independent of disease severity or HIV status.		
Additional Factors to be considered		Disease Severity			
If several regimens are possible	Patient or Family preferences.				
	Access and cost of regimen component drugs.				

For severe Pulmonary TB and all other extrapulmonary TB:

The total duration ranges from 6-12 months with the following:

- Core Regimen
  - 2HRZE/4HR (6 months) severe PTB
  - 2HRZE/10HR (12 months) tuberculous meningitis, osteoarticular tb, other EPTB, severe PTB
- Alternative short regimen
  - 6HRZEto
  - Adjuvant steroids
  - TBM: mortality or severe disability, disease relapse, adverse events
  - TB Pericarditis: death, constrictive pericarditis, treatment adherence (HIV cohort)

Table 38 Dosing for Anti-TB Therapy-weight-band based dosing as per Pakistan TB Program (PTP)

		Duration	Weight band / Number of Tablets						
			Less than 2kg	2-2.9kg	3-3.9kg	4-7.9kg	8-11.9kg	12-15.9kg	16-24.9kg
Initial Phase	HRZ (50/75/150)	2 months	1/4	1/2	3/4	1 Tab	2 Tab	3	4
Continuous daily phase	E 100	3 months	1/4	1/2	3/4	1	2	3	4
	HR (50/75)	4 months	1/4	1/2	3/4	1	2	3	4

Management of co-infection (HIV and TB):

Timing of therapy for both infections minimize the chance of IRIS.

- ART Naïve:
  - Start ATT FIRST
    - Initiate ART after 4-6 weeks of ATT intensive phase
    - Choice of ART may change (3 NRTIs)
      - Dosage of ART may change (double dose of LPV-r, DTG)
    - **ART-experienced:**
  - **Add ATT to ongoing ART**
    - Choice of ART may change (3 NRTIs)
      - Dosage of ART may change (double dose of LPV-r, DTG)

Dose adjustment if nevirapine, lopinavir-ritonavir or dolutegravir are part of the regimen is essential as rifampicin decreases their levels.

Table 39 Caveats in HIV and TB Follow-up Care

ART	ATT
Strategy (Lifelong) Identify main caregiver and back-up discuss at initiation and before changing regimens Lifelong treatment Adherence and its impact on 'wellness' Administration and relation to food Toxicity of drugs Storage of drugs Assess adherence on EVERY visit (other than VL) Aim Once daily regimen with low pill count soon as weight allows	• Strategy (Finite) • Identify main caregiver and back-up • discuss at initiation and before changing regimens • Finite treatment • Adherence and its impact on 'wellness' • Administration and relation to food • Toxicity of drugs • Storage of drugs • Assess adherence on EVERY visit

Monitoring for Adherence and Side Effects:

The family has to be counselled about adherence and the following dynamics explored at start of therapy and on follow up visits

- Caregiver readiness
- Patient-Provider relationship
- Patient health status
- Patient drug adverse effects

Table 40 Common Side-Effects of First Line TB Medications

Adverse Reaction	Drugs
Rash	PZA, INH, RIF, EMB
Gastrointestinal intolerance	PZA, RIF
Liver toxicity	PZA, INH, RIF
Peripheral neuropathy	INH
Optic neuritis	EMB
Gout	PZA

TB Prevention (TB Preventive Therapy TPT):

Historically every child under 5 years exposed to an adult index case with Pulmonary TB was screened for disease and If no signs and symptoms found, received isoniazid preventive therapy for 6 months. With increasing isoniazid resistance, now twod rugs are sued for a shorter duration of three months and this regimen is called TPT.

Table 41 Dosing chart for TB Preventive Therapy (TPT)

TB Prophylaxis regimens for children's								
		3-5.9kg	6-9.9kg	10-13.9kg	14-19.9kg	20-24.9kg		
B6	50mg	-	-	-	0.5	0.5	50	1
6H**	100mg	0.5	1	1.5	2	2.5	300mg	1
	4-7.9KG	8-11.9KG	12-15.9KG	16-24.9KG	25.39.9KG		40-45.9KG	
3RH	75/50	1	2	3	4	5	150/75	3
			10-14KG	14.1-25KG	25.1-32kg		32-49.9KG	
3HP	Isoniazid (100mg) + Rifapentine 150mg			(25mg/kg rounded)* + (300mg) 2tabwkly For 12wk	(25mg/kg rounded)* + (450mg) 3tabwkly For 12wk	(25mg/kg rounded)* (600mg) + 4tabwkly For 12wk	Isoniazid 100mg)* + Rifapentine 150mg For 12wk	(15mg/kg rounded)* (750mg) + 5tabs per week For 12wk

References TB:

Use of TB IGRAs in LMICs: Policy statement. Geneva, WHO, 2011 (WHO/HTM/2011.18)

Tuberculosis (NICE 2016)

Revised BCG vaccination guidelines for infants at risk for HIV infection. Weekly Epidemiological Record, 2007, 82:193-196

Tuberculosis Guidelines WHO 2020

National Consolidation Guidelines for Management of HIV in Pakistan 2020

Chapter 06

Opportunistic Infections in Children

Opportunistic infections strike when the child living with HIV becomes severely immune-suppressed. These infections mimic common childhood infections and may present just as pneumonias, meningitides, chronic diarrhoea, skin lesions caused by common organisms. Caveat for clinicians: when children with moderate to severe immunesuppression have seemingly 'common' infections but encounter an uncommon delay or no response to standard treatment, start thinking about opportunistic infections which present similarly.

How does CD4 count alert physician to risk of opportunistic infections?

CD4 is recommended for all children at baseline or at any timepoint where virological, immunological or clinical failure is suspected. It primes the physician on what opportunistic infections to screen for in immunologically suppressed but clinically well child and also which ones to rule out as differentials of ongoing illnesses.

Table 42 shows the child with age related severe immune suppression

Immunological Status	Age of Child Living with HIV (CLHIV)					
	<12 months		1-5 years		6-12 years	
	Cells/μL	%	Cells/μL	%	Cells/μL	%
No Suppression	>1500	>25	>1000	>25	>500	>25
Moderate Suppression	750-1499	15-24	500-999	15-24	200-499	15-24
Severe Suppression	<750	<15	<500	<15	<200	<15

Opportunistic Infections common in children based on etiological group are as below:

1. Mycobacteria:
   a. Tuberculosis (Pulmonary TB>TB Meningitis)
   b. Mycobacterium Avium Complex Disease
2. Fungi
   a. Candidiasis
   b. Cryptococcosis (including meningitis)
   c. Pneumocystis Jirovecii Pneumonia
3. Parasites
   a. Toxoplasmosis
   b. Cryptosporidiosis
4. Viruses
   a. CMV
   b. HSV
   c. EBV
   d. HPV
   e. VZV
   f. JC Virus
   g. MC

Mycobacterium Avium Complex Disease:

Clinical Scenario Example

Imagine a five-year-old child, let's call her Sarah, living in Larkana where access to healthcare is a challenge. Sarah was diagnosed with HIV at birth and has been receiving antiretroviral therapy (ART). Despite the treatment, Sarah starts experiencing persistent fever, weight loss, and a persistent cough. Concerned, her caregivers take her to the nearest health facility. The physician questions the family on adherence and finds out the caretaker grandmother passed away 2 months ago and since then the child has not been taking ART. Her CD4 count is 39cells/UL.

Definition

Mycobacterium Avium Complex (MAC) disease is an opportunistic infection caused by a group of bacteria known as Mycobacterium avium complex. It primarily affects individuals with weakened immune systems, such as those with HIV/AIDS. MAC disease can manifest in various forms, including disseminated infection, lymphadenitis, pulmonary disease, and gastrointestinal involvement.

Epidemiology

MAC disease has been a significant concern in the HIV/AIDS epidemic, particularly in resource-limited settings where access to healthcare and advanced diagnostic tools may be limited. Children living with HIV are particularly vulnerable to MAC disease due to their immature immune systems and higher susceptibility to infections.

Risk Factors

The primary risk factor for developing MAC disease is immunosuppression, especially due to HIV/AIDS. Other risk factors include inadequate access to healthcare, poor nutrition, lack of appropriate prophylaxis, and non-adherence to ART.

Clinical Features in Children with HIV

In children with HIV, MAC disease often presents with nonspecific symptoms, making diagnosis challenging. Common clinical features include:

1. **Fever**: Persistent or intermittent fever is a hallmark symptom of MAC disease.
2. **Weight Loss**: Unexplained weight loss despite adequate nutritional intake.
3. **Respiratory Symptoms**: Persistent cough, dyspnea, and chest pain may indicate pulmonary involvement.
4. **Gastrointestinal Symptoms**: Abdominal pain, diarrhea, and hepatomegaly may suggest gastrointestinal MAC disease.
5. **Lymphadenopathy**: Enlarged lymph nodes, particularly cervical lymphadenopathy, can occur in disseminated MAC infection.

Diagnostic Tests

Diagnosing MAC disease in children with HIV requires a combination of clinical evaluation, imaging studies, and microbiological tests. Diagnostic tests may include:

1. **Blood Cultures**: Isolation of Mycobacterium avium complex from blood cultures confirms disseminated infection.
2. **Sputum Culture**: In cases of pulmonary involvement, obtaining sputum samples for acid-fast bacilli (AFB) staining and culture is essential.
3. **Imaging**: Chest X-ray or CT scan may reveal pulmonary infiltrates or lymphadenopathy.
4. **Biopsy**: Tissue biopsy, such as lymph node or bone marrow biopsy, may be necessary for definitive diagnosis, especially in cases of extrapulmonary MAC disease.

Treatment

The treatment of MAC disease in children with HIV involves multidrug therapy to eradicate the infection and prevent relapse. The regimen typically includes:

1. **Clarithromycin or Azithromycin**: Macrolide antibiotics are the cornerstone of MAC treatment due to their efficacy against Mycobacterium avium complex.
2. **Ethambutol**: Often used in combination with macrolides to prevent the development of resistance.
3. **Rifabutin**: A rifamycin derivative with activity against MAC, commonly included in the treatment regimen.
4. **Adjunctive Therapy**: In severe cases, corticosteroids may be considered to reduce inflammation and improve clinical outcomes.

Prophylaxis

Given the high risk of MAC disease in children with advanced HIV infection, **prophylaxis with azithromycin or clarithromycin is recommended for those with low CD4 counts (<50 cells/mm^3).** Prophylactic therapy has been shown to significantly reduce the incidence of MAC disease and improve outcomes in HIV-infected children.

Complications of Disease

Untreated or inadequately treated MAC disease can lead to severe complications and increased mortality in children with HIV. Complications may include:

1. **Disseminated Disease**: MAC infection can spread to various organs, including the liver, spleen, bone marrow, and central nervous system, resulting in organ dysfunction and failure.
2. **Immune Reconstitution Inflammatory Syndrome (IRIS)**: In some cases, initiation of ART may paradoxically exacerbate symptoms due to the restoration of immune function, leading to an exaggerated inflammatory response known as IRIS.
3. **Drug Toxicity**: Long-term use of antimycobacterial agents, particularly macrolides, can cause adverse effects such as hepatotoxicity, gastrointestinal disturbances, and QT interval prolongation.

In conclusion, Mycobacterium Avium Complex disease poses a significant threat to children living with HIV, particularly in resource-limited settings. Early diagnosis, prompt initiation of appropriate therapy, and implementation of prophylactic measures are crucial for improving outcomes and reducing morbidity and mortality associated with this opportunistic infection.

Prophylaxis:

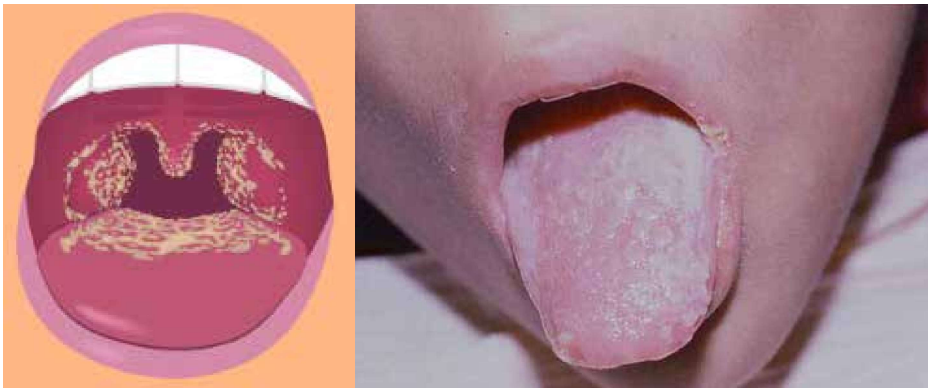
- Primary Prophylaxis
  - Azithromycin (20mg per kg per WEEK) or
  - Clarithromycin (500 mg orally twice daily) or
  - Rifabutin (300 mg orally daily)
- Secondary Prophylaxis
  - Lifelong continuation of therapy for MAC Disease unless MAC-IRIS occurs
    - IP:3 DRUG
    - **CP: 2 drug**
- Discontinuing Prophylaxis
  - Primary prophylaxis
    - **$CD4^+$ T cell count is >100/μL** for 3 months and HIV VL is suppressed
  - Secondary Prophylaxis
    - after 12 months of MAC treatment if CD4>100 and HIV VL is suppressed

Candidiasis

Clinical Scenario Example

Meet Danish, a seven-year-old boy living with HIV in a resource-limited area. Despite receiving antiretroviral therapy (ART), Daniel developed oral thrush, characterized by white patches on his tongue and inner cheeks. Concerned, his caregivers seek medical attention at the local health center.

Figure 32 Oral Candidiasis



Definition

Candidiasis is an opportunistic fungal infection caused by Candida species, primarily Candida albicans. It encompasses a spectrum of clinical manifestations, including oral thrush, esophageal candidiasis, cutaneous candidiasis, and invasive candidiasis. In children with HIV, candidiasis commonly occurs due to immunosuppression, predisposing them to fungal overgrowth and infection.

Epidemiology

Candidiasis is a prevalent opportunistic infection in children living with HIV, particularly in resource-limited settings where access to healthcare may be limited. The incidence of candidiasis is inversely proportional to CD4 cell counts, with higher rates observed in children with advanced HIV disease and severe immunosuppression. Additionally, candidiasis is more common in infants and young children with HIV due to their immature immune systems.

Risk Factors

Several factors increase the risk of candidiasis in children with HIV:

1. **Immunosuppression**: Low CD4 cell counts predispose children to fungal infections, including candidiasis.
2. **Poorly controlled HIV infection**: Inadequate ART adherence or treatment failure can lead to persistent immunosuppression and increased susceptibility to opportunistic infections.
3. **Infant feeding practices**: Breastfeeding infants with HIV are at risk of oral and nipple thrush, especially if the mother has untreated candidiasis.
4. **Malnutrition**: Poor nutritional status weakens the immune system, making children more susceptible to fungal infections.
5. **Coexisting conditions**: Underlying conditions such as diabetes mellitus or use of immunosuppressive medications further increase the risk of candidiasis.

Clinical Features in Children with HIV

Candidiasis can present with various clinical manifestations in children with HIV, including:

1. **Oral Thrush**: White, curd-like patches on the tongue, inner cheeks, palate, and oropharynx.
2. **Esophageal Candidiasis**: Difficulty swallowing (dysphagia), odynophagia (painful swallowing), retrosternal pain, and weight loss.
3. **Cutaneous Candidiasis**: Intertrigo (inflammatory rash in skin folds), diaper rash, and pruritus.
4. **Invasive Candidiasis**: Fever, abdominal pain, hepatosplenomegaly, and signs of systemic infection (e.g., sepsis).

Diagnostic Tests

Diagnosing candidiasis in children with HIV involves clinical evaluation and laboratory tests:

1. **Physical Examination**: Identification of characteristic clinical findings, such as oral thrush or cutaneous lesions.
2. **Microscopic Examination**: Microscopic examination of oral or cutaneous swabs or scrapings using potassium hydroxide (KOH) preparation can reveal budding yeast cells and pseudohyphae**.**
3. **Culture**: Culture of clinical specimens on Sabouraud dextrose agar or chromogenic media can confirm the presence of Candida species and determine antifungal susceptibility.

4. **Endoscopy**: Esophagogastroduodenoscopy (EGD) may be indicated in children with suspected esophageal candidiasis to visualize mucosal lesions and obtain biopsy samples for histopathological examination.

Treatment

The management of candidiasis in children with HIV involves antifungal therapy tailored to the clinical presentation and severity of infection:

1. **Topical Antifungals**: Oral thrush and cutaneous candidiasis are often treated with topical agents such as nystatin oral suspension or clotrimazole cream.
2. **Systemic Antifungals**: Severe or invasive candidiasis may require systemic therapy with azole antifungals (e.g., fluconazole, itraconazole) or echinocandins (e.g., caspofungin**, micafungin).**
3. **Adjunctive Measures**: Proper oral hygiene practices, such as regular mouth rinses with saline or bicarbonate solution, can help alleviate symptoms of oral thrush.

Prophylaxis

In children with HIV at high risk of recurrent candidiasis (e.g., low CD4 counts), long-term suppressive antifungal therapy may be considered as prophylaxis to prevent recurrence of infection. Fluconazole is commonly used for oral prophylaxis in children with advanced HIV disease.

Complications of Disease

Untreated or recurrent candidiasis can lead to complications in children with HIV:

1. **Esophageal Stricture**: Chronic esophageal candidiasis may result in fibrosis and narrowing of the esophagus, leading to dysphagia and strictures.
2. **Disseminated Candidiasis**: Invasive candidiasis can disseminate to other organs, causing systemic infection and sepsis, particularly in immunocompromised children.
3. **Nutritional Deficiencies**: Oral thrush and esophageal candidiasis can impair oral intake and lead to malnutrition, growth failure, and weight loss in children with HIV.

In summary, candidiasis is a common opportunistic infection in children with HIV, particularly in those with advanced disease and severe immunosuppression. Prompt recognition, appropriate diagnostic evaluation, and targeted antifungal therapy are essential for the effective management of candidiasis and prevention of complications in this vulnerable population.Top of Form

Cryptococcosis

Clinical Scenario Example

Meet Sakina, a nine-year-old girl living with HIV in a rural area with limited access to healthcare. Despite being on antiretroviral therapy (ART), Sakina develops severe headaches, confusion, and neck stiffness. Concerned about her worsening condition, her caregivers rush her to the nearest hospital for evaluation.

Definition

Cryptococcosis is an opportunistic fungal infection caused by the encapsulated yeast Cryptococcus neoformans or Cryptococcus gattii. It primarily affects immunocompromised individuals, including those with HIV/AIDS. Cryptococcosis can manifest as pulmonary cryptococcosis, cryptococcal meningitis, or disseminated disease, with cryptococcal meningitis being the most common presentation in children with HIV.

Epidemiology

Cryptococcosis is a significant cause of morbidity and mortality in children with HIV, particularly in resource-limited settings. The incidence of cryptococcosis is highest in regions with a high prevalence of HIV/AIDS and limited access to antifungal therapy. Cryptococcus neoformans is the predominant species causing infection in immunocompromised individuals, including children with HIV.

Risk Factors

Several factors increase the risk of cryptococcosis in children with HIV:

1. **Immunosuppression**: Children with advanced HIV disease and low CD4 cell counts are at increased risk of developing cryptococcosis.
2. **Non-adherence to ART**: Inadequate suppression of HIV replication increases the risk of opportunistic infections, including cryptococcosis.
3. **Environmental Exposure**: Cryptococcus neoformans and Cryptococcus **gattii** are ubiquitous in the environment, with inhalation of fungal spores being the primary mode of transmission.
4. **Geographic Location**: Certain regions, particularly tropical and subtropical areas, have a higher prevalence of cryptococcosis due to environmental factors favoring fungal growth.
5. **Coexisting Conditions**: Concurrent infections, such as tuberculosis or cytomegalovirus (CMV) infection, may further compromise the immune system and increase susceptibility to cryptococcosis.

Clinical Features in Children with HIV

Cryptococcosis can present with various clinical manifestations in children with HIV, including:

1. **Cryptococcal Meningitis**: Headache, fever, altered mental status, neck stiffness, photophobia, nausea, and vomiting.
2. **Pulmonary Cryptococcosis**: Cough, dyspnea, chest pain, and respiratory failure in severe cases.
3. **Disseminated Cryptococcosis**: Cryptococcal infection involving multiple organs, such as the skin, bones, lymph nodes, and central nervous system.

In children with HIV, cryptococcal meningitis is the most common presentation and carries a high risk of morbidity and mortality if not promptly diagnosed and treated.

Diagnostic Tests

Diagnosing cryptococcosis in children with HIV involves clinical evaluation and laboratory tests:

1. **Cerebrospinal Fluid (CSF) Analysis**: Lumbar puncture with CSF analysis is essential for diagnosing cryptococcal meningitis. CSF examination typically reveals elevated opening pressure, lymphocytic pleocytosis, elevated protein levels, and a positive India ink stain or cryptococcal antigen test.
2. **Blood Cultures**: Blood cultures may yield positive results in cases of disseminated cryptococcal infection.
3. Cryptococcal Antigen Blood Test
4. **Imaging Studies**: Chest X-ray or CT scan may reveal pulmonary infiltrates in cases of pulmonary cryptococcosis.

Treatment

The management of cryptococcosis in children with HIV involves antifungal therapy and supportive care:

1. **Induction Therapy**: Initial treatment typically consists of amphotericin B-based regimens, such as liposomal amphotericin B or amphotericin B deoxycholate, in combination with flucytosine.
2. **Consolidation Therapy**: Following induction therapy, consolidation therapy with fluconazole or other oral azoles is initiated to complete the treatment course.
3. **Maintenance Therapy**: Long-term suppressive therapy with oral fluconazole may be necessary to prevent relapse, particularly in children with advanced HIV disease.
4. **Adjunctive Measures**: Supportive care measures, including management of intracranial hypertension, electrolyte abnormalities, and immune reconstitution inflammatory syndrome (IRIS), are essential for optimizing clinical outcomes.

Prophylaxis

In children with HIV at high risk of cryptococcosis (e.g., low CD4 counts), primary prophylaxis with fluconazole may be considered to prevent the development of cryptococcal infection. Secondary prophylaxis with long-term suppressive antifungal therapy may also be indicated in children with a history of cryptococcal disease or recurrent episodes.

Complications of Disease

Untreated or inadequately treated cryptococcosis can lead to severe complications and increased mortality in children with HIV:

1. **Cryptococcal Meningitis Complications**: Intracranial hypertension, hydrocephalus, cerebral infarction, and cranial nerve palsies.
2. **Disseminated Cryptococcosis**: Cryptococcal infection involving multiple organs can result in organ dysfunction, sepsis, and multi-organ failure.
3. **Immune Reconstitution Inflammatory Syndrome (IRIS)**: Initiation of ART may trigger an exaggerated inflammatory response, leading to IRIS manifestations such as worsening meningitis or paradoxical clinical deterioration.

In conclusion, cryptococcosis poses a significant threat to children living with HIV, particularly in regions with high HIV prevalence and limited access to healthcare. Early recognition, prompt diagnosis, and aggressive antifungal therapy are crucial for improving outcomes and reducing morbidity and mortality associated with this opportunistic fungal infection.

Pneumocystis Jirovecii Pneumonia

Clinical Scenario Example

Meet Amina, a nine-year-old girl living with HIV in a rural area with limited access to healthcare. Despite being on antiretroviral therapy (ART), Emily develops severe headaches, confusion, and neck stiffness. Concerned about her worsening condition, Emily's caregivers rush her to the nearest hospital for evaluation.

Definition

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Cryptococcosis is a significant cause of morbidity and mortality in children with HIV, particularly in resource-limited settings. The incidence of cryptococcosis is highest in regions with a high prevalence of HIV/AIDS and limited access to antifungal therapy. Cryptococcus neoformans is the predominant species causing infection in immunocompromised individuals, including children with HIV.

Risk Factors

Several factors increase the risk of cryptococcosis in children with HIV:

1. **Immunosuppression**: Children with advanced HIV disease and low CD4 cell counts are at increased risk of developing cryptococcosis.
2. **Non-adherence to ART**: Inadequate suppression of HIV replication increases the risk of opportunistic infections, including cryptococcosis.
3. **Environmental Exposure**: Cryptococcus neoformans and Cryptococcus gattii are ubiquitous in the environment, with inhalation of fungal spores being the primary mode of transmission.
4. **Geographic Location**: Certain regions, particularly tropical and subtropical areas, have a higher prevalence of cryptococcosis due to environmental factors favoring fungal growth.
5. **Coexisting Conditions**: Concurrent infections, such as tuberculosis or cytomegalovirus (CMV) infection, may further compromise the immune system and increase susceptibility to cryptococcosis.

Clinical Features in Children with HIV

Cryptococcosis can present with various clinical manifestations in children with HIV, including:

1. **Cryptococcal Meningitis**: Headache, fever, altered mental status, neck stiffness, photophobia, nausea, and vomiting.
2. **Pulmonary Cryptococcosis**: Cough, dyspnea, chest pain, and respiratory failure in severe cases.
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In children with HIV, cryptococcal meningitis is the most common presentation and carries a high risk of morbidity and mortality if not promptly diagnosed and treated.

Diagnostic Tests

Diagnosing cryptococcosis in children with HIV involves clinical evaluation and laboratory tests:

1. **Cerebrospinal Fluid (CSF) Analysis**: Lumbar puncture with CSF analysis is essential for diagnosing cryptococcal meningitis. CSF examination typically reveals elevated opening pressure, lymphocytic pleocytosis, elevated protein levels, and a positive India ink stain or cryptococcal antigen test.
2. **Blood Cultures**: Blood cultures may yield positive results in cases of disseminated cryptococcal infection.
3. **Imaging Studies**: Chest X-ray or CT scan may reveal pulmonary infiltrates in cases of pulmonary cryptococcosis.

Treatment

The management of cryptococcosis in children with HIV involves antifungal therapy and supportive care:

1. **Induction Therapy**: Initial treatment typically consists of amphotericin B-based regimens, such as liposomal amphotericin B or amphotericin B deoxycholate, in combination with flucytosine.
2. **Consolidation Therapy**: Following induction therapy, consolidation therapy with fluconazole or other oral azoles is initiated to complete the treatment course.
3. **Maintenance Therapy**: Long-term suppressive therapy with oral fluconazole may be necessary to prevent relapse, particularly in children with advanced HIV disease.
4. **Adjunctive Measures**: Supportive care measures, including management of intracranial hypertension, electrolyte abnormalities, and immune reconstitution inflammatory syndrome (IRIS), are essential for optimizing clinical outcomes.

Prophylaxis

In children with HIV at high risk of cryptococcosis (e.g., low CD4 counts), primary prophylaxis with fluconazole may be considered to prevent the development of cryptococcal infection. Secondary prophylaxis with long-term suppressive antifungal therapy may also be indicated in children with a history of cryptococcal disease or recurrent episodes.

Complications of Disease

Untreated or inadequately treated cryptococcosis can lead to severe complications and increased mortality in children with HIV:

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2. **Disseminated Cryptococcosis**: Cryptococcal infection involving multiple organs can result in organ dysfunction, sepsis, and multi-organ failure.
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In conclusion, cryptococcosis poses a significant threat to children living with HIV, particularly in regions with high HIV prevalence and limited access to healthcare. Early recognition, prompt diagnosis, and aggressive antifungal therapy are crucial for improving outcomes and reducing morbidity and mortality associated with this opportunistic fungal infection.

Pneumocystis jirovecii Pneumonia in Children with HIV

Clinical Scenario Example

Consider Mariam, a six-year-old girl living with HIV in a low-resource setting. Despite receiving antiretroviral therapy (ART), Mariam develops a persistent dry cough, fever, and progressive shortness of breath. Concerned about her worsening symptoms, her caregivers bring her to the local healthcare facility for evaluation.

Definition

Pneumocystis jirovecii pneumonia (PJP), formerly known as Pneumocystis carinii pneumonia (PCP), is an opportunistic fungal infection caused by the yeast-like fungus Pneumocystis jirovecii. It primarily affects immunocompromised individuals, including those with HIV/AIDS, and is a leading cause of morbidity and mortality in this population. PJP typically presents as an interstitial pneumonia, characterized by bilateral pulmonary infiltrates and hypoxemia.

Epidemiology

PJP remains a significant concern in children living with HIV, particularly in resource-limited settings where access to healthcare and prophylactic measures may be limited. The incidence of PJP has declined with the widespread use of ART and prophylactic regimens; however, it continues to be a common opportunistic infection in children with advanced HIV disease and severe immunosuppression.

Risk Factors

Several factors increase the risk of PJP in children with HIV:

1. **Immunosuppression**: Children with advanced HIV disease, particularly those with low CD4 cell counts, are at increased risk of developing PJP.

2. **Non-adherence to ART**: Inadequate suppression of HIV replication increases the risk of opportunistic infections, including PJP.
3. **Lack of Prophylaxis**: Failure to receive appropriate prophylactic therapy with trimethoprim-sulfamethoxazole (TMP-SMX) increases the risk of PJP in children with HIV.
4. **Young Age**: Infants and young children with HIV are particularly susceptible to PJP due to their immature immune systems and higher risk of severe immunosuppression.

Clinical Features in Children with HIV

PJP can present with various clinical manifestations in children with HIV, including:

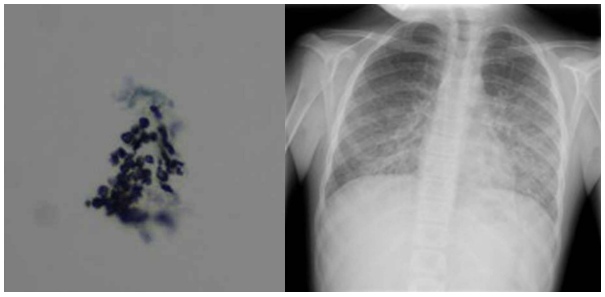
1. **Respiratory Symptoms**: Progressive dyspnea, tachypnea, and hypoxemia are hallmark features of PJP in children. The cough may be dry or nonproductive.
2. **Fever**: Persistent or intermittent fever is common in children with PJP and may be the presenting symptom.
3. **Chest Pain**: Children with PJP may experience pleuritic chest pain, particularly during inspiration.
4. **Malaise and Fatigue**: Generalized weakness, fatigue, and malaise may accompany respiratory symptoms in children with PJP.
5. **Signs of Respiratory Distress**: Tachycardia, nasal flaring, intercostal retractions, and cyanosis may indicate severe respiratory compromise in children with PJP.

Diagnostic Tests

Diagnosing PJP in children with HIV involves clinical evaluation and laboratory tests:

1. **Chest Radiography**: Chest X-ray typically reveals bilateral interstitial infiltrates, often described as a "ground-glass" appearance, although findings may be variable.
2. **Arterial Blood Gas (ABG) Analysis**: ABG analysis may demonstrate hypoxemia and respiratory alkalosis in children with PJP.

Figure 33 Ground glass appearance on CXR



3. **Bronchoalveolar Lavage (BAL)**: BAL with microscopic examination and fungal staining (Grocott-Gomori methenamine silver stain) (Fig 6.3) can confirm the presence of Pneumocystis jirovecii organisms.
4. **Serologic Tests**: Serum (1→3)-β-D-glucan assay and Pneumocystis jirovecii polymerase chain reaction (PCR) testing may be used to support the diagnosis of PJP in children with HIV.

Treatment

The management of PJP in children with HIV involves antimicrobial therapy and supportive care:

1. **Trimethoprim-Sulfamethoxazole (TMP-SMX)**: TMP-SMX is the preferred treatment for PJP in children, given orally or intravenously depending on the severity of illness.
2. **Adjunctive Corticosteroids**: Systemic corticosteroids, such as prednisone, may be indicated in children with moderate to severe PJP and hypoxemia to reduce inflammation and improve oxygenation.
3. **Supplemental Oxygen**: Oxygen therapy is essential for maintaining adequate oxygenation in children with respiratory distress due to PJP.
4. **Intravenous Fluids**: Hydration and electrolyte management are important aspects of supportive care in children with PJP.

Prophylaxis

Primary prophylaxis with TMP-SMX is recommended for children with HIV and CD4 counts below certain thresholds to prevent the development of PJP. Secondary prophylaxis with long-term suppressive therapy may be necessary in children with a history of PJP or recurrent episodes.

Complications of Disease

Untreated or inadequately treated PJP can lead to severe complications and increased mortality in children with HIV:

1. **Respiratory Failure**: Progressive hypoxemia and respiratory compromise may result in respiratory failure requiring mechanical ventilation.
2. **Acute Respiratory Distress Syndrome (ARDS)**: Severe PJP can lead to ARDS, characterized by diffuse alveolar damage and impaired gas exchange.
3. **Secondary Infections**: PJP-associated immunosuppression can predispose children to secondary bacterial or fungal infections, further complicating the clinical course.
4. **Neurological Complications**: Hypoxemia and cerebral hypoperfusion may lead to neurological sequelae such as encephalopathy or seizures in severe cases of PJP.

In conclusion, Pneumocystis jirovecii pneumonia remains a significant opportunistic infection in children living with HIV, particularly in regions with limited access to healthcare and prophylactic measures. Early recognition, prompt diagnosis, and aggressive treatment are crucial for improving outcomes and reducing morbidity and mortality associated with this potentially life-threatening fungal infection.

Toxoplasmosis

Clinical Scenario Example

Consider Latif, a four-year-old boy living with HIV in a rural area with limited access to healthcare. Despite being on antiretroviral therapy (ART), Latif develops seizures, altered mental status, and weakness on one side of his body. Concerned about his worsening condition, Lucas' caregivers rush him to the nearest hospital for evaluation.

Definition

Toxoplasmosis is an opportunistic infection caused by the protozoan parasite Toxoplasma gondii. It primarily affects immunocompromised individuals, including those with HIV/AIDS. Toxoplasmosis can manifest as toxoplasmic encephalitis, cerebral toxoplasmosis, or disseminated disease, with central nervous system involvement being the most common presentation in children with HIV.

Epidemiology

Toxoplasmosis is a significant cause of morbidity and mortality in children with HIV, particularly in resource-limited settings where access to healthcare and preventive measures may be limited. The incidence of toxoplasmosis has decreased with the widespread use of ART and prophylactic regimens; however, it remains an important opportunistic infection in children with advanced HIV disease and severe immunosuppression.

Risk Factors

Several factors increase the risk of toxoplasmosis in children with HIV:

1. **Immunosuppression**: Children with advanced HIV disease, particularly those with low CD4 cell counts, are at increased risk of developing toxoplasmosis.
2. **Non-adherence to ART**: Inadequate suppression of HIV replication increases the risk of opportunistic infections, including toxoplasmosis.
3. **Exposure to Cats**: Contact with cats or ingestion of undercooked meat contaminated with Toxoplasma gondii increases the risk of toxoplasmosis.
4. **Prenatal Exposure**: Congenital toxoplasmosis can occur if the mother acquires Toxoplasma gondii infection during pregnancy, leading to vertical transmission to the fetus.

Clinical Features in Children with HIV

Toxoplasmosis can present with various clinical manifestations in children with HIV, including:

1. **Neurological Symptoms**: Headache, seizures, altered mental status, focal neurological deficits (e.g., hemiparesis), and signs of increased intracranial pressure.
2. **Fever**: Persistent or intermittent fever may be present, although it is less common in children with toxoplasmosis.
3. **Behavioral Changes**: Irritability, lethargy, and personality changes may occur in children with toxoplasmosis, particularly those with central nervous system involvement.

4. **Ocular Symptoms**: Toxoplasmic retinochoroiditis, characterized by unilateral eye pain, blurred vision, and scotomas, may occur in children with congenital toxoplasmosis or disseminated disease.

Diagnostic Tests

Diagnosing toxoplasmosis in children with HIV involves clinical evaluation and laboratory tests:

1. **Neuroimaging**: Brain imaging studies, such as computed tomography (CT) or magnetic resonance imaging (MRI), may reveal characteristic ring-enhancing lesions in the basal ganglia, thalamus, or cerebral cortex suggestive of toxoplasmic encephalitis.
2. **Serologic Tests**: Serologic testing for Toxoplasma-specific antibodies, including immunoglobulin G (IgG) and immunoglobulin M (IgM), can aid in the diagnosis of acute toxoplasmosis.
3. **Cerebrospinal Fluid (CSF) Analysis**: Lumbar puncture with CSF analysis may reveal lymphocytic pleocytosis, elevated protein levels, and a positive Toxoplasma-specific polymerase chain reaction (PCR) test in children with cerebral toxoplasmosis.

Treatment

The management of toxoplasmosis in children with HIV involves antimicrobial therapy and supportive care:

1. **Pyrimethamine and Sulfadiazine**: The combination of pyrimethamine and sulfadiazine is the preferred treatment for toxoplasmosis in children, given orally or intravenously depending on the severity of illness.
2. **Leucovorin**: Leucovorin (**folinic** acid) supplementation is administered to prevent hematologic toxicity associated with pyrimethamine therapy.
3. **Adjunctive Corticosteroids**: Systemic corticosteroids may be indicated in children with cerebral toxoplasmosis and significant perilesional edema to reduce inflammation and minimize neurological sequelae.
4. **Anticonvulsants**: Anticonvulsant medications may be necessary to control seizures in children with toxoplasmosis-associated encephalopathy.

Prophylaxis

Primary prophylaxis with trimethoprim-sulfamethoxazole (TMP-SMX) is recommended for children with HIV and low CD4 counts to prevent the development of toxoplasmosis. Secondary prophylaxis with long-term suppressive therapy may be necessary in children with a history of toxoplasmosis or recurrent episodes.

Complications of Disease

Untreated or inadequately treated toxoplasmosis can lead to severe complications and increased mortality in children with HIV:

1. **Neurological Sequelae:** Toxoplasmic encephalitis can result in permanent neurological deficits, including cognitive impairment, motor dysfunction, and seizures.

2. **Hydrocephalus**: Obstructive hydrocephalus may occur due to mass effect from **toxoplasmic** brain lesions, leading to increased intracranial pressure and neurological deterioration.
3. **Visual Impairment:** Toxoplasmic retinochoroiditis can cause irreversible damage to the retina, resulting in vision loss and permanent visual impairment.
4. **Reactivation of Latent Infection**: Immune reconstitution inflammatory syndrome (IRIS) may occur in children with HIV following initiation of ART, leading to worsening symptoms due to the restoration of immune function and exaggerated inflammatory response.

In conclusion, toxoplasmosis remains a significant opportunistic infection in children living with HIV, particularly in regions with limited access to healthcare and preventive measures. Early recognition, prompt diagnosis, and aggressive treatment are crucial for improving outcomes and reducing morbidity and mortality associated with this potentially devastating parasitic infection.

Cryptosporidiosis

Clinical Scenario Example

Imagine Sabina, a six-year-old girl living with HIV in a rural area with limited access to clean water. Despite receiving antiretroviral therapy (ART), Sarah develops severe diarrhea, abdominal cramps, and weight loss. Concerned about her worsening condition, Sabinas caregivers seek medical attention at the local health center.

Definition

Cryptosporidiosis is an opportunistic protozoal infection caused by the parasite Cryptosporidium spp., commonly Cryptosporidium parvum and Cryptosporidium hominis. It primarily affects immunocompromised individuals, including those with HIV/AIDS. Cryptosporidiosis is transmitted through ingestion of contaminated water or food, contact with infected animals, or person-to-person transmission via the fecal-oral route.

Epidemiology

Cryptosporidiosis is a significant cause of morbidity in children with HIV, particularly in resource-limited settings where access to clean water and sanitation infrastructure is limited. The incidence of cryptosporidiosis is highest in areas with poor hygiene and sanitation practices. Children with HIV/AIDS, particularly those with advanced disease and severe immunosuppression, are at increased risk of developing severe and prolonged cryptosporidiosis.

Risk Factors

Several factors increase the risk of cryptosporidiosis in children with HIV:

1. **Immunosuppression**: Children with advanced HIV disease, particularly those with low CD4 cell counts, are at increased risk of developing cryptosporidiosis.
2. **Environmental Exposure**: Contact with contaminated water sources, including drinking water, swimming pools, and recreational water facilities, increases the risk of cryptosporidiosis transmission.

3. **Poor Hygiene Practices**: Inadequate hand hygiene, consumption of unpasteurized milk or dairy products, and exposure to infected animals increase the risk of cryptosporidiosis.
4. **Malnutrition**: Malnourished children are more susceptible to cryptosporidiosis due to impaired immune function and compromised intestinal barrier function.

Clinical Features in Children with HIV

Cryptosporidiosis can present with various clinical manifestations in children with HIV, including:

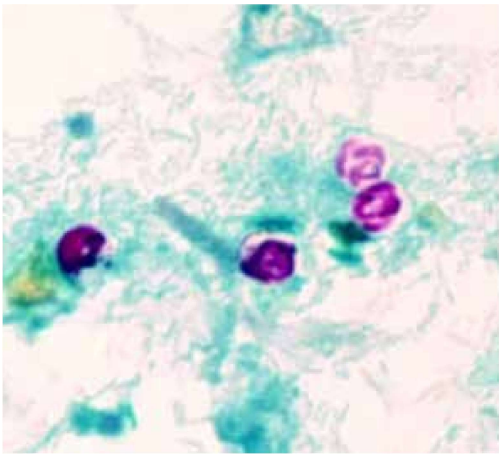
1. **Diarrhea**: Watery diarrhea, which may be profuse, persistent, and recurrent, is the hallmark symptom of cryptosporidiosis in children. Diarrhea may be accompanied by abdominal cramps, bloating, and urgency.
2. **Weight Loss**: Chronic diarrhea and malabsorption can lead to weight loss, failure to thrive, and nutritional deficiencies in children with cryptosporidiosis.
3. **Dehydration**: Prolonged diarrhea and fluid loss can result in dehydration, electrolyte imbalances, and metabolic acidosis, particularly in severe cases.
4. **Immunodeficiency**: Children with advanced HIV disease and severe immunosuppression may experience disseminated cryptosporidiosis, involving extraintestinal organs such as the biliary tract, lungs, or central nervous system.

Diagnostic Tests

Diagnosing cryptosporidiosis in children with HIV involves clinical evaluation and laboratory tests:

1. **Stool Examination**: Microscopic examination of stool samples using acid-fast staining or immunofluorescence microscopy can detect Cryptosporidium oocysts.
2. **Polymerase Chain Reaction (PCR)**: Molecular testing of stool samples using PCR can provide sensitive and specific detection of Cryptosporidium DNA.
3. **Antigen Detection**: Commercially available enzyme immunoassays (EIAs) or rapid diagnostic tests (RDTs) for Cryptosporidium antigen detection in stool samples may offer rapid and accurate diagnosis of cryptosporidiosis.

Figure 34 Cryptosporidium oocysts stained with modified acid fast (bright red against black of green background) (https://www.cdc.gov/dpdx/cryptosporidiosis/index.html)



Treatment

The management of cryptosporidiosis in children with HIV involves supportive care and antimicrobial therapy:

1. **Rehydration**: Oral rehydration therapy with electrolyte solutions is essential for correcting fluid and electrolyte imbalances in children with cryptosporidiosis-associated diarrhea.

2. **Antimicrobial Therapy**: There is no universally effective antimicrobial therapy for cryptosporidiosis in children with HIV. Nitazoxanide may be considered for severe or persistent cases, although its efficacy in immunocompromised individuals is limited.
3. **Nutritional Support**: Adequate nutritional support, including provision of high-calorie, high-protein diets and micronutrient supplementation, is crucial for promoting recovery and preventing malnutrition in children with cryptosporidiosis.

Prophylaxis

Primary prophylaxis for cryptosporidiosis in children with HIV/AIDS is not routinely recommended due to the lack of highly effective preventive measures. However, strategies to improve water quality, promote hygiene practices, and provide access to clean drinking water may help reduce the risk of cryptosporidiosis transmission in vulnerable populations.

Complications of Disease

Untreated or inadequately treated cryptosporidiosis can lead to severe complications and increased mortality in children with HIV:

1. **Severe Dehydration**: Prolonged diarrhea and fluid loss can result in severe dehydration, electrolyte imbalances, and metabolic acidosis, requiring aggressive fluid resuscitation and supportive care.
2. **Malnutrition**: Chronic diarrhea and malabsorption can lead to malnutrition, growth failure, and micronutrient deficiencies, exacerbating the clinical course of cryptosporidiosis.
3. **Chronic Illness**: Persistent or recurrent cryptosporidiosis can lead to chronic illness, impaired quality of life, and long-term sequelae, particularly in children with advanced HIV disease and severe immunosuppression.
4. **Opportunistic Infections**: Cryptosporidiosis-associated immunosuppression may predispose children to other opportunistic infections, further complicating the clinical management and prognosis.

In summary, cryptosporidiosis remains a significant opportunistic infection in children living with HIV, particularly in regions with limited access to clean water and sanitation infrastructure. Early recognition, prompt diagnosis, and supportive care are essential for improving outcomes and reducing morbidity associated with this challenging parasitic infection Top of Form Bottom of Form

Cytomegalovirus Disease (CMV)

Meet ARIF, a three-year-old boy living with HIV. Despite receiving antiretroviral therapy (ART), Arif develops persistent fever, hepatosplenomegaly, and thrombocytopenia. Concerned about his worsening condition, Arif's caregivers bring him to the hospital for evaluation.

Definition

CMV disease refers to clinical manifestations resulting from infection with cytomegalovirus (CMV), a member of the herpesvirus family. CMV is a common opportunistic pathogen in immunocompromised individuals, including those with HIV/AIDS. CMV disease can affect various organ systems, including the lungs, gastrointestinal tract, liver, central nervous system, and eyes.

Epidemiology

CMV infection is widespread in the general population, with a seroprevalence approaching 60-90% in adults worldwide. In children with HIV/AIDS, CMV disease occurs primarily in those with advanced immunosuppression and severe CD4 depletion. Despite the widespread use of ART, CMV remains a significant cause of morbidity and mortality in children living with HIV.

Risk Factors

Several factors increase the risk of CMV disease in children with HIV:

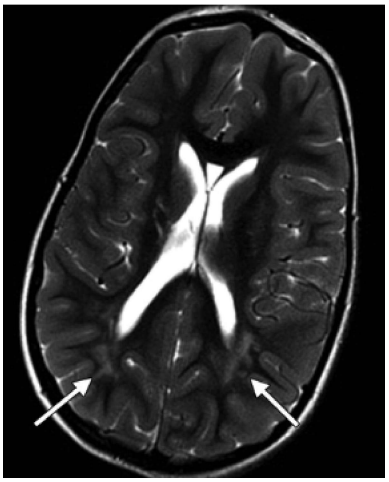
1. **Immunosuppression**: Severe immunosuppression, indicated by low CD4 cell counts, predisposes children with HIV to CMV disease.
2. **Non-adherence to ART**: Inadequate viral suppression due to non-adherence or treatment failure increases the risk of CMV reactivation and disease progression.
3. **Perinatal CMV Transmission**: Congenital CMV infection acquired from an HIV-infected mother or through breastfeeding may lead to symptomatic CMV disease in children with HIV.
4. **Transplant Recipients**: Children with HIV who undergo solid organ or hematopoietic stem cell transplantation are at increased risk of CMV disease due to intense immunosuppressive therapy.

Clinical Features in Children with HIV

CMV disease can present with various clinical manifestations in children with HIV, including:

1. **Fever**: Persistent or recurrent fever is a common presenting symptom of CMV disease in children with HIV.
2. **Hepatosplenomegaly**: Enlargement of the liver and spleen may occur due to CMV-induced hepatocellular and splenic inflammation.
3. **Thrombocytopenia**: Low platelet counts are frequently observed in children with CMV-associated bone marrow suppression.
4. **Pneumonitis**: CMV pneumonitis can manifest with respiratory symptoms such as cough, dyspnea, and hypoxemia, particularly in severely immunocompromised children.
5. **Gastrointestinal Symptoms**: CMV enteritis or colitis may present with abdominal pain, diarrhea, bloody stools, and weight loss in children with HIV.

Figure 35 showing patchy periventricular white matter lesions, mild ventricular prominence and normal gyration.



6. **Neurological Manifestations**: CMV encephalitis or meningoencephalitis can lead to seizures, altered mental status, focal neurological deficits, and intracranial hypertension.

Diagnostic Tests

Diagnosing CMV disease in children with HIV involves clinical evaluation and laboratory tests:

1. **Viral Culture**: Isolation of CMV from blood, urine, or other clinical specimens can confirm active CMV infection.
2. **Serologic Testing**: Serologic assays for CMV-specific immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies may indicate recent or past CMV infection, respectively.
3. **Polymerase Chain Reaction (PCR)**: Molecular testing of blood, urine, or tissue samples using PCR can detect CMV DNA and provide sensitive and specific diagnosis of CMV disease.
4. **Histopathological Examination**: Biopsy specimens from affected organs, such as the liver, lungs, or gastrointestinal tract, may reveal characteristic CMV inclusion bodies on histopathological examination.
5. **MRI Brain**: MRI may should ventriculitis or T2 flair hyperintensities in periventricular white matter

Treatment

The management of CMV disease in children with HIV involves antiviral therapy and supportive care:

1. **Antiviral Therapy**: Treatment of CMV disease typically involves the use of antiviral medications such as ganciclovir, valganciclovir, or foscarnet. Intravenous ganciclovir is often used for severe cases of CMV disease, while oral valganciclovir may be considered for less severe disease or maintenance therapy.
2. **Adjunctive Measures**: Supportive care measures, including hydration, nutritional support, and management of complications such as thrombocytopenia or pneumonitis, are essential for optimizing clinical outcomes in children with CMV disease.

Prophylaxis

Primary prophylaxis for CMV disease in children with HIV/AIDS is not routinely recommended due to the lack of highly effective preventive measures. However, strategies to optimize ART adherence, monitor CD4 cell counts, and prevent opportunistic infections may help reduce the risk of CMV reactivation and disease progression in this population.

Complications of Disease

Untreated or inadequately treated CMV disease can lead to severe complications and increased mortality in children with HIV:

1. **Disseminated Disease**: CMV disease can disseminate to multiple organ systems, leading to multi-organ failure, sepsis, and death, particularly in severely immunocompromised children.
2. **Organ Dysfunction**: CMV-associated end-organ damage, such as hepatocellular necrosis, pneumonitis, or encephalitis, can result in permanent organ dysfunction and long-term sequelae.
3. **Opportunistic Infections**: CMV-induced immunosuppression may predispose children to other opportunistic infections, further complicating the clinical management and prognosis.

4. **Neurodevelopmental Impairment**: CMV encephalitis or meningoencephalitis can cause neurological sequelae such as cognitive impairment, motor dysfunction, and developmental delay in surviving children.

In summary, CMV disease remains a significant opportunistic infection in children living with HIV, particularly in those with advanced immunosuppression. Early recognition, prompt diagnosis, and aggressive antiviral therapy are crucial for improving outcomes and reducing morbidity associated with this challenging viral infection.

Warts

Clinical Scenario Example

Consider Bushra, a nine-year-old girl living with HIV. Despite being on antiretroviral therapy (ART), Bushra develops painful oral ulcers and genital warts. Concerned about her worsening symptoms, her caregivers bring her to the pediatric clinic for evaluation.

Definition

Herpes simplex virus (HSV) and human papillomavirus (HPV) infections are common opportunistic infections in children with HIV. HSV typically presents with oral or genital ulcers, while HPV may manifest as warts or other cutaneous lesions. These infections can cause significant morbidity and may indicate underlying immunosuppression in children with HIV.

Epidemiology

HSV and HPV infections are prevalent worldwide, with HSV-1 and HSV-2 affecting approximately 67% and 11% of the global population, respectively. HPV is the most common sexually transmitted infection globally, with an estimated 79 million Americans currently infected. In children with HIV, the prevalence and severity of HSV and HPV infections are higher compared to the general population, particularly in those with advanced disease and severe immunosuppression.

Risk Factors

Several factors increase the risk of HSV and HPV infections in children with HIV:

1. **Immunosuppression**: Severe immunosuppression, indicated by low CD4 cell counts, predisposes children with HIV to HSV and HPV infections.

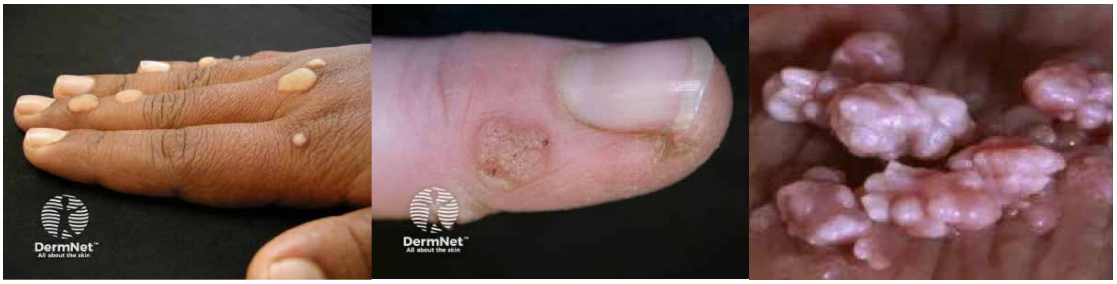
2. **Non-adherence to ART**: Inadequate viral suppression due to non-adherence or treatment failure increases the risk of HSV and HPV reactivation and disease progression.

3. **Sexual Activity**: Sexual activity, including oral-genital or anal-genital contact, increases the risk of acquiring HSV and HPV infections in adolescents with HIV.

4. **Vertical Transmission**: Children born to mothers with genital HSV or HPV infections may acquire the virus during childbirth, leading to symptomatic or asymptomatic infection in infancy or childhood.

Clinical Features in Children with HIV

Figure 36 Warts in children with HIV (periungual, perianal)



HSV and HPV infections can present with various clinical manifestations in children with HIV, including:

1. **HSV Oral Ulcers**: Painful oral ulcers or herpetic stomatitis are common manifestations of HSV infection in children with HIV. Lesions may be localized to the lips, gums, tongue, or oral mucosa and may recur intermittently.
2. **HSV Genital Ulcers**: Genital herpes, caused by HSV-2, may present with painful genital ulcers, vesicles, or erosions in children with HIV, particularly those who are sexually active or perinatally infected.
3. **HPV Warts**: Cutaneous or mucosal warts caused by HPV may occur in various anatomical locations, including the genital area, perianal region, hands, feet, and oral cavity. Genital warts (**condylomata** acuminata) are common in sexually active adolescents with HIV and may be associated with HPV types 6 and 11.
4. **Dysplastic Lesions**: Persistent or recurrent HPV infection may lead to the development of dysplastic lesions, such as cervical intraepithelial neoplasia (CIN) or anal intraepithelial neoplasia (AIN), in children with HIV, particularly those with longstanding immunosuppression.

Diagnostic Tests

Diagnosing HSV and HPV infections in children with HIV involves clinical evaluation and laboratory tests:

1. **Viral Culture**: Isolation of HSV from oral, genital, or cutaneous lesions can confirm active HSV infection. However, viral culture may have limited sensitivity, particularly in cases of recurrent or healed lesions.
2. **Polymerase Chain Reaction (PCR)**: Molecular testing of lesion swabs or biopsy specimens using PCR can detect HSV or HPV DNA and provide sensitive and specific diagnosis of infection.
3. **Histopathological Examination**: Biopsy specimens from dysplastic or suspicious lesions may reveal characteristic histological changes indicative of HPV-associated neoplasia, such as koilocytosis or dyskeratosis.

Treatment

The management of HSV and HPV infections in children with HIV involves antiviral therapy and wart removal:

1. **Antiviral Therapy for HSV**: Oral antiviral medications, such as acyclovir, valacyclovir, or famciclovir, are used to treat HSV infections in children with HIV. These medications can reduce the duration and severity of symptoms and may prevent recurrent episodes.
2. **Topical Treatments for Warts**: Topical agents such as podophyllotoxin, imiquimod, or trichloroacetic acid (TCA) may be used to treat external genital warts (**condylomata** acuminata) caused by HPV in children with HIV. Cryotherapy or surgical excision may be necessary for larger or resistant warts.

Prophylaxis

Primary prophylaxis for HSV and HPV infections in children with HIV/AIDS is not routinely recommended due to the lack of highly effective preventive measures. However, strategies to optimize ART adherence, promote safe sexual practices, and educate caregivers about the risks and symptoms of HSV and HPV infections may help reduce the incidence and transmission of these viruses.

Complications of Disease

Untreated or inadequately treated HSV and HPV infections can lead to severe complications and increased morbidity in children with HIV:

1. **Disseminated HSV Infection**: Severe HSV infections, particularly in immunocompromised individuals, may disseminate to multiple organ systems, leading to systemic complications such as hepatitis, pneumonitis, or encephalitis.
2. **Malignant Transformation**: Persistent or recurrent HPV infection may lead to the development of cervical, anal, or oropharyngeal cancer in children with HIV, particularly those with longstanding immunosuppression and high-risk HPV genotypes.
3. **Psychosocial Impact**: Genital warts and other visible manifestations of HSV and HPV infections may cause psychological distress, stigma, and impaired quality of life in children and adolescents with HIV, affecting social relationships and self-esteem.

In summary, HSV and HPV infections are common opportunistic infections in children living with HIV/AIDS. Early recognition, prompt diagnosis, and appropriate treatment are essential for managing these infections and preventing complications in this vulnerable population.

EBV associated Lymphoid Interstitial Pneumonia (LIP)

Clinical Scenario Example

Meet Noman, a six-year-old boy living with HIV. Despite being on antiretroviral therapy (ART), Noman develops progressive cough, dyspnea, and fatigue. His chest X-ray reveals diffuse interstitial infiltrates suggestive of pneumonia. Concerned about his worsening respiratory symptoms, his caregivers bring him to the hospital for further evaluation.

Definition

EBV-associated lymphoid interstitial pneumonitis (LIP) is a rare but potentially serious opportunistic infection characterized by inflammatory infiltration of the lung **interstitium** and hyperplasia of lymphoid tissue. It occurs in immunocompromised individuals, including those with HIV/AIDS, and is associated with Epstein-Barr virus (EBV) infection. LIP can lead to respiratory failure and significant morbidity in affected children.

Epidemiology

Lymphoid interstitial pneumonitis is relatively rare in children with HIV/AIDS, but its incidence is higher in those with advanced disease and severe immunosuppression. EBV infection is widespread in the general population, with seroprevalence approaching 90-95% by adulthood. In children with HIV, EBV-associated LIP occurs more commonly in those with profound immunodeficiency and impaired cellular immunity.

Risk Factors

Several factors increase the risk of EBV-associated LIP in children with HIV:

1. **Severe Immunodeficiency**: Children with advanced HIV disease and severe CD4 depletion are at increased risk of developing EBV-associated LIP due to impaired cellular immunity and ineffective viral control.
2. **EBV Co-infection**: Concurrent or recent EBV infection may trigger lymphoproliferative disorders, including LIP, in children with HIV/AIDS, particularly those with defective T-cell function.
3. **Non-adherence to ART**: Inadequate viral suppression due to non-adherence or treatment failure increases the risk of EBV reactivation and lymphoproliferative complications in children with HIV.

Clinical Features in Children with HIV

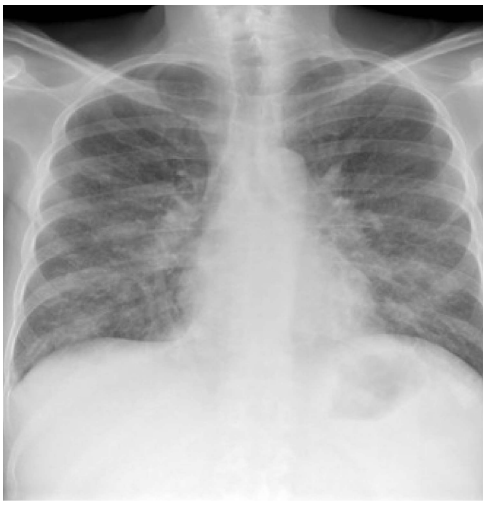
EBV-associated LIP can present with various clinical manifestations in children with HIV, including:

1. **Respiratory Symptoms**: Progressive cough, dyspnea, tachypnea, and respiratory distress are common presenting symptoms of EBV-associated LIP in children with HIV. Respiratory symptoms may be acute or subacute in onset and may worsen over time.
2. **Systemic Symptoms**: Fever, fatigue, malaise, and weight loss may occur in children with EBV-associated LIP, reflecting the systemic inflammatory response and underlying viral infection.
3. **Lymphadenopathy**: Generalized lymphadenopathy, hepatosplenomegaly, and peripheral lymphocytosis may be observed in children with EBV-associated LIP due to systemic lymphoid hyperplasia and immune activation.
4. **Radiographic Findings**: Chest radiography or computed tomography (CT) imaging may reveal diffuse interstitial infiltrates, ground-glass opacities, and peribronchovascular thickening characteristic of lymphocytic interstitial pneumonitis.

Diagnostic Tests

Diagnosing EBV-associated LIP in children with HIV involves clinical evaluation and laboratory tests:

Figure 37 CXR showing diffuse, bilateral reticulonodular lung opacities most prominent at the base



1. **Serologic Testing**: Serologic assays for EBV-specific antibodies, including viral capsid antigen (VCA) IgM and IgG, can indicate recent or past EBV infection but may not differentiate between active and latent infection.
2. **EBV DNA PCR**: Molecular testing of blood or respiratory specimens using polymerase chain reaction (PCR) can detect EBV DNA and provide evidence of active viral replication in children with suspected EBV-associated LIP.
3. **Bronchoalveolar Lavage (BAL)**: BAL fluid analysis may reveal lymphocytic predominance, elevated CD4/CD8 ratio, and increased levels of EBV DNA in children with EBV-associated LIP, supporting the diagnosis.
4. **Histopathological Examination**: Lung biopsy specimens obtained via transbronchial biopsy or surgical lung biopsy may demonstrate lymphocytic interstitial infiltrates, germinal center hyperplasia, and EBV-infected lymphocytes on histopathological examination, confirming the diagnosis of EBV-associated LIP.

Treatment

The management of EBV-associated LIP in children with HIV involves antiretroviral therapy and supportive care:

1. **Antiretroviral Therapy (ART)**: Optimizing ART adherence and achieving viral suppression are essential for controlling HIV replication and restoring immune function in children with EBV-associated LIP.
2. **Corticosteroids**: Systemic corticosteroid therapy, such as prednisone or methylprednisolone, may be considered for children with severe or progressive respiratory symptoms due to EBV-associated LIP. Corticosteroids can reduce inflammation, alleviate respiratory distress, and improve clinical outcomes.
3. **Oxygen Therapy**: Supplemental oxygen therapy may be necessary for children with hypoxemia or respiratory failure secondary to EBV-associated LIP, particularly in cases of severe interstitial lung disease.

Prophylaxis

Primary prophylaxis for EBV-associated LIP in children with HIV/AIDS is not routinely recommended due to the lack of highly effective preventive measures. However, strategies to optimize ART adherence, monitor CD4 cell counts, and prevent opportunistic infections may help reduce the risk of EBV reactivation and lymphoproliferative complications in this population.

Complications of Disease

Untreated or inadequately treated EBV-associated LIP can lead to severe complications and increased mortality in children with HIV:

1. **Respiratory Failure**: Progressive interstitial lung disease and respiratory compromise can result in respiratory failure and the need for mechanical ventilation in children with EBV-associated LIP.
2. **Pulmonary Fibrosis**: Chronic inflammation and fibrotic remodeling of the lung interstitium may lead to irreversible pulmonary fibrosis and impaired lung function in survivors of EBV-associated LIP.
3. **Secondary Infections**: Immunosuppression secondary to EBV-associated LIP may predispose children to secondary bacterial, fungal, or viral infections, further complicating the clinical management and prognosis.

In summary, EBV-associated lymphoid interstitial pneumonitis is a rare but potentially life-threatening opportunistic infection in children living with HIV/AIDS. Early recognition, prompt diagnosis, and aggressive management are essential for improving outcomes and reducing morbidity associated with this challenging viral complication of HIV infection.

Varicella Zoster infections

Clinical Scenario Example

Consider **Maha**, a seven-year-old girl living with HIV. Despite receiving antiretroviral therapy (ART), Maha develops a painful rash with fluid-filled blisters on her trunk and face. Concerned about her worsening symptoms, her caregivers bring her to the pediatric clinic for evaluation.

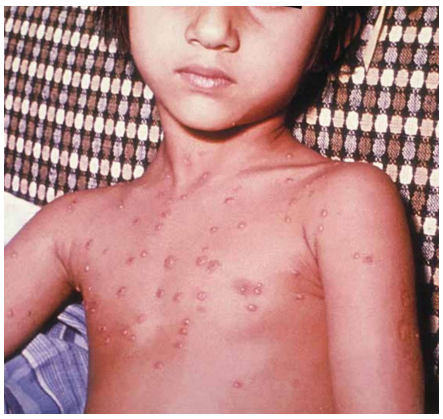
Definition

Varicella zoster virus (VZV) is a highly contagious herpesvirus that causes two distinct clinical syndromes: varicella (chickenpox) and herpes zoster (shingles). Varicella occurs primarily in VZV-naïve individuals, while herpes zoster represents reactivation of latent VZV infection, typically manifesting as a painful dermatomal rash. In children with HIV/AIDS, VZV disease and reactivation can lead to significant morbidity and may indicate underlying immunosuppression.

Epidemiology

Varicella is a common childhood infection, with approximately 90% of individuals experiencing primary VZV infection by adulthood. Herpes zoster occurs more commonly in older adults but can also affect immunocompromised individuals, including children with HIV/AIDS. Incidence and severity of VZV disease and reactivation are higher in children with advanced HIV disease and impaired cellular immunity.

Figure 38 Child with varicella (vesicular lesions)



Risk Factors

Several factors increase the risk of VZV disease and reactivation in children with HIV:

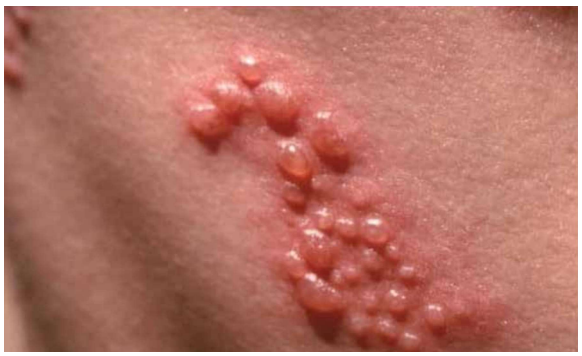
1. **Immunosuppression**: Severe immunosuppression, indicated by low CD4 cell counts, predisposes children with HIV to VZV disease and reactivation due to impaired cellular immunity and ineffective viral control.
2. **Non-adherence to ART**: Inadequate viral suppression due to non-adherence or treatment failure increases the risk of VZV reactivation and disease progression in children with HIV.
3. **VZV Exposure**: Close contact with individuals with active varicella or herpes zoster increases the risk of VZV transmission and disease acquisition in susceptible children with HIV/AIDS.

Clinical Features in Children with HIV

VZV disease and reactivation can present with various clinical manifestations in children with HIV, including:

1. Varicella (Chickenpox):

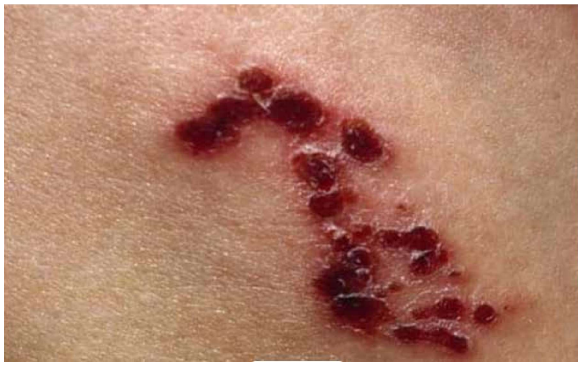
Figure 39 Acute Zoster lesions in patient with HIV



- Rash: Varicella typically presents with a pruritic rash characterized by erythematous papules, vesicles, and crusts distributed in crops on the face, trunk, and extremities.
- Fever: Low-grade fever may precede the onset of the rash in children with varicella, accompanied by malaise and irritability.
- Complications: Children with HIV/AIDS are at increased risk of severe varicella complications, including pneumonia, encephalitis, disseminated disease, and death.

2. Herpes Zoster (Shingles):

Figure 40 Healed Zoster lesions in patient with HIV



- Rash: Herpes zoster presents as a painful, unilateral vesicular rash following the distribution of a sensory nerve dermatome, commonly the thoracic or lumbar region.
- Pain: Herpes zoster-associated pain may precede the onset of the rash and persist after rash resolution, known as postherpetic neuralgia.
- Complications: Children with HIV/AIDS are at increased risk of herpes zoster complications, including disseminated disease, visceral organ involvement, and neurological sequelae.

Diagnostic Tests

Diagnosing VZV disease and reactivation in children with HIV involves clinical evaluation and laboratory tests:

1. **Clinical Presentation**: The characteristic rash morphology and distribution of vesicles along dermatomal patterns are often sufficient to diagnose varicella or herpes zoster clinically.
2. **Viral Culture or PCR**: Laboratory testing of vesicular fluid or swab specimens using viral culture or polymerase chain reaction (PCR) can confirm VZV infection and differentiate between varicella and herpes zoster.
3. **Serologic Testing**: Serologic assays for VZV-specific antibodies, including varicella-zoster virus IgM and IgG, may indicate recent or past VZV infection but are not routinely used for diagnosis in clinical practice.

Treatment

The management of VZV disease and reactivation in children with HIV involves antiviral therapy and supportive care:

1. **Antiviral Therapy**: Oral antiviral medications, such as acyclovir, valacyclovir, or famciclovir, are used to treat VZV infections in children with HIV/AIDS. Antiviral therapy can reduce the duration and severity of symptoms and may prevent complications associated with varicella and herpes zoster.
2. **Pain Management**: Analgesic medications, including nonsteroidal anti-inflammatory drugs (NSAIDs) or opioids, may be necessary to alleviate pain associated with herpes zoster, particularly in children with postherpetic neuralgia.
3. **Hydration and Rest**: Adequate hydration, rest, and symptomatic relief measures, such as cool compresses and oatmeal baths for pruritus, can help alleviate discomfort and promote recovery in children with VZV disease.

Prophylaxis

Primary prophylaxis for varicella zoster virus disease in children with HIV/AIDS is recommended in certain circumstances:

1. **VZV Vaccination**: Varicella vaccination is recommended for VZV-seronegative children with HIV who have evidence of immune reconstitution with ART and CD4 counts ≥ 200 cells/mm^3. The live attenuated varicella vaccine is contraindicated in severely immunocompromised children with HIV/AIDS.
2. **Post-Exposure Prophylaxis**: Varicella-zoster immune globulin (VZIG) may be considered for VZV-seronegative children with HIV who have significant exposure to varicella or herpes zoster, particularly those with advanced disease or no evidence of immune reconstitution.

Complications of Disease

Untreated or inadequately treated VZV disease and reactivation can lead to severe complications

and increased morbidity in children with HIV:

1. **Pneumonia**: Varicella pneumonia is a potentially life-threatening complication of varicella in children with HIV/AIDS, characterized by respiratory failure, hypoxemia, and diffuse pulmonary infiltrates.
2. **Encephalitis**: Varicella encephalitis can occur in children with HIV/AIDS, presenting with altered mental status, seizures, and focal neurological deficits due to viral invasion of the central nervous system.
3. **Postherpetic Neuralgia**: Herpes zoster-associated postherpetic neuralgia can cause chronic pain and functional impairment in affected children, requiring long-term management and analgesic therapy.

In summary, varicella zoster virus disease and reactivation represent significant opportunistic infections in children living with HIV/AIDS. Vaccination, antiviral therapy, and supportive care measures are essential for preventing complications and improving outcomes in this vulnerable population.

JC Virus related Progressive multifocal leukoencephalopathy (PML)

Clinical Scenario Example

Meet Akash, a twelve-year-old boy living with HIV. Despite being on antiretroviral therapy (ART), Akash begins to experience progressive weakness in his right arm and leg, along with cognitive difficulties and visual disturbances. Concerned about his neurological symptoms, his caregivers bring him to the hospital for evaluation.

Definition

Progressive multifocal leukoencephalopathy (PML) is a rare and severe demyelinating disease of the central nervous system (CNS) caused by reactivation of the JC virus (JCV), a polyomavirus. In children with HIV/AIDS, PML occurs as a result of profound immunosuppression and impaired cellular immunity, leading to uncontrolled viral replication and progressive neurological dysfunction.

Epidemiology

PML is relatively rare in children with HIV/AIDS but represents a significant neurological complication of advanced immunodeficiency. The incidence of PML has declined with the widespread use of combination antiretroviral therapy (**cART**) but remains higher in children with severe immunosuppression and inadequate viral suppression. JCV infection is widespread in the general population, with seroprevalence rates exceeding 50% by adulthood.

Risk Factors

Several factors increase the risk of JC virus-associated PML in children with HIV:

1. **Severe Immunodeficiency**: Children with advanced HIV disease and severe CD4 depletion are at increased risk of developing PML due to impaired cellular immunity and ineffective viral control.
2. **Non-adherence to ART**: Inadequate viral suppression due to non-adherence or treatment failure increases the risk of JCV reactivation and PML development in children with HIV.

3. **Duration of HIV Infection**: Longer duration of untreated HIV infection is associated with increased risk of PML in children, as prolonged immunosuppression allows for JCV reactivation and CNS invasion.
4. **Co-existing Opportunistic Infections**: Concurrent opportunistic infections, particularly those affecting the CNS, may exacerbate immunosuppression and increase the risk of PML in children with HIV/AIDS.

Clinical Features in Children with HIV

JC virus-associated PML can present with various neurological manifestations in children with HIV, including:

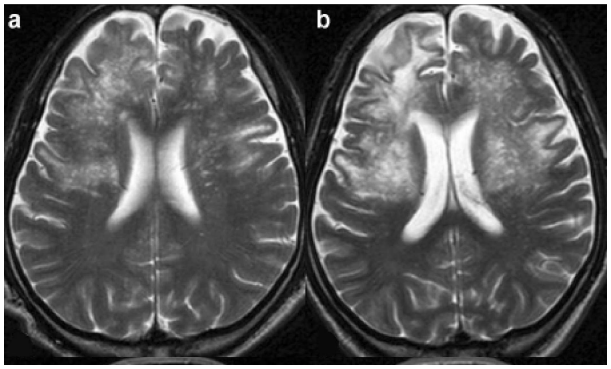
1. **Progressive Neurological Deficits**: PML typically manifests with progressive weakness, ataxia, sensory disturbances, cognitive impairment, and visual deficits due to multifocal demyelination and CNS damage.
2. **Cerebellar Dysfunction**: Ataxia, dysmetria, and intention tremor may occur in children with PML involving the cerebellum, leading to impaired coordination and balance.
3. **Pyramidal Signs**: Weakness, spasticity, and hyperreflexia in the extremities may indicate corticospinal tract involvement and pyramidal tract dysfunction in children with PML.
4. **Cognitive Decline**: PML-associated cognitive impairment may manifest with memory deficits, executive dysfunction, language disturbances, and behavioral changes, reflecting multifocal CNS involvement.

Diagnostic Tests

Diagnosing JC virus-associated PML in children with HIV involves clinical evaluation and diagnostic testing:

1. **Neuroimaging**: Magnetic resonance imaging (MRI) of the brain may reveal characteristic findings of PML, including multifocal white matter lesions with T2 hyperintensity and contrast enhancement. Lesions typically involve the subcortical white matter and progress over time.

Figure 41 Lesion progression in patients with PML on T2 weighted images



2. **Cerebrospinal Fluid (CSF) Analysis**: CSF examination may show mild lymphocytic pleocytosis, elevated protein levels, and detection of JCV DNA by polymerase chain reaction (PCR), supporting the diagnosis of PML.
3. **Brain Biopsy**: Stereotactic brain biopsy may be considered in children with atypical clinical presentation or diagnostic uncertainty, allowing for histopathological confirmation of PML and exclusion of other CNS disorders.

Treatment

The management of JC virus-associated PML in children with HIV is challenging and primarily involves supportive care:

1. **Antiretroviral Therapy (ART)**: Optimizing ART adherence and achieving viral suppression are essential for controlling HIV replication and restoring immune function in children with PML. Immune reconstitution may help control JCV replication and improve clinical outcomes.
2. **Symptomatic Management**: Treatment of PML-related symptoms may include physical therapy, occupational therapy, speech therapy, and supportive care measures to address neurological deficits and functional impairment.
3. **Experimental Therapies**: Investigational therapies for PML, including antiviral agents, immunomodulatory drugs, and monoclonal antibodies targeting JCV-infected cells, are under investigation in clinical trials but have not yet demonstrated consistent efficacy in children with HIV/AIDS.

Prophylaxis

Primary prophylaxis for JC virus-associated PML in children with HIV/AIDS is not routinely recommended due to the lack of highly effective preventive measures. However, strategies to optimize ART adherence, monitor CD4 cell counts, and prevent opportunistic infections may help reduce the risk of PML development in this population.

Complications of Disease

Untreated or inadequately treated JC virus-associated PML can lead to severe neurological complications and increased mortality in children with HIV:

1. **Functional Impairment**: Progressive neurological deficits and cognitive decline associated with PML may lead to significant functional impairment, disability, and dependence on caregivers for activities of daily living.
2. **Immune Reconstitution Inflammatory Syndrome (IRIS)**: Immune reconstitution following ART initiation may trigger an inflammatory response within CNS lesions, exacerbating neurological symptoms and causing paradoxical deterioration in some children with HIV/AIDS and PML.
3. **Mortality**: JC virus-associated PML carries a poor prognosis in children with HIV, with high rates of morbidity and mortality despite aggressive supportive care measures and ART optimization.

In summary, JC virus-associated progressive multifocal leukoencephalopathy is a rare but devastating neurological complication of advanced HIV disease in children. Early recognition, prompt diagnosis, and aggressive management of underlying immunosuppression are crucial for improving outcomes and reducing morbidity associated with this challenging opportunistic infection.

Molluscum Contagiosum Disease in Children with HIV

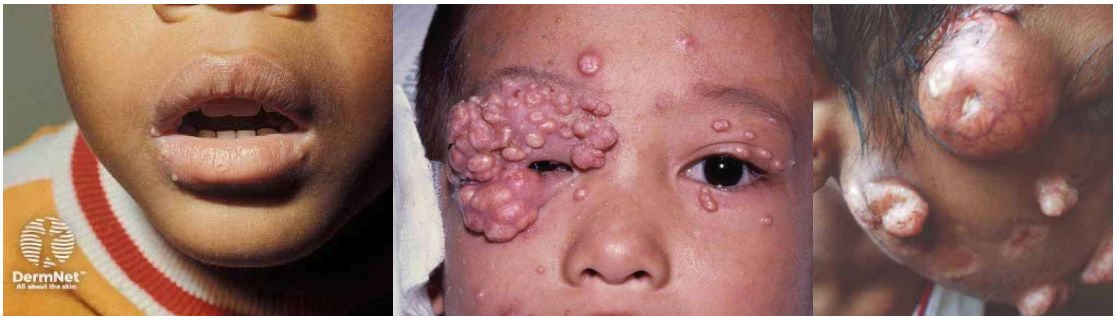
Clinical Scenario Example

Meet Sarah, a five-year-old girl living with HIV. Despite being on antiretroviral therapy (ART), Sarah develops multiple small, painless, flesh-colored papules on her face, trunk, and extremities. Concerned about the appearance of these lesions, Sarah's caregivers bring her to the pediatric clinic for evaluation.

Definition

Molluscum contagiosum is a benign viral skin infection caused by the molluscum contagiosum virus (MCV), a member of the Poxviridae family. In children with HIV/AIDS, molluscum contagiosum can manifest as multiple discrete papules or nodules on the skin and mucous membranes, representing an opportunistic infection associated with immunosuppression.

Figure 42 Molluscum Contagiosum in children with HIV



Epidemiology

Molluscum contagiosum is a common childhood skin infection worldwide, with an estimated prevalence of 5-20% in the general pediatric population. In children with HIV/AIDS, the incidence and severity of molluscum contagiosum are higher compared to immunocompetent individuals, particularly in those with advanced disease and severe immunosuppression.

Risk Factors

Several factors increase the risk of molluscum contagiosum in children with HIV:

1. **Immunosuppression**: Severe immunosuppression, indicated by low CD4 cell counts, predisposes children with HIV to molluscum contagiosum infection due to impaired cellular immunity and inadequate viral control.
2. **Close Contact**: Direct skin-to-skin contact with individuals with active molluscum lesions increases the risk of transmission and disease acquisition in susceptible children with HIV/AIDS.
3. **Poor Hygiene**: Inadequate hygiene practices and crowded living conditions may facilitate the spread of molluscum contagiosum virus among children, particularly in institutional settings.

Clinical Features in Children with HIV

Molluscum contagiosum in children with HIV/AIDS can present with the following clinical features:

1. **Skin Lesions**: Molluscum contagiosum lesions typically appear as flesh-colored, dome-shaped papules with central umbilication, ranging in size from 2 to 5 millimeters in diameter. Lesions may be solitary or multiple and can occur on any body surface, including the face, trunk, extremities, and genital area.
2. **Distribution**: Molluscum contagiosum lesions may be localized to specific areas or involve multiple anatomical sites in children with HIV/AIDS, reflecting widespread viral dissemination and impaired immune control.
3. **Pruritus**: Some children with molluscum contagiosum may experience mild pruritus or discomfort at the site of lesions, although symptoms are generally minimal compared to other skin conditions.
4. **Secondary Infection**: Secondary bacterial infection or superinfection of molluscum contagiosum lesions may occur in children with HIV/AIDS, leading to erythema, pain, and purulent discharge.

Diagnostic Tests

Diagnosing molluscum contagiosum in children with HIV involves clinical evaluation and examination of skin lesions:

1. **Clinical Presentation**: The characteristic morphology of molluscum contagiosum lesions, including their appearance as flesh-colored papules with central umbilication, is often sufficient to diagnose the infection clinically.
2. **Dermoscopy:** Dermoscopic examination of molluscum contagiosum lesions may reveal characteristic features such as central umbilication, white curd-like material (molluscum bodies), and peripheral vascular structures, aiding in diagnosis.
3. **Skin Biopsy**: If the diagnosis is uncertain or atypical, a skin biopsy of a molluscum lesion may be performed to confirm the presence of eosinophilic cytoplasmic inclusions (molluscum bodies) within epidermal cells.

Treatment

The management of molluscum contagiosum in children with HIV/AIDS involves various treatment modalities:

1. **Observation**: Spontaneous resolution of molluscum contagiosum lesions may occur within months to years without specific intervention in immunocompetent individuals. Observation alone may be appropriate for children with HIV/AIDS with mild or limited lesions.
2. **Topical Treatments**: Topical therapies such as imiquimod cream, podophyllotoxin solution, or tretinoin cream may be used to induce immune-mediated clearance of molluscum contagiosum lesions in children with HIV/AIDS. These treatments may require prolonged application and can cause local skin irritation.
3. **Physical Removal**: Physical methods such as curettage, cryotherapy, or laser therapy may be employed to remove individual molluscum lesions in children with HIV/AIDS, particularly those

with extensive or symptomatic disease. These procedures should be performed by trained healthcare providers to minimize scarring and complications.

Prophylaxis

Primary prophylaxis for molluscum contagiosum in children with HIV/AIDS is not routinely recommended due to the lack of highly effective preventive measures. However, strategies to optimize ART adherence, promote good hygiene practices, and minimize close contact with individuals with active lesions may help reduce the risk of transmission and disease acquisition.

Complications of Disease

Molluscum contagiosum is generally a benign and self-limiting condition in children with HIV/AIDS. However, untreated or inadequately managed molluscum contagiosum may lead to the following complications:

1. **Secondary Infection**: Superinfection of molluscum contagiosum lesions with bacteria or fungi may occur, leading to localized inflammation, pain, and purulent discharge. Prompt recognition and treatment of secondary infections are essential to prevent complications.
2. **Cosmetic Concerns**: Extensive or disfiguring molluscum contagiosum lesions may cause cosmetic concerns and psychosocial distress in children with HIV/AIDS, particularly adolescents. Timely intervention and appropriate management can help minimize aesthetic impact and improve quality of life.

In summary, molluscum contagiosum is a common viral skin infection in children with HIV/AIDS, particularly those with advanced immunosuppression. Early recognition, prompt diagnosis, and appropriate management are essential for minimizing morbidity and preventing complications associated with this opportunistic infection.

Recurrent Salmonellosis in Children with HIV

Clinical Scenario Example

Meet Daud, a six-year-old boy living with HIV. Despite receiving antiretroviral therapy (ART), Daud **has experienced** multiple episodes of diarrhea, abdominal pain, and fever over the past year. Each episode requires hospitalization and treatment for Salmonella infection. Concerned about the frequency and severity of his recurrent illness, his caregivers seek medical advice to address the underlying cause and prevent future recurrences.

Definition

Recurrent salmonellosis refers to the repeated episodes of Salmonella infection in individuals, particularly children, with HIV/AIDS. Salmonella is a common cause of gastroenteritis worldwide, but recurrent infections in the setting of HIV suggest underlying immunodeficiency and impaired host defense mechanisms.

Epidemiology

Salmonella infections are prevalent in children with HIV/AIDS, particularly in resource-limited settings with inadequate access to clean water, sanitation, and healthcare. The incidence of recurrent salmonellosis in children with HIV/AIDS varies depending on factors such as age, disease severity, nutritional status, and exposure to contaminated food or water sources.

Risk Factors

Several factors increase the risk of recurrent salmonellosis in children with HIV/AIDS:

1. **Immunosuppression**: Severe immunosuppression, characterized by low CD4 cell counts and impaired cellular immunity, predisposes children with HIV to recurrent Salmonella infections due to inadequate pathogen clearance and immune response.
2. **Malnutrition**: Undernutrition and micronutrient deficiencies compromise gut integrity and mucosal immunity, increasing susceptibility to Salmonella colonization and invasive disease in children with HIV/AIDS.
3. **Co-existing Gastrointestinal Conditions**: Concurrent gastrointestinal disorders such as enteropathy, malabsorption, and inflammatory bowel disease may predispose children with HIV/AIDS to recurrent salmonellosis by disrupting the gut microbiota and mucosal barrier function.
4. **Environmental Factors**: Poor hygiene practices, unsafe food handling, and contaminated water sources contribute to the transmission and spread of Salmonella infection in children living with HIV/AIDS, particularly in crowded or unsanitary environments.

Clinical Features in Children with HIV

Recurrent salmonellosis in children with HIV/AIDS can present with the following clinical features:

1. **Gastrointestinal Symptoms**: Episodes of diarrhea, abdominal pain, nausea, and vomiting are common manifestations of recurrent Salmonella infection, ranging from mild to severe depending on the extent of gut involvement.
2. **Fever**: Recurrent episodes of fever may accompany gastrointestinal symptoms or precede them, indicating systemic inflammatory response to Salmonella infection in children with HIV/AIDS.
3. **Dehydration**: Prolonged or severe diarrhea can lead to dehydration and electrolyte imbalances, particularly in young children with HIV/AIDS, necessitating prompt fluid resuscitation and supportive care.
4. **Extra-intestinal Manifestations**: Invasive Salmonella infection may result in extra-intestinal complications such as bacteremia, sepsis, meningitis, osteomyelitis, or focal abscesses in children with HIV/AIDS, requiring targeted antimicrobial therapy and close monitoring.

Diagnostic Tests

Diagnosing recurrent salmonellosis in children with HIV/AIDS involves clinical evaluation and laboratory testing:

1. **Stool Culture**: Microbiological examination of stool specimens for Salmonella isolation and identification is the primary diagnostic test for confirming recurrent salmonellosis in children with HIV/AIDS.

2. **Blood Culture**: Blood cultures may be indicated in children with HIV/AIDS presenting with systemic symptoms or signs of invasive Salmonella infection, such as bacteremia or sepsis.
3. **Serological Testing**: Serologic assays for Salmonella-specific antibodies, including serum IgM and IgG titers, may provide supportive evidence of recent or past infection but are not routinely used for acute diagnosis in clinical practice.

Treatment

The management of recurrent salmonellosis in children with HIV/AIDS involves antimicrobial therapy and supportive care:

1. **Antibiotic Treatment**: Empirical or targeted antibiotic therapy with fluoroquinolones, third-generation cephalosporins, or azithromycin is recommended for children with HIV/AIDS with recurrent Salmonella infection, particularly those with invasive disease or systemic symptoms.
2. **Fluid and Electrolyte Replacement**: Oral or intravenous fluid therapy is essential for correcting dehydration, electrolyte imbalances, and metabolic acidosis associated with recurrent salmonellosis in children with HIV/AIDS.
3. **Nutritional Support**: Adequate nutrition and micronutrient supplementation are important for optimizing immune function, promoting gut healing, and reducing the risk of recurrent Salmonella infections in children with HIV/AIDS.

Prophylaxis

Preventive measures for recurrent salmonellosis in children with HIV/AIDS include:

1. **Food and Water Safety**: Educating caregivers about safe food handling practices, proper hand hygiene, and avoidance of contaminated water sources can help reduce the risk of Salmonella transmission and recurrent infections in children living with HIV/AIDS.
2. **Immunization**: Routine childhood immunization with vaccines against Salmonella typhi (typhoid fever) and non-typhoidal Salmonella serotypes may help prevent invasive Salmonella infections and reduce the risk of recurrent salmonellosis in children with HIV/AIDS, particularly in endemic regions.
3. **ART Adherence**: Achieving and maintaining viral suppression with antiretroviral therapy is essential for restoring immune function and reducing the risk of opportunistic infections, including recurrent salmonellosis, in children with HIV/AIDS.

Complications of Disease

Untreated or inadequately treated recurrent salmonellosis in children with HIV/AIDS can lead to severe complications and increased morbidity:

1. **Dehydration and Electrolyte Imbalance**: Prolonged or severe diarrhea can result in dehydration, electrolyte imbalances, and metabolic acidosis, requiring aggressive fluid resuscitation and supportive care measures.
2. **Bacteremia and Sepsis**: Invasive Salmonella infection may lead to bacteremia, sepsis, and systemic inflammatory response syndrome (SIRS) in children with HIV/AIDS, necessitating hospitalization and parenteral antibiotic therapy.

3. **Chronic Carriage and Recurrence**: Some children with HIV/AIDS may become chronic carriers of Salmonella, experiencing recurrent episodes of infection despite antibiotic treatment, highlighting the importance of adherence to preventive measures and close monitoring of clinical status.

In summary, recurrent salmonellosis represents a significant clinical challenge in children living with HIV/AIDS, necessitating early recognition, prompt diagnosis, and appropriate management to prevent complications and improve outcomes in this vulnerable population.

Kaposi Sarcoma

Clinical Scenario Example

Meet Erum Fatima, a ten-year-old girl living with HIV. Despite being on antiretroviral therapy (ART), Erum develops painless, purple-colored lesions on her skin, along with swelling in her legs. Concerned about the appearance of these lesions and their potential significance, Erums caregivers bring her to the hospital for evaluation.

Definition

Kaposi sarcoma (KS) is a rare, vascular tumor characterized by the proliferation of spindle cells and the formation of vascular spaces, leading to the development of purple, red, or brown visceral, oral or skin lesions. In children with HIV/AIDS, KS is considered an opportunistic infection caused by human herpesvirus 8 (HHV-8), also known as Kaposi sarcoma-associated herpesvirus (KSHV). Many children present with lymphadenopathy alone while others have HSHV inflammatory cytokine syndrome (KICS).

Epidemiology

Before the widespread use of combination antiretroviral therapy (cART), KS was a common malignancy in children with HIV/AIDS, particularly those with advanced immunosuppression. Although the incidence of KS has declined significantly in the cART era, it remains an important opportunistic infection in children with poorly controlled HIV infection or inadequate access to healthcare.

Risk Factors

Several factors increase the risk of Kaposi sarcoma in children with HIV/AIDS:

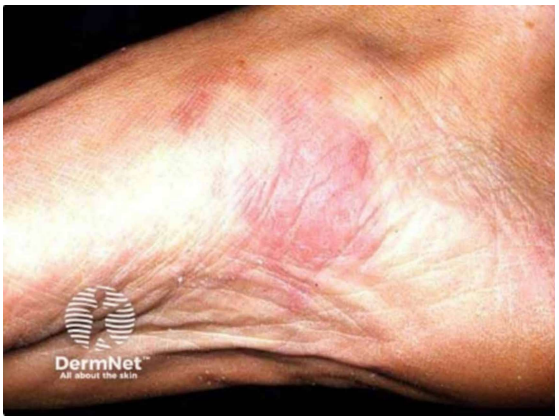
1. **Immunosuppression**: Severe immunosuppression, indicated by low CD4 cell counts and high viral load, predisposes children with HIV to Kaposi sarcoma due to impaired immune surveillance and inadequate control of HHV-8 infection.
2. **HHV-8 Coinfection**: Infection with HHV-8, the causative agent of Kaposi sarcoma, is a significant risk factor for developing KS in children with HIV/AIDS, particularly in regions with high HHV-8 prevalence and endemic KS.
3. **Age**: Adolescents and older children with HIV/AIDS are at higher risk of developing Kaposi sarcoma compared to younger children, possibly due to prolonged exposure to HHV-8 and cumulative immunosuppression.
4. **Geographic Location**: Geographic variation in HHV-8 prevalence and KS incidence influences the risk of Kaposi sarcoma in children with HIV/AIDS, with higher rates observed in sub-Saharan Africa, Eastern Europe, and certain regions of the United States.

Clinical Features in Children with HIV

Kaposi sarcoma in children with HIV/AIDS can present with the following clinical features:

1. **Cutaneous Lesions**: Kaposi sarcoma lesions typically manifest as painless, violaceous or reddish-purple macules, papules, or nodules on the skin, mucous membranes, or internal organs. Lesions may vary in size, shape, and distribution and can occur anywhere on the body, including the face, trunk, extremities, and genital area.
2. **Lymphadenopathy**: Regional or generalized lymphadenopathy may accompany cutaneous Kaposi sarcoma lesions in children with HIV/AIDS, reflecting lymphatic spread of the tumor and immune response to HHV-8 infection.
3. **Edema**: Edema of the lower extremities, known as Kaposi sarcoma-associated lymphedema (KSAL), may occur in children with HIV/AIDS with advanced or extensive cutaneous Kaposi sarcoma lesions, leading to swelling, pain, and functional impairment.
4. Visceral and/or disseminated cutaneous/oral

Figure 43 Kaposi Sarcoma Skin lesion in patient with HIV



Diagnostic Tests

Diagnosing Kaposi sarcoma in children with HIV/AIDS involves clinical evaluation and diagnostic testing:

1. **Clinical Examination**: The characteristic appearance of cutaneous lesions, along with associated symptoms such as lymphadenopathy and edema, is often sufficient to establish a clinical diagnosis of Kaposi sarcoma in children with HIV/AIDS.
2. **Biopsy**: Histopathological examination of a skin biopsy specimen is essential for confirming the diagnosis of Kaposi sarcoma and ruling out other skin conditions. Biopsy findings typically reveal spindle cell proliferation, vascular spaces, and extravasated red blood cells characteristic of KS.
3. **Immunohistochemistry**: Immunohistochemical staining for HHV-8 antigens, such as latency-associated nuclear antigen (LANA-1), can help confirm the presence of HHV-8 infection and support the diagnosis of Kaposi sarcoma in children with HIV/AIDS.

Treatment

The management of Kaposi sarcoma in children with HIV/AIDS involves multimodal therapy:

1. **Antiretroviral Therapy (ART)**: Optimizing ART adherence and achieving viral suppression are essential for controlling HIV replication, restoring immune function, and reducing the risk of Kaposi sarcoma progression in children with HIV/AIDS.
2. **Local Therapy**: Local treatment modalities for cutaneous Kaposi sarcoma lesions may include topical chemotherapy (e.g., imiquimod cream), intralesional chemotherapy (e.g., vincristine injection), cryotherapy, or laser therapy, aimed at reducing tumor burden and improving cosmesis.

3. **Systemic Therapy**: Systemic chemotherapy with agents such as liposomal doxorubicin (doxorubicin liposomal), paclitaxel, or vincristine may be indicated for children with HIV/AIDS with extensive or symptomatic Kaposi sarcoma lesions, particularly those with visceral involvement or progressive disease.
4. **Supportive Care**: Supportive care measures, including pain management, wound care, nutritional support, and psychosocial support, are important components of comprehensive care for children with HIV/AIDS with Kaposi sarcoma, addressing symptom control and improving quality of life.

Prophylaxis

Preventive measures for Kaposi sarcoma in children with HIV/AIDS include:

1. **Screening and Early Detection**: Regular clinical evaluation and skin examination for cutaneous lesions, particularly in high-risk populations such as adolescents and older children with HIV/AIDS, can facilitate early detection and prompt intervention for Kaposi sarcoma.
2. **HHV-8 Testing**: Screening for HHV-8 infection, either by serological testing for HHV-8 antibodies or molecular testing for viral DNA, may be considered in children with HIV/AIDS at high risk of Kaposi sarcoma, guiding preventive strategies and monitoring for disease progression.
3. **Behavioral Counseling**: Education about safe sex practices, avoidance of high-risk behaviors such as intravenous drug use, and reduction of HHV-8 transmission through saliva exchange can help prevent HHV-8 acquisition and reduce the risk of Kaposi sarcoma in children with HIV/AIDS.

Complications of Disease

Untreated or inadequately treated Kaposi sarcoma in children with HIV/AIDS can lead to severe complications and increased morbidity:

1. **Disseminated Disease**: Kaposi sarcoma may disseminate to internal organs such as the lungs, gastrointestinal tract, or lymph nodes in children with HIV/AIDS, resulting in systemic symptoms, organ dysfunction, and poor prognosis.
2. **Immune Reconstitution Inflammatory Syndrome (IRIS)**: Immune reconstitution following ART initiation may trigger an exaggerated inflammatory response to latent HHV-8 infection, leading to paradoxical worsening of Kaposi sarcoma lesions and clinical deterioration in children with HIV/AIDS.
3. **Secondary Infections**: Extensive cutaneous Kaposi sarcoma lesions may predispose children with HIV/AIDS to secondary bacterial, fungal, or viral infections, complicating management and contributing to morbidity and mortality.

In summary, Kaposi sarcoma is an important opportunistic infection in children with HIV/AIDS, particularly those with advanced immunosuppression and HHV-8 coinfection. Early recognition, prompt diagnosis, and appropriate management are essential for optimizing outcomes and preventing complications associated with this malignant neoplasm in children living with HIV/AIDS.

Syphilis in Children with HIV

Clinical Scenario Example

Consider Sarah, a six-year-old girl living with HIV. Sarah presents to the clinic with a painless sore on her genital area. Her caregiver reports that the sore appeared a few weeks ago and has not healed. Concerned about the possibility of sexually transmitted infections (STIs) in a child with HIV, the healthcare provider performs a thorough evaluation to determine the cause of the genital lesion and assess for potential complications.

Definition

Syphilis is a sexually transmitted infection caused by the bacterium Treponema pallidum. In children with HIV, syphilis is considered an opportunistic infection due to their heightened vulnerability to sexually transmitted pathogens and increased risk of complications associated with immunosuppression.

Epidemiology

The prevalence of syphilis in children with HIV varies depending on factors such as age, geographic location, and sexual behavior. In resource-limited settings with high HIV and STI burden, children with HIV may be at increased risk of acquiring syphilis through vertical transmission from infected mothers or horizontal transmission through sexual abuse or exposure.

Risk Factors

Several factors increase the risk of syphilis in children with HIV:

1. **Vertical Transmission**: Infants born to mothers with untreated syphilis during pregnancy are at risk of congenital syphilis, acquiring the infection transplacentally or during delivery, particularly if the mother is coinfected with HIV.
2. **Sexual Abuse**: Children with HIV may be at increased risk of sexual abuse or exploitation, leading to exposure to STIs such as syphilis through non-consensual sexual contact with infected individuals.
3. **High-Risk Sexual Behavior**: Older children and adolescents with HIV/AIDS may engage in high-risk sexual behaviors, including unprotected sex and multiple sexual partners, increasing their susceptibility to STIs such as syphilis.

Clinical Features in Children with HIV

Syphilis in children with HIV/AIDS can present with the following clinical features:

1. **Primary Syphilis**: Primary syphilis manifests as a painless, indurated chancre at the site of Treponema pallidum inoculation, commonly on the genitalia, perianal area, or oral mucosa. The chancre may go unnoticed or be mistaken for other benign lesions, delaying diagnosis and treatment.
2. **Secondary Syphilis**: Secondary syphilis presents with systemic symptoms such as fever, malaise, headache, and generalized lymphadenopathy, along with characteristic mucocutaneous manifestations including maculopapular rash, **condylomata** lata, mucous patches, and alopecia. Children with HIV/AIDS may have atypical or severe secondary syphilis manifestations due to immunosuppression.

3. **Congenital Syphilis**: Congenital syphilis in children with HIV/AIDS may present with a wide range of clinical manifestations, including rhinitis, hepatosplenomegaly, rash, jaundice, skeletal abnormalities, neurologic deficits, and failure to thrive. The diagnosis of congenital syphilis should be considered in infants born to mothers with untreated or inadequately treated syphilis during pregnancy.

Diagnostic Tests

Diagnosing syphilis in children with HIV/AIDS involves clinical evaluation and laboratory testing:

1. **Physical Examination**: Clinical assessment of genital lesions, mucocutaneous manifestations, and systemic symptoms is essential for identifying suspected cases of syphilis in children with HIV/AIDS and determining the need for further diagnostic testing.
2. **Serological Tests**: Serological assays for syphilis-specific antibodies, including non-treponemal tests (e.g., Venereal Disease Research Laboratory [VDRL] test, Rapid Plasma **Reagin** [RPR] test) and treponemal tests (e.g., fluorescent treponemal antibody absorption [FTA-ABS] test, treponemal pallidum particle agglutination [TP-PA] test), are used to confirm the diagnosis of syphilis and differentiate between active and past infection.
3. **Dark-Field Microscopy**: Dark-field microscopy of lesion exudate or tissue biopsy specimens may be performed to visualize Treponema pallidum spirochetes directly, aiding in the diagnosis of primary syphilis in children with HIV/AIDS.

Treatment

The management of syphilis in children with HIV/AIDS involves antimicrobial therapy and supportive care:

1. **Antibiotic Treatment**: Penicillin remains the treatment of choice for syphilis in children with HIV/AIDS, with parenteral penicillin G benzathine or penicillin G aqueous crystalline administered according to the stage of disease and age of the child. Alternative antibiotic regimens may be considered for children with HIV/AIDS with penicillin allergy or intolerance.
2. **Follow-Up Evaluation**: Children with HIV/AIDS treated for syphilis should undergo close clinical monitoring and serological follow-up to assess treatment response, evaluate for treatment failure or reinfection, and ensure resolution of clinical manifestations and serological abnormalities.
3. **Partner Notification and Testing**: Identification and treatment of sexual partners and household contacts of children with HIV/AIDS diagnosed with syphilis are essential for preventing transmission, reducing the risk of reinfection, and promoting sexual health and wellbeing.

Prophylaxis

Preventive measures for syphilis in children with HIV/AIDS include:

1. **Prenatal Screening and Treatment**: Routine antenatal screening for syphilis during pregnancy, followed by prompt treatment with benzathine penicillin for infected mothers, can help prevent vertical transmission and congenital syphilis in children born to HIV-positive women.
2. **Behavioral Counseling**: Education about safe sex practices, sexual health, and the prevention of sexually transmitted infections, including syphilis, is important for children with HIV/AIDS as they reach adolescence and become sexually active, reducing the risk of STI acquisition and transmission.

Complications of Disease

Untreated or inadequately treated syphilis in children with HIV/AIDS can lead to severe complications and increased morbidity:

1. **Congenital Syphilis Complications**: Congenital syphilis in children with HIV/AIDS may result in adverse pregnancy outcomes such as stillbirth, neonatal death, preterm birth, low birth weight, and congenital anomalies affecting multiple organ systems, including the central nervous system, cardiovascular system, and skeletal system.
2. **Neurosyphilis**: Children with HIV/AIDS with untreated or inadequately treated syphilis are at risk of developing neurosyphilis, leading to neurologic deficits, cognitive impairment, sensorimotor dysfunction, and ophthalmologic abnormalities if left untreated.
3. **Secondary Infections**: Genital or anal ulcers associated with primary or secondary syphilis in children with HIV/AIDS may predispose to secondary bacterial, viral, or fungal infections, complicating management and contributing to morbidity and mortality.

In summary, syphilis is an important opportunistic infection in children with HIV/AIDS, requiring early recognition, prompt diagnosis, and appropriate management to prevent complications and improve outcomes in this vulnerable population.

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Chapter 07

Syndromic Approach to Common Childhood Infections

Introduction:

In resource-limited settings, where access to healthcare facilities and diagnostic tools may be limited, syndromic management plays a crucial role in the timely identification and treatment of common childhood infections, especially in children living with HIV. The Integrated Management of Childhood Illness (IMNCI) and World Health Organization (WHO) pneumonia guidelines provide structured approaches for the assessment and management of pediatric infections based on presenting symptoms and clinical signs. This chapter aims to outline a syndromic approach to common childhood infections in children with HIV, incorporating IMNCI and WHO pneumonia guidelines.

Section 1: Fever with Cough

Clinical Scenario Example: Asim, a 7-year-old boy with HIV, presents with a 3-day history of fever and cough. He has no difficulty breathing but appears tired and lethargic.

Differentials:

1. Pneumonia (bacterial or viral)
2. Tuberculosis
3. Pneumocystis jirovecii pneumonia (PJP)
4. **Bronchiolitis**
5. Asthma exacerbation

Investigations:

1. Chest X-ray (if available)
2. Sputum or induced sputum for microscopy, culture, and sensitivity
3. Tuberculin skin test (TST) or interferon-gamma release assay (IGRA)
4. HIV viral load and CD4 count (if not previously done)

Clinical Diagnosis: Bacterial pneumonia based on clinical findings of fever, cough, and signs of respiratory distress.

Treatment:

1. Antibiotics (e.g., amoxicillin or co-trimoxazole) for bacterial pneumonia.
2. Consider empiric treatment for TB if suspicion is high.
3. Supportive care, including hydration and antipyretics.
4. Ensure adherence to ART and prophylaxis for opportunistic infections.

Section 2: Fever without Focus

Clinical Scenario Example: Fatima, a 5-year-old girl with HIV, is brought to the clinic with a high-grade fever for the past 5 days. She appears irritable but has no localizing symptoms.

Differentials:

1. **Bacteremia/sepsis**
2. Malaria
3. Viral infection (e.g., respiratory syncytial virus, influenza)
4. **Urinary tract infection (UTI)**
5. Typhoid fever

Investigations:

1. Blood culture
2. **Malaria rapid diagnostic test (RDT) or microscopy**
3. Complete blood count (CBC) with differential
4. Urinalysis and urine culture
5. Widal test or blood culture for typhoid fever (if indicated)

Clinical Diagnosis: Sepsis secondary to bacterial infection based on clinical findings of fever and irritability with no localizing signs.

Treatment:

1. **Empiric antibiotics** cover common pathogens (e.g., amoxicillin or ceftriaxone).
2. Antimalarial therapy if malaria is diagnosed.
3. **Supportive care, including hydration and antipyretics.**
4. Ensure adherence to ART and prophylaxis for opportunistic infections.

Section 3: Fever with Rash

Clinical Scenario Example: Junaid, a 3-year-old boy with HIV, presents with a 2-day history of fever and a maculopapular rash involving the trunk and extremities.

Differentials:

1. **Measles**
2. Rubella
3. Varicella (chickenpox)
4. **Drug rash**
5. Kawasaki disease

Investigations:

1. Serological testing for measles, rubella, and varicella IgM antibodies
2. Complete blood count (CBC) with platelet count
3. CRP or ESR to assess for inflammation (if available)

Clinical Diagnosis: Varicella infection based on clinical findings of fever and a characteristic maculopapular rash.

Treatment:

1. **Supportive care, including antipyretics and analgesics.**
2. Maintain skin hygiene to prevent secondary bacterial infection.
3. Consider acyclovir therapy for severe or complicated cases.
4. Ensure adherence to ART and prophylaxis for opportunistic infections.

Section 4: Fever with Ear Discharge or Otalgia

Clinical Scenario Example: Sophia, a 6-year-old girl with HIV, **presents** a 1-day history of fever and ear pain. On examination, purulent discharge is noted from the right ear.

Differentials:

1. **Acute otitis media (AOM)**
2. Otitis externa
3. Mastoiditis
4. Temporomandibular joint (TMJ) disorder
5. **Dental infection**

Investigations:

1. Otoscopy to visualize the tympanic membrane
2. Culture and sensitivity of ear discharge (if available)
3. Complete blood count (CBC) with differential (if systemic signs of infection)

Clinical Diagnosis: Acute otitis media based on clinical findings of fever, ear pain, and purulent discharge from the ear.

Treatment:

1. Antibiotics targeting common pathogens (e.g., amoxicillin or co-amoxiclav).
2. Analgesics for pain relief.
3. Topical antibiotics (e.g., ofloxacin ear drops) for otitis externa.
4. Ensure adherence to ART and prophylaxis for opportunistic infections.

Section 5: Fever with Dysuria

Clinical Scenario Example: Danish, a 9-year-old boy with HIV, complains of fever and pain during urination for the past 2 days. He is reluctant to pass urine due to discomfort.

Differentials:

1. Urinary tract infection (UTI)
2. Sexually transmitted infection (STI) (e.g., gonorrhea, chlamydia)
3. Urethritis
4. Pyelonephritis
5. Genital ulcer disease (GUD)

Investigations:

1. Urinalysis and urine culture
2. STI screening (if indicated)
3. Renal ultrasound (if pyelonephritis is suspected)

Clinical Diagnosis: Urinary tract infection (UTI) based on clinical findings of fever and dysuria with positive urine culture.

Treatment:

1. Empiric antibiotics targeting common uropathogens (e.g., co-amoxiclav or ceftriaxone).
2. Encourage fluid intake and frequent voiding.
3. Ensure adherence to ART and prophylaxis for opportunistic infections.

Section 6: Fever with Skin and Soft Tissue Infections

Clinical Scenario Example: Liam, a 4-year-old boy with HIV, presents with a 3-day history of fever and multiple painful skin lesions on the buttocks and thighs.

Differentials:

1. Cellulitis
2. Abscess (e.g., furuncle, carbuncle)
3. Folliculitis
4. Ecthyma
5. Impetigo

Investigations:

1. Clinical examination of skin lesions
2. Culture and sensitivity of pus or wound swab (if indicated)
3. Complete blood count (CBC) with differential (if systemic signs of infection)

Clinical Diagnosis: Folliculitis based on clinical findings of fever and painful, erythematous papules or pustules involving hair follicles.

Treatment:

1. Warm compresses and incision and drainage for abscesses.
2. Empiric antibiotics targeting common skin pathogens (e.g., co-amoxiclav or clindamycin).
3. Topical antiseptics or antibiotics for superficial infections.
4. Ensure adherence to ART and prophylaxis for opportunistic infections.

Conclusion:

A syndromic approach to common childhood infections in children with HIV, guided by IMNCI and WHO pneumonia guidelines, enables healthcare providers in resource-limited settings to promptly diagnose and treat pediatric infections based on presenting symptoms and clinical signs. Early recognition and appropriate management of childhood infections are essential for improving outcomes and reducing morbidity and mortality in children living with HIV.

Chapter 08

Non-Communicable Sequelae in Children Living with HIV

Introduction:

As children living with HIV survive into adolescence and adulthood due to the widespread availability of antiretroviral therapy (ART), they face an increasing burden of non-communicable diseases (NCDs) that affect various organ systems. These NCDs significantly impact the quality of life and long-term outcomes of children living with HIV. This chapter explores the non-communicable sequelae in children living with HIV across different systems, including the Brain, Locomotor System, Heart, Lung, Gastrointestinal Tract, Kidney, Eye, Blood and Bone Marrow, and Skin and Soft Tissue. Each system is divided into subsections with a focus on common conditions, diagnostic approaches, and management strategies.

1. Brain

Common List of Conditions:

1. HIV-associated neurocognitive disorders (HAND)
2. Cerebrovascular disease
3. HIV-associated encephalopathy
4. Opportunistic infections (e.g., toxoplasmosis, cryptococcal meningitis)
5. HIV-associated neurodevelopmental delays

How to Diagnose:

1. Clinical assessment: Evaluation of neurological symptoms and signs, cognitive function, and developmental milestones.
2. Neuroimaging: Magnetic resonance imaging (MRI) or computed tomography (CT) scan of the brain to detect structural abnormalities or opportunistic infections.
3. Cerebrospinal fluid analysis: Lumbar puncture with cerebrospinal fluid (CSF) examination for cell count, protein, glucose, and specific tests for opportunistic infections.

How to Manage:

1. Antiretroviral therapy (ART): Early initiation and adherence to ART to suppress HIV viral load and prevent neurological complications.
2. Pharmacological treatment: Antiretroviral drugs with good central nervous system penetration, antimicrobial agents for opportunistic infections, and symptomatic management of neurological symptoms.
3. Supportive care: Multidisciplinary interventions, including neurocognitive rehabilitation, developmental support, and social services to optimize outcomes

2. Locomotor System

Common List of Conditions:

1. HIV-associated osteopenia and osteoporosis
2. Osteonecrosis
3. Avascular necrosis of the hip
4. HIV-associated arthritis
5. Osteomyelitis

How to Diagnose:

1. Clinical evaluation: Assessment of musculoskeletal symptoms, joint function, and mobility.
2. Imaging studies: X-rays, magnetic resonance imaging (MRI), or bone scans to evaluate bone density, joint integrity, and the presence of osteonecrosis or osteomyelitis.
3. Laboratory tests: Serum markers of bone turnover, including calcium, phosphate, alkaline phosphatase, and vitamin D levels.

How to Manage:

1. Lifestyle modifications: Encourage weight-bearing exercises, adequate nutrition, and sun exposure to promote bone health.
2. Pharmacological interventions: Calcium and vitamin D supplementation, bisphosphonates for osteoporosis, and analgesics for pain management.
3. Surgical intervention: Joint replacement surgery for advanced osteonecrosis or severe arthritis.
4. ART optimization: Ensure adherence to ART to reduce HIV-related inflammation and improve bone health.

3. Heart

Common List of Conditions:

1. HIV-associated cardiomyopathy
2. Heart failure
3. Myocarditis
4. Arrhythmias
5. Endocarditis

How to Diagnose:

1. Clinical evaluation: Assessment of cardiac symptoms, including dyspnea, fatigue, palpitations, and exercise intolerance.
2. Electrocardiography (ECG): Recording of cardiac electrical activity to detect arrhythmias, conduction abnormalities, or signs of myocardial ischemia.

3. Echocardiography: Ultrasound imaging of the heart to evaluate cardiac structure, function, and chamber dimensions.
4. Cardiac biomarkers: Measurement of serum troponin levels and brain natriuretic peptide (BNP) or N-terminal pro-BNP (NT-proBNP) levels to assess for myocardial injury or heart failure.

How to Manage:

1. Pharmacological therapy: Angiotensin-converting enzyme (ACE) inhibitors, beta-blockers, diuretics, and digoxin for heart failure management.
2. ART optimization: Ensure adherence to ART to suppress HIV viral load and reduce HIV-related inflammation, which may contribute to cardiac dysfunction.
3. Device therapy: Implantable cardioverter-defibrillators (ICDs), cardiac resynchronization therapy (CRT), or pacemakers for arrhythmia management or heart failure with electrical conduction abnormalities.
4. Surgical intervention: Valve repair or replacement, coronary artery bypass grafting (CABG), or ventricular assist device (VAD) placement for structural heart disease or end-stage heart failure.

4. Lung

Common List of Conditions:

1. Chronic obstructive pulmonary disease (COPD)
2. Pulmonary hypertension
3. Pulmonary fibrosis
4. HIV-associated lung infections (e.g., Pneumocystis jirovecii pneumonia, tuberculosis)
5. Bronchiectasis

How to Diagnose:

1. Clinical evaluation: Assessment of respiratory symptoms, including cough, dyspnea, and exercise intolerance.
2. Pulmonary function tests: Spirometry, lung volumes, and diffusion capacity to evaluate lung function and assess for obstructive or restrictive patterns.
3. Imaging studies: Chest X-ray or CT scan to detect structural lung abnormalities, infiltrates, or signs of fibrosis.
4. Microbiological tests: Sputum culture, bronchoalveolar lavage, or nucleic acid amplification tests to identify respiratory pathogens.

How to Manage:

1. Smoking cessation: Encourage smoking cessation and avoidance of environmental pollutants to prevent COPD exacerbations.
2. Pulmonary rehabilitation: Exercise training, breathing exercises, and education to improve respiratory muscle strength and functional capacity.

3. Pharmacological therapy: Bronchodilators, inhaled corticosteroids, oxygen therapy, and targeted therapies for pulmonary hypertension or fibrosis.
4. Antimicrobial treatment: Prompt initiation of antimicrobial therapy for HIV-associated lung infections to reduce morbidity and mortality.

5. Gastrointestinal Tract

Common List of Conditions:

1. HIV-associated diarrhea
2. Gastroesophageal reflux disease (GERD)
3. Esophageal candidiasis
4. Inflammatory bowel disease (IBD)
5. Gastrointestinal malignancies (e.g., Kaposi sarcoma, lymphoma)

How to Diagnose:

1. Clinical assessment: Evaluation of gastrointestinal symptoms, including diarrhea, abdominal pain, dysphagia, and weight loss.
2. Endoscopic evaluation: Upper endoscopy or colonoscopy with biopsy to visualize gastrointestinal mucosa, detect lesions, and obtain tissue samples for histological examination.
3. Stool studies: Stool culture, microscopy, and polymerase chain reaction (PCR) assays for infectious pathogens, including parasites, bacteria, and viruses.
4. Imaging studies: Barium swallow, upper gastrointestinal series, or abdominal CT scan to assess for structural abnormalities, strictures, or masses.

How to Manage:

1. Symptomatic treatment: Antidiarrheal agents, proton pump inhibitors, and dietary modifications to alleviate gastrointestinal symptoms.
2. Antimicrobial therapy: Antifungal agents for esophageal candidiasis, antibiotics for bacterial infections, and antiparasitic drugs for parasitic infections.
3. Immunosuppressive therapy: Corticosteroids, immunomodulators, or biologic agents for inflammatory bowel disease or refractory symptoms.
4. Surgical intervention: Surgical resection or palliative procedures for gastrointestinal malignancies or complications such as strictures or fistulas.

6. Kidney

Common List of Conditions:

1. HIV-associated nephropathy (HIVAN)
2. Acute kidney injury (AKI)
3. Chronic kidney disease (CKD)
4. Renal tubular dysfunction
5. HIV-associated glomerular diseases

How to Diagnose:

1. Clinical evaluation: Assessment of renal function, including serum creatinine, estimated glomerular filtration rate (eGFR), and urinary protein excretion.
2. Renal imaging: Ultrasound, CT scan, or MRI to evaluate renal size, structure, and presence of cysts or masses.
3. Urinalysis: Dipstick testing for proteinuria, hematuria, and urinary sediment examination to detect abnormalities suggestive of glomerular or tubular dysfunction.
4. Renal biopsy: Histological examination of renal tissue to establish a definitive diagnosis, assess disease severity, and guide management decisions.

How to Manage:

1. Blood pressure control: Antihypertensive therapy (e.g., ACE inhibitors, angiotensin receptor blockers) to manage hypertension and reduce the risk of kidney disease progression.
2. Antiretroviral therapy (ART): Initiation and optimization of ART to suppress HIV viral load and prevent HIV-associated nephropathy.
3. Renoprotective strategies: Avoid nephrotoxic medications, maintain euvolemia, and monitor electrolyte balance and renal function regularly.
4. Dialysis and transplantation: Renal replacement therapy (hemodialysis or peritoneal dialysis) or kidney transplantation for end-stage kidney disease or refractory complications.

7. Eye

Common List of Conditions:

1. Cytomegalovirus (CMV) retinitis
2. HIV-associated neuroretinal disorder (HIV-NRD)
3. Uveitis
4. Retinal detachment
5. Optic neuropathy

How to Diagnose:

1. Ophthalmic examination: Dilated fundoscopic examination, visual acuity testing, and intraocular pressure measurement to assess for retinal lesions, optic nerve abnormalities, or visual impairment.
2. Optical coherence tomography (OCT): High-resolution imaging of retinal layers and optic nerve head to evaluate structural changes or edema.
3. Fluorescein angiography: Intravenous injection of fluorescein dye followed by retinal imaging to detect vascular abnormalities or leakage.
4. Polymerase chain reaction (PCR) assays: Molecular testing of ocular fluid or tissue samples for viral DNA or RNA to diagnose viral retinitis or other infectious etiologies.

How to Manage:

1. Antiviral therapy: Systemic or intravitreal antiviral medications (e.g., ganciclovir, foscarnet) for CMV retinitis or other viral infections.
2. Corticosteroids: Topical, periocular, or systemic corticosteroids for uveitis or inflammatory ocular conditions.
3. Immunomodulatory therapy: Immunosuppressive agents (e.g., methotrexate, cyclosporine) for refractory uveitis or autoimmune-mediated eye diseases.
4. Surgical intervention: Vitrectomy, retinal laser photocoagulation, or scleral buckling for retinal detachment or other structural abnormalities.

8. Blood and Bone Marrow

Common List of Conditions:

1. Anemia
2. Thrombocytopenia
3. Neutropenia
4. Hematologic malignancies (e.g., lymphoma, leukemia)
5. Bone marrow suppression

How to Diagnose:

1. Complete blood count (CBC): Assessment of hemoglobin, platelet count, and white blood cell count to detect anemia, thrombocytopenia, or leukopenia.
2. Peripheral blood smear: Examination of blood film for morphological abnormalities of red blood cells, white blood cells, and platelets.
3. Bone marrow biopsy: Invasive procedure to obtain bone marrow samples for histological examination, cytogenetic analysis, and flow cytometry.
4. Coagulation studies: Measurement of prothrombin time (PT), activated partial thromboplastin time (aPTT), and fibrinogen levels to evaluate coagulation status and detect bleeding disorders.

How to Manage:

1. Supportive care: Blood transfusion, erythropoietin-stimulating agents, or granulocyte colony-stimulating factor (G-CSF) for anemia, thrombocytopenia, or neutropenia.
2. Antiretroviral therapy (ART): Initiation and optimization of ART to suppress HIV viral load and restore immune function, which may alleviate hematologic abnormalities.
3. Chemotherapy or targeted therapy: Treatment regimens tailored to specific hematologic malignancies, including lymphoma, leukemia, or myelodysplastic syndromes.
4. Hematopoietic stem cell transplantation: Curative option for selected patients with hematologic malignancies or severe bone marrow suppression refractory to conventional therapies.

9. Skin and Soft Tissue

Common List of Conditions:

1. HIV-associated dermatoses (e.g., seborrheic dermatitis, eosinophilic folliculitis)
2. Cutaneous manifestations of opportunistic infections (e.g., herpes simplex virus, varicella-zoster virus)
3. Drug reactions (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis)
4. Cutaneous malignancies (e.g., Kaposi sarcoma, non-Hodgkin lymphoma)
5. Skin and soft tissue infections (e.g., cellulitis, abscess)

How to Diagnose:

1. Dermatological examination: Evaluation of skin lesions, rash distribution, morphology, and associated symptoms.
2. Skin biopsy: Excisional or punch biopsy with histopathological examination to establish a definitive diagnosis, identify infectious agents, or rule out malignancy.
3. Microbiological tests: Culture, microscopy, or nucleic acid amplification tests (NAATs) of skin swabs or tissue samples to detect bacterial, fungal, or viral pathogens.
4. Patch testing: Application of allergens to the skin to diagnose drug hypersensitivity reactions or contact dermatitis.

How to Manage:

1. Topical therapy: Emollients, topical corticosteroids, antifungal creams, or antimicrobial agents for localized skin lesions or infections.
2. Systemic therapy: Oral or parenteral antibiotics, antivirals, or antifungals for severe or disseminated infections.
3. Symptomatic treatment: Pain management, wound care, and supportive measures for cutaneous adverse drug reactions or toxic epidermal necrolysis.
4. Surgical intervention: Excision, cryotherapy, or laser therapy for benign or malignant cutaneous lesions requiring removal or destruction.
5. Oncological management: Chemotherapy, radiotherapy, or immunotherapy for cutaneous malignancies such as Kaposi sarcoma or non-Hodgkin lymphoma.

Conclusion:

Non-communicable sequelae in children living with HIV encompass a wide range of conditions affecting multiple organ systems. Early recognition, comprehensive evaluation, and multidisciplinary management are essential for optimizing outcomes and improving the quality of life for children living with HIV. A holistic approach that addresses both HIV-related and non-HIV-related morbidities is crucial for achieving optimal health outcomes in this vulnerable population.

Chapter 09

Common Skin Rashes and Infections in Children with HIV

Clinical Scenario Example

Consider Akbar, a nine-year-old child living with HIV. Despite being on antiretroviral therapy (ART), Akbar develops a widespread rash with associated itching and discomfort. Concerned about the appearance of the rash and its potential implications for his health, his caregivers seek medical evaluation to determine the cause and appropriate management.

Definition

Children with HIV are susceptible to various skin rashes and infections due to their impaired immune function, which predisposes them to opportunistic infections and inflammatory dermatoses. These skin conditions can range from benign and self-limiting to severe and potentially life-threatening, impacting the quality of life and overall health of affected children.

Epidemiology

The prevalence and incidence of skin rashes and infections in children with HIV vary depending on factors such as the degree of immunosuppression, exposure to opportunistic pathogens, and adherence to antiretroviral therapy. Common skin conditions in this population include viral, bacterial, and fungal infections, as well as inflammatory dermatoses and drug reactions.

Risk Factors

Several factors increase the risk of skin rashes and infections in children with HIV:

1. **Immunosuppression**: Severe immunosuppression, indicated by low CD4 cell counts and high viral load, increases the susceptibility of children with HIV to opportunistic infections and inflammatory skin conditions.
2. **Non-adherence to ART**: Inadequate viral suppression due to non-adherence or treatment failure predisposes children with HIV to recurrent or persistent skin infections and dermatoses.
3. **Environmental Factors**: Poor hygiene overcrowded living conditions, and close contact with individuals with active skin infections increase the risk of transmission and disease acquisition in susceptible children with HIV/AIDS.
4. **Co-existing Medical Conditions**: Underlying medical conditions such as malnutrition, concomitant infections, and systemic diseases may exacerbate immunosuppression and contribute to the development of skin rashes and infections in children with HIV.

Clinical Features in Children with HIV

Common skin rashes and infections in children with HIV/AIDS include the following:

Viral Infections:

- **Herpes Simplex Virus (HSV) Infection**: Presents with grouped vesicles on an erythematous base, typically around the mouth or genital area.
- **Varicella Zoster Virus (VZV) Infection**: Characterized by a pruritic rash with vesicles in various stages of development, following a dermatomal distribution.
- **Molluscum Contagiosum**: Presents as flesh-colored, dome-shaped papules with central umbilication, commonly on the face, trunk, and extremities.

Bacterial Infections:

- **Impetigo**: Presents with honey-colored crusted lesions or pustules, often occurring in intertriginous areas or areas of skin trauma.
- **Folliculitis**: Presents with erythematous papules or pustules involving hair follicles, commonly on the face, neck, and trunk.
- **Cellulitis**: Presents with erythema, warmth, swelling, and tenderness of the affected skin, often associated with fever and systemic symptoms.

Fungal Infections:

- **Tinea Corporis**: Presents with annular, scaly plaques with central clearing and raised borders, commonly on the trunk and extremities.
- **Candidiasis**: Presents with erythematous plaques with satellite papules and pustules, commonly in intertriginous areas such as the groin and axillae.

Inflammatory Dermatoses:

- **Atopic Dermatitis**: Presents with pruritic, erythematous papules, plaques, and excoriated lesions, commonly affecting flexural areas in children with HIV.
- **Seborrheic Dermatitis**: Presents with greasy, yellowish scales on erythematous patches, commonly involving the scalp, face, and intertriginous areas.

Diagnostic Tests

Diagnosing skin rashes and infections in children with HIV involves clinical evaluation and diagnostic testing:

1. **Clinical Examination**: The characteristic morphology and distribution of skin lesions are often sufficient to establish a clinical diagnosis of common skin rashes and infections in children with HIV/AIDS.

2. **Microbiological Tests**: Microscopic examination, culture, and sensitivity testing of skin scrapings, swabs, or biopsy specimens may be performed to identify the causative pathogens, including bacteria, fungi, and viruses.
3. **Histopathological Examination**: Skin biopsy and histopathological examination may be indicated in cases of atypical or refractory skin lesions, providing additional diagnostic information and guiding management decisions.

Treatment

The management of skin rashes and infections in children with HIV involves various treatment modalities:

1. **Antimicrobial Therapy**: Topical or systemic antimicrobial agents, including antiviral, antibacterial, and antifungal medications, may be prescribed based on the suspected or confirmed etiology of the skin infection.
2. **Topical Corticosteroids**: Topical corticosteroids may be used to reduce inflammation and pruritus associated with inflammatory dermatoses such as atopic dermatitis and seborrheic dermatitis.
3. **Emollients and Moisturizers**: Emollients and moisturizers may help hydrate and soothe dry, irritated skin in children with HIV/AIDS, particularly those with eczematous or xerotic dermatoses.
4. **Supportive Care Measures**: Symptomatic relief measures such as cool compresses, oatmeal baths, and oral antihistamines may alleviate pruritus and discomfort associated with various skin rashes and infections in children with HIV/AIDS.

Prophylaxis

Preventive measures for common skin rashes and infections in children with HIV/AIDS include:

1. **Good Hygiene Practices**: Encouraging regular bathing, handwashing, and cleanliness of skin and clothing can help prevent the transmission and spread of skin infections in susceptible children with HIV.
2. **Prompt Treatment of Skin Infections**: Early recognition and treatment of skin infections, including bacterial, fungal, and viral infections, can help prevent complications and reduce the risk of secondary transmission.
3. **Optimization of ART**: Achieving and maintaining viral suppression with antiretroviral therapy is essential for restoring immune function and reducing the risk of opportunistic infections, including skin rashes and infections, in children with HIV/AIDS.

Complications of Disease

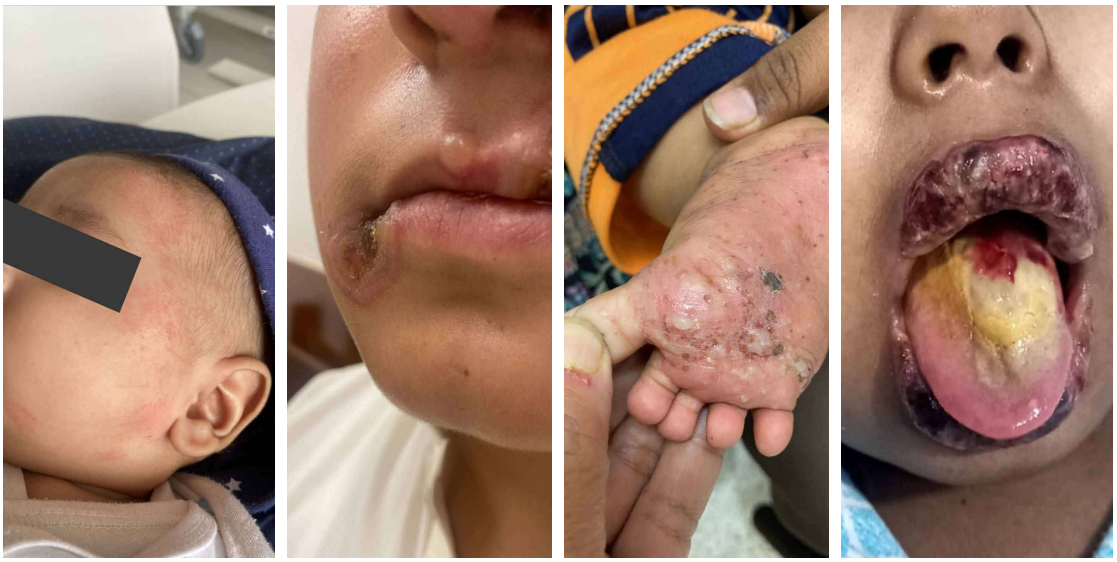
Complications of common skin rashes and infections in children with HIV/AIDS may include:

1. **Secondary Infection**: Superinfection of skin lesions with bacteria, fungi, or viruses may occur, leading to localized inflammation, cellulitis, abscess formation, and systemic complications.
2. **Chronic or Recurrent Disease**: Inadequately treated or recurrent skin infections may lead to chronic or recurrent disease, requiring prolonged or alternative treatment modalities to achieve resolution.

3. **Psychosocial Impact**: Skin rashes and infections in children with HIV/AIDS may cause psychosocial distress, stigma, and social isolation, affecting self-esteem, quality of life, and mental health outcomes.

In summary, common skin rashes and infections represent significant clinical challenges in children living with HIV/AIDS, requiring early recognition, accurate diagnosis, and appropriate management to optimize outcomes and prevent complications associated with these dermatological conditions.

Figure 44 Myriad of skin and mucosal lesions encountered in children with HIV



Chapter 10

Approach to a child with HIV on a follow-up visit in clinic

10.1 History taking for the Program Physician on return visit

This history taking is shorter and smoother as rapport between patient and physician improves over time.

10.2 Objective of follow-up visit of a child with HIV:

a. Program Deliverables
    i. History
        1. To review missing information in baseline and previous visit note
        2. document laboratory and radiology reports since last visit
        3. Interpret and add action to rolling ART plan
    ii. Examination
        1. Weight/Height/Vitals
        2. General Physical Examination
        3. Clinical Staging
        4. Tuberculosis Evaluation (See chapter xyz)
    iii. Assess vaccination coverage gaps
    iv. Document CD4 and VL with date since last visit
    v. Document Regimen with starting date/stopping date/switching reason
    vi. Document adherence (from previous visit date)
        1. Total number of doses to be taken – missed doses/total doses x 100
            a. <85%
            b. 86-95%
            c. >95%
    vii. Document disclosure
    viii. Patient can correctly identify prescribed medication Yes No
b. Patient Deliverables
    i. Investigations and Special Investigations
        1. Document HBV and HCV positive or negative status
        2. Screen for Pulmonary TB
        3. Assess Immunological Status (CD4 absolute count)
        4. Screen for likely OI if Clinical Stage 3-4 and/or CD4<200

c. Physician Deliverables

i. ART as per Program

ii. Prophylaxis (cotrimoxazole preventive therapy (CPT), MAC Prophylaxis, TB Preventive Therapy (TPT)) as per Program

iii. Macronutrient Supplements (if Severe Acute Malnutrition

iv. Micronutrient Supplements (Iron, Vitamin D)

v. Treatment of acute common childhood infections

vi. Treatment of uncommon opportunistic infections and co-infections

vii. Recognition of poor resource to manage serious illness and expedited referral to higher center

viii. School and Home Plan (Psychosocial Support)

ix. Other needs (referral to higher specialized centre for suspected advanced disese: motor delays etc)

x. Family Caregiver HIV and health status

xi. Recommend family testing (mother, father, siblings, extended family in same household) and check for compliance on every visit till complete

3.3 History Taking for the Program

The medical files provided by the Program contain deliverables required by the funding agencies (The Global Fund/UNDP) in a sequence relevant to the agency and not the treating physician.

For example the follow-up visit note starts with family situation (staying with own family, at center with family contact, at center without family contact), who is the caregiver (parent, relative, friends and their HIV status), caregiver highest education, gender of patient and age, member of high risk group or not. Followed by examination

There is an abrupt jumping to birth history and then vaccination history before ART and CD4 and VL status are documented.

Follow the sequence which makes best sense to you as physician and document at end of the visit if easier. Else follow sequence in booklet.

a. Program Deliverables

xii. History

1. To review missing information in baseline and previous visit note
2. document laboratory and radiology reports since last visit
3. Interpret and add action to rolling ART plan
4. Ascertain caregiver
5. Ascertain family testing status
6. Ascertain risk factor group

xiii. Examination

1. Weight/Height/Vitals
2. General Physical Examination
3. Clinical Staging
4. Tuberculosis Evaluation (See chapter xyz)

xiv. Assess vaccination coverage gaps

xv. Document CD4 and VL with date since last visit

xvi. Document Regimen with starting date/stopping date/switching reason

xvii. Document adherence (from previous visit date)

1. Total number of doses to be taken – missed doses/total doses x 100
   a. <85%
   b. 86-95%
   c. >95%

xviii. Document disclosure

xix. Patient can correctly identify prescribed medication Yes No

Chapter 11

Helping Children in Pakistan Live with HIV

Understanding HIV

HIV, or Human Immunodeficiency Virus, is a virus that attacks the immune system, specifically targeting CD4 cells, a type of white blood cell that plays a crucial role in fighting infections. When HIV weakens the immune system, children become more susceptible to infections and other diseases.

- **Effects on the Body of a Child:** HIV can lead to various health issues in children, including recurrent infections, failure to thrive, and neurological complications. Without treatment, HIV can progress to Acquired Immunodeficiency Syndrome (AIDS), which is characterized by severe immune suppression and opportunistic infections.
- **Effects on the Mind and Development of a Child:** Children living with HIV may experience developmental delays, cognitive impairments, and behavioral problems due to the impact of the virus on the central nervous system. HIV-associated neurocognitive disorders (HAND) can affect memory, attention, and executive functioning, hindering a child's academic and social development.
- **Transmission to and from a Child:** HIV can be transmitted to a child through vertical transmission from an HIV-infected mother during pregnancy, childbirth, or breastfeeding. Horizontal transmission can occur through unprotected sexual contact, sharing contaminated needles or syringes, or exposure to infected blood or bodily fluids. However, with proper precautions and prevention methods, the risk of transmission can be significantly reduced.
- **Role of Antiretroviral Therapy (ART):** ART plays a crucial role in the management of HIV in children by suppressing viral replication, preserving immune function, and preventing disease progression. ART regimens typically consist of a combination of antiretroviral drugs, tailored to the child's age, weight, and HIV disease stage. With effective ART, children with HIV can lead healthy lives and reduce the risk of transmitting the virus to others.

Stigma

Stigma surrounding HIV/AIDS remains a significant barrier to care and support for children living with the virus in Pakistan.

- **Within Family:** Children living with HIV may face stigma and discrimination within their own families due to misconceptions about the disease, fear of transmission, and cultural taboos surrounding HIV/AIDS. Some family members may blame or isolate the child, leading to feelings of shame, guilt, and low self-esteem.
- **Within Neighborhood and Community:** Community attitudes towards HIV/AIDS can contribute to stigma and discrimination, leading to social exclusion, bullying, and marginalization of children living with HIV. Negative perceptions of HIV/AIDS may deter families from seeking healthcare services or disclosing their child's HIV status, further perpetuating stigma and discrimination.
- **School and Workplace:** Children living with HIV may encounter stigma and discrimination in school settings, including harassment from peers, exclusion from activities, and refusal of enrollment or participation. Similarly, parents or caregivers of children with HIV may face discrimination in the workplace, affecting their employment opportunities and economic stability.

Caring for Caregivers

- Caring for a child with HIV can be emotionally and physically demanding for caregivers, who may also face stigma and discrimination.
    - **Chronic Illness:** Caregivers of children with HIV often experience stress, anxiety, and depression related to managing their child's chronic illness, navigating the healthcare system, and coping with uncertainty about the future.
    - **Stigma:** Caregivers may face stigma and discrimination within their communities, leading to social isolation, rejection, and loss of social support networks.
    - **Daily Medications:** Managing a child's daily medications, medical appointments, and healthcare needs can be overwhelming for caregivers, especially in resource-limited settings with limited access to healthcare services and support networks.

Disclosure of HIV Status to Child

Disclosure of HIV status to a child is a complex and sensitive process that requires careful consideration of the child's age, cognitive development, and emotional readiness.

- **Birth-1 Year:** Disclosure is not typically recommended during the first year of life due to the child's limited understanding and cognitive development. However, caregivers should prioritize early initiation of ART and preventive measures to reduce the risk of disease progression and transmission.
- **1-3 Years:** Caregivers can begin introducing age-appropriate concepts of health, illness, and medication adherence through play, storytelling, and routine medical appointments. However, full disclosure of HIV status may not be necessary at this stage.
- **3-5 Years:** Children in this age group may have a basic understanding of illness and may ask questions about their health or medications. Caregivers can provide simple and honest explanations, emphasizing the importance of taking medications to stay healthy.
- **Older Children:** As children grow older and become more cognitively and emotionally mature, caregivers can gradually disclose their HIV status in a supportive and non-judgmental manner, providing accurate information, reassurance, and ongoing support.

Talking with Children about HIV

Open and honest communication about HIV is essential for empowering children with knowledge, reducing stigma, and promoting adherence to treatment.

- **Why Knowing is Good:** Knowing about HIV helps children understand their health condition, make informed decisions about their care, and protect themselves and others from HIV transmission. It also promotes resilience, self-esteem, and social connectedness.
- **How to Teach Children:** Caregivers can use age-appropriate language, visual aids, and interactive activities to teach children about HIV, emphasizing key concepts such as virus transmission, medication adherence, and stigma reduction.
- **Parental Fears about Disclosure:** Parents may fear that disclosing their child's HIV status will lead to rejection, discrimination, or emotional distress. However, withholding information can create feelings of secrecy, shame, and confusion for the child, affecting their trust in caregivers and their ability to cope with their diagnosis.

- **Physician Fears about Disclosure:** Healthcare providers may hesitate to discuss HIV with children due to concerns about emotional distress, parental reactions, or legal and ethical considerations. However, providing support and guidance to families can facilitate open communication and empower children to actively participate in their care.

Helping Children with Grief and Loss

Children living with HIV may experience grief and loss related to the death of a caregiver or family member due to HIV/AIDS-related complications.

- **Caregiver Death:** The death of a caregiver can have a profound impact on a child's emotional well-being, stability, and sense of security. Providing bereavement support, counseling, and psychosocial services can help children cope with their loss and adjust to changes in their caregiving arrangements.

Helping Dying Child

When a child is facing end-of-life care due to advanced HIV/AIDS-related complications, parental support and comfort care are essential for ensuring dignity, comfort, and quality of life.

- **Parental Support:** Parents should be supported to provide emotional support, physical care, and comfort measures for their child, including pain management, symptom control, and spiritual support.
- **Comfort Care:** Comfort care focuses on meeting the child's physical, emotional, and spiritual needs, prioritizing pain relief, symptom management, and psychosocial support to enhance the child's quality of life and promote a peaceful and dignified death.

Prevention of Mother-to-Child Transmission (PMTCT)

Preventing mother-to-child transmission of HIV is critical for reducing the burden of pediatric HIV/AIDS in Pakistan.

- **Antenatal Care:** Ensuring pregnant women living with HIV receive timely antenatal care, HIV testing, and ART initiation to reduce the risk of vertical transmission to their infants.
- **Intrapartum Care:** Providing access to safe delivery practices, including elective cesarean section and avoidance of breastfeeding, for HIV-positive women to further reduce the risk of vertical transmission during childbirth.
- **Postnatal Care:** Offering infant feeding counseling, early infant diagnosis, and access to pediatric ART for HIV-exposed infants to prevent mother-to-child transmission and ensure optimal health outcomes.

Community Support

Community support plays a vital role in addressing the needs of children living with HIV and their families, promoting acceptance, and reducing stigma and discrimination.

- **Peer Support Groups:** Establishing peer support groups for children and families affected by HIV/AIDS to provide emotional support, share experiences, and access practical resources and information.
- **Community Education:** Conducting community-based education and awareness campaigns to dispel myths and misconceptions about HIV/AIDS, promote acceptance, and encourage compassion and empathy towards children living with HIV.
- **Local Resources:** Identifying and strengthening local resources, such as community health centers, support networks, and advocacy groups, to provide comprehensive care, support services, and referrals for children and families affected by HIV/AIDS.

Conclusion:

Helping children in Pakistan live with HIV requires a holistic approach that addresses the physical, emotional, and social needs of children and families affected by the disease. By promoting awareness, reducing stigma, providing psychosocial support, and fostering community engagement, we can create a supportive environment that enables children living with HIV to thrive and lead fulfilling lives.

Chapter 12

Prevention of HIV

Prevention of Parent to Child Transmission of HIV (PPCT):

Since the Program's inception in 2006, PPTCT has been an offered service for Women with HIV. Its success has not been documented due to failure in quantifying HIV infection rate in infants where mother-baby pairs have received interventions. The strategy of elimination of vertical transmission of HIV is now in process of alignment with elimination of vertical transmission of syphilis and Hepatitis B (triple elimination). Triple elimination is now a 'Priority Area' (HIV Prioritized interventions) of the Global Fund and will include the following steps:

1. Integrated HIV testing and rapid ART initiation among pregnant and breastfeeding women including adolescents and key populations at facility and community delivery points
2. Treatment continuity and retention of mother-infant pairs throughout breastfeeding period.
3. Prevention of new HIV infections among pregnant and breastfeeding women.
4. Infant prophylaxis
5. Early infant diagnosis and follow-up HIV testing for infants through the breastfeeding period and linkage to pediatric HIV treatment
6. Integrated service delivery with Sexual Reproductive Health (SRH) and Maternal, Neonatal and Child Health (MNCH)

Prevention of Parent to Child Transmission of HIV: The Science

Time frames of risk of mother to child transmission of HIV:

During Pregnancy

- High maternal viral load (>1000) during pregnancy (whether maternal HIV status is known or unidentified) increases risk of pre-partum transmission to fetus
- Mother receiving ART duration < 4 weeks by time of delivery increases risk of pre-partum transmission to fetus

During Delivery

- High maternal viral load (>1000) at delivery (whether maternal HIV status is known or unidentified) increases risk of peri-partum transmission to baby
- Low but detectable maternal viral load (<1000) at delivery (whether maternal HIV status is known or unidentified) increases risk of peri-partum transmission to baby
- Mother receiving ART duration < 4 weeks by time of delivery increases risk of peri-partum transmission to baby
- Any of above AND Vaginal Delivery increase risk of peri-partum transmission to baby

During Postpartum Period

- breastfeeding with high or low viremia and no ART or non-compliance to ART increases risk of post-partum transmission of HIV to baby
- breastfeeding with zero viremia and maternal compliance to ART and infant prophylaxis decreases risk of post-partum transmission to <2% (not zero)

What makes WRA/Adolescent Female vulnerable to HIV in Pakistan

Modes of Transmission

- Parenteral Transmission
  - Unsafe blood transfusions
  - Unsterilized instrumentation or procedures
  - Unsafe injections

Sexual Transmission

  - Sexual partner/spouse is positive and/or highly viremic
  - Sexual partner/spouse at risk but not tested or have not disclosed HIV status
  - Multiple partners
  - Presence of mucosal ulceration or other STD in either partner

Sexual Practices

- Higher risk
  - Unprotected anal insertive
  - Unprotected vaginal receptive
- Infection risk documented
  - Unprotected anal insertive
  - Unprotected vaginal insertive (↑ during menses)
  - Unprotected oral receptive
  - Unprotected oral insertive

For a gentle reminder, each of the following risk factors have a risk of infection per encounter.

Table 43 Routes of Exposure to HIV in Female Adolescents and WRA

Infection Route	Risk of Infection
Sexual Transmission	
Female to male transmission	1 in 700 to 1 in 3000
Male to female transmission	1 in 200 to 1 in 2000
Male to male transmission	1 in 10 to 1 in 1600
Fellatio?	0 to 6%
Parenteral Transmission	
Transfusion of infected Blood	95 in 100
Needle-sharing	1 in 150
Needle-stick	1 in 300
Needle stick-AZT PEP	1 in 10000
Vertical Transmission	
Without ART mother	1 in 4

Prevention of Parent To Child Transmission: Service Delivery

The strategy is divided into 4 prongs (components) however service delivery of each is shared by more than 1 program (Table 12.2)

Table 44 Gamut of Services comprising comprehensive PPTCT and umbrella programs

Prong 1: Identify Women with HIV	Prong 2: Care for Pregnant Women with HIV	Prong 3: Care for Women with HIV after Pregnancy	Prong 4: Care for HIV-exposed Infant
MNCH	**NACP**	**MNCH/SRH/HIV**	**NACP**
Risk assessment during healthcare visits	Offer Risk-based testing Offer CHTC Provide ART during Pregnancy	ART for woman	Infant Prophylaxis and Feeding Counselling Breastfeeding (AFASS) vs Formula Feeding
Offer CHTC	Safe Delivery (CSEC vs VD)	Reproductive health care: Family planning and contraception counselling	Early Infant Diagnosis
Test and link to care	Breastfeeding (AFASS) vs Formula Feeding	Nutritional support	Vaccination

Prong 1: Identify Women with HIV	Prong 2: Care for Pregnant Women with HIV	Prong 3: Care for Women with HIV after Pregnancy	Prong 4: Care for HIV-exposed Infant
MNCH	**NACP**	**MNCH/SRH/HIV**	**NACP**
	Linkages to long-term treatment, care, support services are critical	Psychosocial and community support	Regular follow-up during first two years of life for monitoring of feeding, nutrition, growth and development

Prong 1: Identify Woman of Reproductive Age (WRA)

This precludes early identification (testing) of HIV in a woman of reproductive age (married or unmarried) and early initiation of ART so that viral load in woman is undetectable and she cannot transmit infection (Undetectable=Untransmissable). The gamut of services for this population are covered by **MNCH** Program where adolescent girls and women of reproductive age (WRA) (15-45 years) seek healthcare.

Caveat: 'Grey' Policy on Testing

There is no universal testing for HIV and Syphilis in antepartum care at present. The only universal testing in Pakistan's antenatal service is for HCV and HBV. Risk-based testing is recommended for HIV testing but the criteria are not validated and not widely known or understood by health providers dealing with this population.

Risk Factors based Testing Criteria recommended by our group:

TEST WOMAN OF REPRODUCTIVE AGE OR PREGNANT WOMAN FOR HIV IF ANY ONE OR MORE OF FOLLOWING:

- Occupation (healthcare worker with increased needlestick injury exposure, sex worker)
- Spouse working abroad or away from home/Spouse HIV+/Spouse intravenous drug user or other Key Population/ANY family member HIV+
- Coinfections: HCV/HBV/TB/STIs in last 5 years
- History of surgery minor or major, obstetric procedures, blood transfusions in last 5 years
- Stage 2-4 conditions (See Table 3.4)

Prong 2 Care for Pregnant Women Living with HIV (PWLHIV)

The gamut of services for this population is covered **by the HIV Program** where HIV+ adolescent girls and women of reproductive age (WRA) (15-45 years) seek healthcare. The services in this prong include:

- ART to pregnant women with HIV
- Safe Delivery to pregnant women testing positive

- Feeding Counselling for HIV-exposed baby
- Infant Prophylaxis Counselling for HIV-exposed baby

Prong 3: Care for Women with HIV after Pregnancy

Caveat: The g202amut of services for this population are covered by **SRH/MNCH** Program where adolescent girls and women of reproductive age (WRA) (15-45 years) seek FP/nutritional care. Psychological support is missing mostly across the country and social support is not channeled through MNCH/SRH/HIV Program.

In order to get a handle on comprehensive PPTCT service delivery information from all three relevant programs (HIV/SRH/MNCH) needs to be collated, interpreted and disseminated to relevant partners and UN Agencies.

- Family Planning Counselling to HIV-positive women after delivery
- Contraception Methods offered
- STI Screening and counselling
- Nutritional counselling
- Psychosocial support

Prong 4 Follow up of Infant with HIV Exposure

Components include:

- Infant Prophylaxis for HIV-exposed baby based on risk-stratification (Table
- Early Infant Diagnosis for HIV-exposed baby (Figure 2.3)
- Vaccinations for HIV-exposed baby
- Feeding, growth and development monitoring for HIV-exposed baby for first 2 years of life

Caveat: This prong comes under the gamut of **National and Provincial AIDS Control Program**. There is a universal failure to achieve the indicators in this component especially for the essential one (EID results at 6-12 weeks).

Infant Prophylaxis for HIV-exposed baby based on risk-stratification

Infants are at high risk of acquiring HIV from mothers when mothers have:

- Newly diagnosed HIV infection during pregnancy or breastfeeding with a prior negative test during pregnancy
- Newly diagnosed HIV infection identified for the first time during the postpartum period, with or without a negative HIV test prenatally
- If VL is not available, have received <4 weeks of ART at the time of delivery.
- If VL is available, have a VL>1000 copies/ml within four weeks before delivery.

Infants with a high risk of acquiring maternal HIV should undergo NAT testing as soon as possible and infant prophylaxis should be initiated:

- Triple drug 'Presumptive ARV Therapy' (AZT+3TC+NVP) at treatment doses

Triple drug presumptive ARV Therapy should be started for the first 6 weeks of life (whether HIV-exposed infant is breastfed, or formula fed). An effort should be made to get **NAAT or HIV PCR as soon as possible after birth** to determine HIV infection status at the earliest or at least till 6 weeks of life. If NAAT or PCR is positive, the baby should be shifted to an appropriate first line regimen (DTG-based). If negative and breastfeeding, the baby should continue on NVP alone or AZT + NVP in prophylactic doses for another 6 weeks.

- 'Dual therapy' (AZT and NVP) in prophylactic doses

Dual therapy can also be started for the first 6 weeks of life (whether **the** HIV-exposed infant is breastfed, or formula fed). An effort should be made to get NAAT or HIV PCR as soon as possible after birth to determine HIV infection status at the earliest or at least till 6 weeks of life. If NAAT or PCR is positive, the baby should be shifted to an appropriate first-line regimen (DTG-based). If negative and breastfeeding, the baby should continue on NVP **alone,** or dual therapy **should continue** for another 6 weeks.

Other Regimens for HIV-exposed infants with **a** 'high' risk of acquiring maternal HIV infection

- AZT for 6 weeks with 3 intermittent doses of NVP (day0, day1, day6)

This regimen has been used in research settings.

- 'Single therapy' (AZT or NVP) in prophylactic doses

This regimen can be used for 6 weeks in a non-breastfed baby and up to 12 weeks in a breastfed baby provided earnest effort is made to get NAAT or HIV PCR as soon as possible after birth to determine HIV infection status at the earliest.

No randomized controlled trials have compared the safety and efficacy of these three regimens and despite the potential of drug toxicity, triple therapy is preferred where the risk of transmission is high. The emphasis should be on getting a baseline HIV Viral load in these infants as soon as possible after birth to determine HIV infection status at the earliest.

A second confirmatory NAT should follow an initial positive NAT. The goal of the new recommendation is to optimize infant prophylaxis and further reduce rates of peripartum and breast milk transmission, especially for infants whose mothers have not benefited from optimal care.

The availability of dispersible AZT/3TC/NVP (FDC) tablets can greatly facilitate the uptake of this recommendation and should be given in treatment doses

Infants at standard (low) risk of acquiring HIV infection from mothers have mothers who have:

- Been on ART>4 weeks before delivery.
- Have VL<1000 copies/ml within 4 weeks of delivery.

Infants with a standard risk of acquiring maternal HIV do not need to undergo NAT at birth. They should be initiated on 6 weeks of once-daily NVP or twice daily AZT whether breastfed or formula-fed and undergo NAT at 6 weeks.

The availability of dispersible NVP tablets and dispersible AZT tablets can greatly facilitate uptake of this recommendation and should be given in prophylactic doses (See Table 12.3: Postnatal Prophylaxis for HIV-exposed infants 0-6 weeks and 6-12 weeks) and Table 4.13. Dosing chart for ART for infants, children and adolescents with HIV (including ART Presumptive Therapy)

Sustainable Development Goals (SDG) for HIV and AIDS viz a viz Pakistan (EMRO) and India (Southeast Asia):

Table 45 SDG targets viz a viz Pakistan

Indicators	Global target	Pakistan
Aware of status	90%	17%
On treatment	90%	61%
Virally suppressed	90%	?
Pregnant women with HIV with access to ART	90%	23%
HIV infection rates in HIV-exposed infants (vertical transmission rates)	90%	?

Post Exposure Prophylaxis (PEP):

When there is a risk of HIV transmission (needle prick, sexual assault), post-exposure prophylaxis should be initiated as soon as possible, within hours, and no later than 72 hours following the potential exposure.

Eligibility for PEP:

Children and adolescents are eligible for PEP if:

- exposure occurred within the past 72 hours; and
- the potentially exposed individual is not infected or not known to be infected with HIV; and
- mucous membrane or non-intact skin was significantly exposed to a potentially infectious body fluid; and
- the source is HIV-infected or the HIV status is unknown

Counselling for PEP:

Counseling for individuals exposed to HIV should include information on post-exposure prophylaxis (PEP) adherence, potential side effects, and transmission risks. This counseling should begin immediately after exposure and include guidance on preventive measures until an HIV test at 28 days and again at six months confirms a negative result. Emotional and mental health support is

crucial, especially for those sexually assaulted. Informed consent should be obtained after providing comprehensive PEP information

Informed consent:

When seeking informed consent for HIV post-exposure prophylaxis (PEP), it's crucial to ensure that the caretakers of the exposed child or the child (if older than 10 years) fully understands several key points. They need to be aware of the specific risk of acquiring HIV from their exposure and the known and unknown efficacy of PEP. The importance of taking an HIV test and receiving post-test counseling is emphasized, even if testing is delayed. If the person has not yet been tested, the possibility of already being infected must be assessed.

Individuals diagnosed with HIV should be referred to a clinic, and any PEP medication should be discontinued. For those with discordant rapid HIV test results, PEP should be offered while waiting for confirmatory testing. PEP will be stopped if an initial HIV test is positive, as the medication is ineffective for those already living with HIV and could lead to drug resistance.

The importance of adhering to the four-week PEP course, understanding potential side effects, and knowing that stopping PEP early reduces its effectiveness is stressed.

Prescribing and dispensing post-exposure prophylaxis medicine:

Stat investigations: HIV Ab testing as soon as possible (preferably before initiation of PEP)

Standard regimen contain three ART (DLT) for 28 days with HIV Ab testing at 6 weeks and 3-6 months after exposure. The HCV Ab and HBsAg tests should also be done at 6 weeks and at 3-6 months.

Negative indications:

Post-exposure prophylaxis is not indicated if:

- The exposed person is HIV-positive from a previous exposure.
- The exposed person has chronic exposure.
- If the exposure does not pose a risk of transmission, that is, after:
    - exposure of intact skin to potentially infectious body fluids
    - sexual intercourse using a condom that remains intact
    - any exposure to non-infectious body fluids (such as faeces, saliva, urine and sweat)
    - exposure to body fluids from a person known to be HIV-negative, unless this person is identified as being at high risk for recent infection and thus likely to be within the window period
    - if the exposure occurred more than 72 hours previously

Program Deliverables for PPTCT:

The Program provides the indicators below to the Global Fund for AIDS, Tuberculosis and Malaria (GFATM).

Physicians compiling center reports have to be mindful of their centers data collection and how the data reflets center performance and patient care quality.

Table 46 Program Indicators reflecting PPTCT Service Delivery

No	Indicator definition	Outcome Indicator catching the PMTCT Cascade
1	Identified HIV+ pregnant women	a. Total number of pregnant WLHIV ever registered in PPTCT clinic till end of the current month.
		b. Total number of pregnant WLHIV registered in PPTCT clinic in current month.
2	ARVs: perinatal transmission Definition: Mum started on ARV soon as diagnosed and continued through pregnancy, labour and delivery (>90%)	Total number of pregnant WLHIV registered in PPTCT clinic and initiated on ART during pregnancy and/or Labour and/or delivery during current month.
3	ARVs: postnatal Transmission Definition: baby started on ARV within 3 days of life for minimum 6 weeks (should be >90%)	Total number of babies born during current month to HIV positive pregnant women registered in PPTCT clinic (ie. HIV-exposed babies) who were registered for infant prophylaxis within 3 days of life for a minimum of 6 weeks
4	Early Infant Diagnosis Testing Definition: testing of HIV status of baby through DNA Xpert (PREFERRED) or RNA VL within 2 months of birth (should be >90%)	Total number of babies born to HIV positive pregnant women registered in PPTCT clinic and, received infant prophylaxis and, got tested for HIV (DNA Xpert or RNA VL) within 2 months of birth (EARLY INFANT DIAGNOSIS) in this current month
5	Early Infant Diagnosis Results Definition: HIV infection rate in HIV-exposed baby where mother-baby received PMTCT (should be <2%)	Total number of babies born HIV positive pregnant women registered in PPTCT clinic and, received infant prophylaxis and, got tested for HIV (DNA Xpert or RNA VL) within 2 months of birth (EARLY INFANT DIAGNOSIS) in this current month and tested POSITIVE

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Post-Exposure Prophylaxis to prevent HIV infection (Joint WHO/ILO guidelines on PEP to prevent HIV infection 2007

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Chapter 13

Implementing Infection Prevention and Control in Healthcare settings in Pakistan

Why do we need 'effective' Infection prevention and control (IPC) in healthcare settings in Pakistan?

Infection Prevention and Control (IPC) is not just a practical necessity—it's a critical, evidence-based approach that saves lives by preventing patients and healthcare workers from falling victim to avoidable infections. The consequences of inadequate IPC are dire; it can lead to severe harm and even death. Without robust IPC measures, achieving high-quality healthcare is impossible.

IPC touches every aspect of healthcare—from hand hygiene and surgical site infections to injection safety and combating antimicrobial resistance. It dictates how hospitals function, both in routine care and during emergencies. This is especially vital in low- and middle-income countries, where the burden of secondary infections can severely compromise healthcare delivery and medical hygiene standards.

Pakistan is a stark example of the consequences of poor IPC. The country has one of the highest rates of unsafe transfusions and injection practices, leading to widespread transmission of HCV, HBV, and multiple HIV outbreaks. These outbreaks, including at least ten instances where HIV spread from key populations to the general population due to inadequate IPC practices, underline the urgent need for improvement (see Fig). Moreover, only a handful of healthcare facilities in Pakistan report on healthcare-associated infections (HAIs) and antimicrobial resistance (AMR) rates, leaving critical gaps in monitoring and response.

For instance, a case-control study on the 2019 HIV outbreak in Larkana identified healthcare facility exposure as a significant risk factor for acquiring HIV. This highlights the catastrophic impact that defective IPC can have on public health. Strengthening IPC is not optional; it is essential for safeguarding lives and ensuring that healthcare systems, especially in Pakistan, can deliver the safe, quality care that every patient deserves.

What are its core components? What the Minimum requirements for each core component?

An effective Infection Prevention and Control (IPC) program is built on eight core components, each crucial for safeguarding patient and staff health in healthcare settings.

1. **IPC Programmes**: Establishing a robust IPC program is the foundation. It involves setting up a dedicated team to oversee and implement infection control measures across the facility.

Minimum Req: Functional IPC program should have one full-time focal point trained in IPC and a dedicated budget for IPC strategies

2. **IPC Guidelines**: These are essential for standardizing procedures and ensuring that best practices in infection prevention are consistently followed.

3. **Minimum Req**: Evidence based guidelines adapted to local context and reviewed every 5 years eg. SOPs for hand hygiene, decontamination of medical devices and patient care equipment, environmental cleaning, healthcare waste management, injection safety, HCW protection, aseptic techniques for invasive procedures, triage of infectious patients, basic principles of standard and transmission-based precautions including routine monitoring of the implementation of at least some of the IPC SOPs.

4. **IPC Education and Training**: Continuous education and training for healthcare workers are critical to keep them informed about the latest IPC practices and ensure they are equipped to implement these effectively.

Minimum Req: All HCWs should be trained in IPC (in-house training) (frontline clinical staff and cleaners)

5. **Healthcare-Associated Infection Surveillance**: Monitoring infections acquired within the healthcare setting allows for early detection, response, and prevention of outbreaks.

Minimum Req: A multi-disciplinary technical group for HAI surveillance should monitor HAIs according to national or healthcare facility priority including AMR data using resources such as dependable laboratories, medical records, trained staff

6. **Multimodal Strategies**: Implementing a combination of interventions, such as improving hand hygiene, safe injections, antimicrobial stewardship, decontamination of medical instruments, devices and environmental cleaning helps to enhance the effectiveness of IPC measures.

Minimum Req: Choose local priorities **eg.** Reduction of specific infections such as Surgical site infections or catheter associated infections; and implement interventions to improve each on **eof** standard and transmission-based precautions.

7. **Monitoring, Audit, and Feedback**: Regular monitoring and auditing of IPC practices, coupled with timely feedback, ensure that standards are maintained and improvements are made where necessary.

Minimum Req: The multi-disciplinary technical group should develop recommendations for minimum **indicatros** such as hand hygiene (collection of data, analysis, development of protocols, provision of training)

8. **Workload, Staffing, and Bed Occupancy**: Proper management of workload, adequate staffing, and controlled bed occupancy are vital to preventing the spread of infections and ensuring a safe healthcare environment.

Minimum Req: Develop a system for reducing overcrowding (through triage and referral), optimizing staffing levels (develop national norms on patient/staff ratio), standardizing bed occupancy (one person per bed, spacing of at least one metre between beds etc)

9. **Built Environment, Materials, and Equipment**: The design and maintenance of the facility, along with the availability of appropriate materials and equipment, are crucial for supporting effective infection control practices at the facility level.

Minimum Req: This includes Water (to perform IPC measures), hand hygiene materials like alcohol based hand rub and soap and single use towels, minimum of two functional improved sanitation facilities (one for patients, one for staff), sufficient labelled bins for healthcare waste segregation, waste treatment and disposal via autoclaving and incineration or burial, natural ventilation in premises, space for triage and segregation, IPC materials (mops, detergents, disinfectants, PPE, power/fuel).

These components work together to create a comprehensive approach to infection prevention and control, reducing the risk of healthcare-associated infections and improving overall patient safety.

What do standard and transmission-based precautions entail?

Implementation of Standard Precautions for Patient Care include the following:

- Hand hygiene
- Use of Personal Protective Equipment (PPE) when there is an expectation of possible exposure to infectious material
- Follow respiratory hygiene/cough etiquette principles
- Ensure appropriate patient placement
- Properly handle, clean and disinfect patient care equipment and instruments/devices
- Handle textiles and laundry carefully
- Follow safe injection practices

Implementation of Transmission-Based Precautions for Patient Care include the following:

Contact Precautions: Use contact precautions for patients with known or suspected infections that represent increased risk for contact transmission

Droplet Precautions: Use droplet precautions for patients known or suspected to be infected with pathogens transmitted by respiratory droplets that are generated by a patient who is coughing, sneezing or talking

Airborne Precautions: Use airborne precautions for patients known or suspected to be infected with pathogens transmitted by the airborne route (eg TB, measles, chickenpox, disseminated herpes zoster)

What is 'Safe Injection'?

A safe injection does not harm the recipient or expose the healthcare provider to avoidable risks. Healthcare providers should never reuse a needle or syringe on more than one patient. Providers must discard both needles and syringes once used. Reusing the needle and/or syringe is unsafe and can spread disease

What is a Blood Transfusion Safety?

Safe blood transfusion is vital for treating various health conditions, including anemia, pregnancy complications, trauma, and genetic disorders. Despite 120 million annual donations, global shortages persist, with low-income countries receiving up to seven times fewer donations than high-income ones. Regular donations are essential due to the limited storage life of blood. Haemovigilance, a comprehensive system of procedures, ensures the safety and effectiveness of the entire blood transfusion process, from collection to use in healthcare settings. This is lacking in Pakistan because of an unregulated private sector.

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CDC 2023

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