PEDIATRIC HUMAN IMMUNODEFICIENCY VIRUS
DISEASE BURDEN

• There were 3.2 million children living with HIV around the world with 90% residing in sub-Saharan Africa.

• Globally, between 2002 and 2013, there was a 58% reduction in the number of new HIV infections among children.

• More than 240,000 children were infected with HIV during 2013.

• Only 24% of children who needed antiretroviral treatment (ART) received it.

• 190,000 children died of AIDS-related illnesses.
INDIA

• India has the third largest HIV epidemic in the world.
• National adult (15–49 years) HIV prevalence is estimated at 0.26% (0.22%–0.32%) in 2015.
• In 2015, adult HIV prevalence is estimated at 0.30% among males and at 0.22% among females.
• The total number of people living with HIV (PLHIV) is estimated at 21.17 lakhs in 2015 compared with 22.26 lakhs in 2007.
• Children account for 6.54%, while two fifth (40.5%) of total HIV infections are among females.
India is estimated to have around 86 (56–129) thousand new HIV infections in 2015 showing 66% decline in new infections from 2000 and 32% decline from 2007.

- Children accounted for 12% of total new infections.
- Since 2007, when the number of AIDS related deaths (ARD) started to show a declining trend, the annual number of AIDS related deaths has declined by 54%.
DISTRIBUTION OF PEOPLE LIVING WITH HIV IN INDIA

- AP & Telangana: 18%
- Maharashtra: 14%
- Karnataka: 9%
- Gujarat: 8%
- Bihar: 7%
- Uttar Pradesh: 7%
- Tamil Nadu: 7%
- West Bengal: 6%
- Rajasthan: 5%
- Madhya Pradesh: 2%
- Others: 14%
- Odisha: 3%
ETIOLOGY

- Caused by HIV 1 and HIV 2 – belong to Retroviridae.
- Single stranded RNA
- HIV 1 genome
  - GAG- viral core proteins like p24
  - POL- viral enzymes like reverse transcriptase
  - ENV- envelope proteins gp120 and gp41
MODES OF TRANSMISSION IN CHILDREN

- Vertical
  - can occur during intrauterine, intrapartum (most common) or through breast feeding.
  - Rate of transmission from mother to child varies from 12% to 30% with figures as high as 50% reported from Africa.

- Blood Products - 3-6%
MODES OF TRANSMISSION IN CHILDREN

• Other routes
  - Sexual abuse
  - Sharps
  - MSM
  - Unsafe needles
  - IVDU
  - Unknown
PATHOGENESIS

- Attachment to CD4 receptor
- Binding to coreceptor CCR5 or CXCR4
- Fusion inhibitors
- Fusion
- Reverse transcriptase inhibitors
- Reverse transcription of viral RNA genome
- Double-stranded DNA
- Genomic RNA
- Reverse transcription
- Integrase inhibitors
- Proviral RNA
- Integration
- Cell nucleus
- Transcription
- Viral mRNA
- Protease inhibitors
- Cleavage of polypeptides and assembly
- Viral proteins
- Translation
- Maturation
- Viral release
CLINICAL PATTERNS

• Three clinical patterns of HIV disease have been described in children (prior to HAART).
  – Rapid progressors (15-25%)
    • Symptomatic within first year.
  – Short term progressors (60-80%)
    • Symptomatic within 6-7 years.
  – Long term progressors (<5%)
    • Symptomatic within 8-10 years.
• Clinical manifestations of HIV infection vary widely among infants, children and adolescents.
CLINICAL FEATURES CONT.

Important manifestations occurring in infancy and childhood include:

• lymphadenopathy,
• hepatosplenomegaly,
• failure to thrive,
• chronic or recurrent
• diarrhea,
• recurrent pneumonia,
• oral thrush,
CLINICAL FEATURES CONT.

- Recurrent otitis media,
- Tuberculosis (TB),
- PCP,
- Pyrexia of unknown origin, etc.
- Recurrent bacterial infections,
- Chronic parotid swelling,
- Lymphoid interstitial pneumonitis (LIP) and
- Early onset progressive neurologic deterioration are manifestations seen more commonly in children as compared to adults.
## WHO CLINICAL STAGING OF HIV

<table>
<thead>
<tr>
<th>HIV-associated symptoms</th>
<th>WHO clinical stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>1</td>
</tr>
<tr>
<td>Mild symptoms</td>
<td>2</td>
</tr>
<tr>
<td>Advanced symptoms</td>
<td>3</td>
</tr>
<tr>
<td>Severe symptoms</td>
<td>4</td>
</tr>
</tbody>
</table>
### Clinical stage 1
- Asymptomatic
- Persistent generalized lymphadenopathy

### Clinical stage 2
- Unexplained persistent hepatosplenomegaly
- Papular pruritic eruptions
- Fungal nail infection
- Angular cheilitis
- Lineal gingival erythema
- Extensive wart virus infection
- Extensive molluscum contagiosum
- Recurrent oral ulcerations
- Unexplained persistent parotid enlargement
- Herpes zoster
- Recurrent or chronic upper respiratory tract infections
  - (otitis media, otorrhoea, sinusitis or tonsillitis)
### Clinical stage 3

Unexplained moderate malnutrition or wasting not adequately responding to standard therapy
Unexplained persistent diarrhoea (14 days or more)
Unexplained persistent fever (above 37.5°C intermittent or constant, for longer than one month)
Persistent oral candidiasis (after first 6–8 weeks of life)
Oral hairy leukoplakia
Acute necrotizing ulcerative gingivitis or periodontitis
Lymph node tuberculosis
Pulmonary tuberculosis
Severe recurrent bacterial pneumonia
Symptomatic lymphoid interstitial pneumonitis
Chronic HIV-associated lung disease including brochiectasis
Unexplained anaemia (<8 g/dl), neutropaenia (<0.5 × 10⁹ per litre)
and or chronic thrombocytopenia (<50 × 10⁹ per litre)
### Clinical stage 4

- Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy
- Pneumocystis pneumonia
- Recurrent severe bacterial infections (such as empyema, pyomyositis, bone or joint infection or meningitis but excluding pneumonia)
- Chronic herpes simplex infection (orolabial or cutaneous of more than one month's duration or visceral at any site)
- Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
- Extrapulmonary tuberculosis
- Kaposi sarcoma
- Cytomegalovirus infection: retinitis or cytomegalovirus infection affecting another organ, with onset at age older than one month
- Central nervous system toxoplasmosis (after one month of life)
- Extrapulmonary cryptococcosis (including meningitis)
- HIV encephalopathy
- Disseminated endemic mycosis (coccidiomycosis or histoplasmosis)
- Disseminated non-tuberculous mycobacterial infection
- Chronic cryptosporidiosis (with diarrhoea)
- Chronic isosporiasis
- Cerebral or B-cell non-Hodgkin lymphoma
- Progressive multifocal leukoencephalopathy
- Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy
# IMMUNE CLASSIFICATION

<table>
<thead>
<tr>
<th>HIV-associated immunodeficiency</th>
<th>&lt;11 months (%CD4+)</th>
<th>12–35 months (%CD4+)</th>
<th>36–59 months (%CD4+)</th>
<th>&gt;5 years (absolute number per mm$^3$ or %CD4+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None or not significant</td>
<td>&gt;35</td>
<td>&gt;30</td>
<td>&gt;25</td>
<td>&gt; 500</td>
</tr>
<tr>
<td>Advanced</td>
<td>25–29</td>
<td>20–24</td>
<td>15–19</td>
<td>200–349</td>
</tr>
<tr>
<td>Severe</td>
<td>&lt;25</td>
<td>&lt;20</td>
<td>&lt;15</td>
<td>&lt;200 or &lt;15%</td>
</tr>
</tbody>
</table>
HIV – NON SPECIFIC MANIFESTATIONS

• PUO > 1 mo
• Weight loss > 10% in 6 mo
• Diarrhea > 1 mo (10-50%)
• Failure to thrive & Growth retardation (~ 90%)
• Hepato/Spleno megaly
• Generalized Lymphadenopathy
OPPORTUNISTIC INFECTIONS

• Bacterial: Mycobacterial – M. TB, MAI
  Rec. severe pyogenic infections
• Viral:  OI - CMV, Herpes, EBV
  Measles, Varicella, Molluscum
• Fungal:  Candidiasis, C. Neoformans etc.
• Protozoal:  PCP, Toxo., Cryptosporidium
• 30-50% of AIDS patients present with OI
• Recurrent infections – rapid progression of disease
RECURRENT BACTERIAL INFECTIONS

About 20% of AIDS defining illnesses.

• Recurrent, severe, systemic, non responsive
• Mainly capsular organisms

• Poor antibody response in spite of IgG levels
• Internal organ infections/abscess
  - Sepsis                - Septic Arthritis   - Pneumonitis
  - Pyo. Meningitis     - Organ abscesses
  - SSTIs

≥ 2 episodes of invasive infections in 2 years
• Candidiasis:
  – Candidiasis is the most common fungal infection in HIV-infected children.
  – Oral nystatin suspension or clotrimazole can be used for treatment.

• Tuberculosis (TB)
  – All forms of tuberculosis are seen in HIV-infected children including pulmonary, lymph node and extrapulmonary tuberculosis
PNEUMOCYSTIS CARINII (JIROVECI)
PNEUMONIA (PCP):

• This is the most common OI in infants.
• The highest occurrence is at age of 3–6 months.
• The infant presents with acute onset fever, dyspnoea, tachypnea, cough, cyanosis and marked hypoxia.
PNEUMOCYSTIS CARINII (JIROVECI) PNEUMONIA (PCP):

• Investigations: X ray Chest, PFT, Gallium Scan,
• The radiographic findings include interstitial infiltrates or diffuse alveolar disease (which progresses rapidly).
• GM stain sensitivity: Sputum (30%) BAL (60-90%) Biopsy (97%)
• Treatment is with intravenous cotrimoxazole.
PCP PNEUMONIA

PCP GM S⁻
SOME OTHER OI S
RESPIRATORY TRACT

• Lymphoid Interstitial Pneumonia (LIP):

  - Prevalence 40-50%, less common in adults
  - Commonly seen in vertically infected children
  - Older child, insidious onset of dry cough, progressive dyspnea, clubbing
  - ? HIV RNA ? EBV induced
  - Investigations: X ray Chest, Lung biopsy
  - Prognosis: Median survival 60-70 mo after diagnosis
CENTRAL NERVOUS SYSTEM (CNS)

• HIV is a neurotropic virus and can cause primary CNS involvement.
• Neurological manifestations can be caused by the HIV itself, OIs, tumors or drugs.
• Presentation may be -development delay in an infant, poor scholastic performance
• HIV encephalopathy needs early initiation of treatment with highly active anti-retroviral therapy (HAART).
GASTROINTESTINAL AND HEPATIC MANIFESTATIONS

• Candidiasis, periodontal disease, salivary gland disease, oral hairy leukoplakia and oral ulcerations can occur.

• Chronic or recurrent diarrhea with malabsorption, abdominal pain, dysphagia, and failure to thrive are common symptoms of gastrointestinal disease.

• HIV or AIDS enteropathy is the syndrome of malabsorption with partial villous atrophy caused by HIV infection to gut.

• Hepatomegaly is common.

• Fluctuating serum levels of transaminases with or without cholestasis is common.
• The reasons for cardiac involvement can be HIV itself, intercurrent infections, immune-mediated reactions and adverse effects of drug therapy (zidovudine).

• Usually the cardiac involvement is clinically silent.

• Dilated cardiomyopathy, left ventricular hypertrophy, pulmonary hypertension and congestive cardiac failure can occur.
RENAL DISEASE

• Nephropathy is an unusual presenting symptom of HIV infection.
• Focal glomerulosclerosis (80%) progressing to renal failure in 6–9 months, mesangial hyperplasia (10–15%), segmental necrotizing glomerulonephritis and minimal change disease may be seen.
• Nephrotic syndrome is the most common manifestation of paediatric renal HIV disease.
DERMATOLOGICAL DISORDERS

• Cutaneous manifestations are inflammatory or infectious disorders which are not necessarily unique

• Seborrheic dermatitis, severe eczema, recurrent or chronic episodes of HSV, herpes zoster, molluscum contagiosum, anogenital warts, candidial infections, tinea, onychomycosis, impetigo and scabies are common.
HEMATOLOGIC DISORDERS

- Anaemia is frequent (20–70%) and caused due to various reasons.
- Leukopenia occurs in almost one-third of untreated cases (and neutropenia often occurs).
- Thrombocytopenia may occur in up to 20% of patients.
- Patients are predisposed for thrombosis due to:
  - hyperviscosity (due to hypergammaglobulinemia)
  - protein C and protein S deficiency
MALIGNANCIES & OTHER ORGAN INVOLVEMENT

• Malignancies:
  – As compared to adults, malignant diseases are uncommon in children. Non-Hodgkin lymphoma and primary CNS lymphoma are known to occur.
  – Epstein-Barr virus is associated with most lymphomas. Kaposi sarcoma (caused by human herpesvirus 8) is very rare in HIV-infected children.

Other organ involvement:
  HIV-arthropathy, myopathy, rheumatologic, endocrine and metabolic disorders may also be seen.
HIV DIAGNOSIS UNDER 18 MONTHS

Non-breast feeding infant

Virological testing at 6 weeks

+ve test

Repeat +ve test

HIV Infected

-ve test

Not HIV Infected

Breast-feeding infant

Virological testing at 6 weeks

+ve test

Repeat +ve test

HIV Infected

-ve test

Repeat virological test if infant becomes symptomatic

Not HIV Infected

Retest 6-8 wks after stopping Breast-feeding

+ve test

Not HIV Infected

-ve test
HIV DIAGNOSIS OVER 18 MONTHS

Breast-feeding child

HIV antibody test

Confirmed +ve test

Refer for Rx, care & support

Confirmed -ve test

HIV antibody test

-ve test

Not HIV Infected

Retest 6-8 wks after stopping breast-feeding

Non-breast feeding child

HIV antibody test

Confirmed +ve test

HIV Infected

Refer for Rx, care & support

-ve test

Not HIV Infected

Confirmed +ve test

HIV Infected

Refer for Rx, care & support

-ve test

Not HIV Infected
MANAGEMENT OF HIV

• High index of suspicion & timely diagnosis
• Growth monitoring & Nutritional advise
• Breast feeding vs. Replacement feeding
• Psycho-social support
• Immunization
• Management of OI’s & prophylaxis
• Anti-retro viral therapy
• Prevention including PMTCT
HIV TREATMENT - IMMUNISATION

• Asymptomatic HIV - Give all vaccines
• Symptom. HIV - ? Live vaccines avoided
• BCG must in our country
• OPV safe - IPV if available
• All killed/subunit vaccines - Safe
• Monitor seroresponse - Additional doses
• Passive prophylaxis - VZIZ/Measles Ig
ARVT AIMS

- Immune preservation
- Slower disease progression
- Lesser infections
- Better physical growth
- Better neurodevelopment
- Prolong the life
- Improved quality of life
  - ? Cure in future
TYPES OF ANTIRETROVIRAL AGENTS

1. Nucleoside reverse transcriptase inhibitor
   • Zidovudine
   • Didanosine
   • Stavudine
   • Zalcitabine
   • Lamivudine
   • Abacavir

2. Non nucleoside reverse transcriptase inhibitor
   • Nevirapine
   • Delavirdine
   • Efavirenz

3. Protease inhibitor
   • Saquinavir
   • Indinavir
   • Ritonavir
   • Nelfinavir
   • Amprenavir
   • Lopinavir

4. Newer drugs
   • Fusion inhibitor
MECHANISM OF ACTION

• Nucleoside reverse transcriptase inhibitor
  • Blocks the reverse transcriptase enzyme

• Non nucleoside reverse transcriptase inhibitor
  • Blocks RT activity by binding adjacent to the enzymes active site

• Protease inhibitor
  • Blocks HIV protease resulting in formation of immature, non infectious virion
NEWER ANTIRETROVIRALS

• Fusion Inhibitor
  • T 20
  • Inhibits the fusion of HIV virion to the lymphocyte membrane
  • Not available orally
  • To be given either SC or IV twice daily
### RECOMMENDATIONS FOR INITIATING ART IN INFANTS AND CHILDREN

<table>
<thead>
<tr>
<th>WHO Paediatric Stage</th>
<th>Availability of CD4 cell measurements</th>
<th>Age-specific treatment recommendation</th>
<th>&lt;12 months</th>
<th>≥12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>CD4</td>
<td>Treat all</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No CD4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>CD4</td>
<td>Treat all</td>
<td></td>
<td>Treat all, CD4 guided in those children with TB, LIP, OHL, thrombocytopenia</td>
</tr>
<tr>
<td></td>
<td>No CD4</td>
<td></td>
<td></td>
<td>Treat all</td>
</tr>
<tr>
<td>2</td>
<td>CD4</td>
<td>CD4-guided</td>
<td></td>
<td>Do not treat</td>
</tr>
<tr>
<td></td>
<td>No CD4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>CD4</td>
<td>CD4-guided</td>
<td></td>
<td>Do not treat</td>
</tr>
<tr>
<td></td>
<td>No CD4</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
RECOMMENDED FIRST LINE THERAPY

• Regimen of 2 NRTI plus 1 NNRTI
  – AZT + 3TC + NVP/ EFV
  – d4T + 3TC + NVP/ EFV
  – ABC* + 3TC + NVP/ EFV

• ABC presently not available through the national program
• Never use AZT and d4T together
• AZT – 1st choice in non-anemic children (Hb > 9 gm%)
• d4T – 1st choice in those who are anemic

[EFV – HIV and TB]
[Not recommended]
- < 3 yrs
- Adolescent girls
ARVT MONITORING

• Clinical follow up
• CD 4 count & Viral load
• Baseline, at 6 wk., 18-24 wk., and then every 3-6 mo., SOS as required
• In vitro drug sensitivity

Abn. results to be confirmed after 1 wk
Don’t test within 1 wk. of any infection
# Using the WHO Clinical Staging System for Treatment Failure

<table>
<thead>
<tr>
<th>WHO Clinical Stage on ART</th>
<th>Management options</th>
</tr>
</thead>
</table>
| **T 1**                   | ▪ Do not switch to other regimen  
                             ▪ Maintain scheduled follow up visits |
| **T 2**                   | ▪ Treat and manage staging event  
                             ▪ Do not switch to other regimen  
                             ▪ Assess and offer adherence support  
                             ▪ Assess nutritional status and offer support  
                             ▪ Schedule earlier visit for clinical review |
| **T 3**                   | ▪ Treat and manage staging event and monitor response  
                             ▪ Check if on treatment 24 weeks or more  
                             ▪ Assess and offer adherence support  
                             ▪ Assess nutritional status and offer support  
                             ▪ Check CD4 - where available  
                             ▪ **Consider switching regimen**  
                             ▪ Institute more frequent follow up |
| **T 4**                   | Assess and offer adherence support  
                             ▪ Assess nutritional status and offer support  
                             ▪ Document CD4 - where available  
                             ▪ **Switch regimen** |
## DECISION-MAKING REGARDING SWITCHING TO SECOND LINE THERAPY

<table>
<thead>
<tr>
<th>WHO Paediatric Clinical Stage on ART</th>
<th>Availability of CD4 measurements</th>
<th>Management options</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 and T2</td>
<td>No CD4</td>
<td>Do not switch regimen</td>
</tr>
<tr>
<td></td>
<td>CD4</td>
<td>▪ Consider switching regimen only if 2 or more values below age-related threshold for severe immunodeficiency are available/declining values?</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▪ Increase clinical and CD4 follow up if CD4 approaches age-related threshold for severe immunodeficiency</td>
</tr>
<tr>
<td>T3</td>
<td>No CD4</td>
<td>▪ Consider switching regimen</td>
</tr>
<tr>
<td></td>
<td>CD4</td>
<td>▪ Switching regimen is recommended if CD4 at or below age-related threshold for severe immunodeficiency and particularly if child initially had good immune response to ART</td>
</tr>
<tr>
<td>T4</td>
<td>No CD4</td>
<td>▪ Switch regimen, regardless of CD4</td>
</tr>
<tr>
<td></td>
<td>CD4</td>
<td></td>
</tr>
</tbody>
</table>
ARVT DRUG INTERACTIONS

- NRTI: Antifungals, Aminoglycosides, Antacids (except ddI)
- AZT: TMP/SMX, Acyclovir
- ddC: IV Pentamidine
- ddI: Tetracyclines, Quinolones
- NNRTI & PI: Analgesics, Antihistaminic, Cizapride, Sedatives, Hypnotics, Rifampicin, Anticonvulsants
ARVT LONG TERM SIDE EFFECTS

- Altered Blood Sugar – Diabetes Mellitus
- Raised S. Lipid levels
- Abnormal Body fat distribution
- Nephrocalcinosis
- Spontaneous bleeding in Hemophiliacs
- Hepatic damage
- Bone and joint effects
HIV - PREVENTION

- ‘No sex’ is the safest sex!
- Safe blood & blood products
- Disinfection - Bleach, heat
- Universal precautions
  - Gloves, protective measures, Hand washing
  - Disposal of disposables
  - Avoid mouth to mouth methods
- Post Exposure Prophylaxis
- HIV vaccine
- Prevention of PTCT
Five Phases of PMTCT

Phase alpha: Prevent
- Life skills
- STIs
- FP

Phase 1: Inform
- ANC
- VCT

Phase 2: Prophylaxis
- ARV
- Safe Delivery

Phase 3: Infant Feeding
- R.F
- E.BF

Phase omega: Support
- PEP
- Social Support
- PEP
- Social Support
INFANT FEEDING

• ARV prophylaxis administered to the mother and infant reduces PTCT

• 5 to 20% of infants breastfed by HIV-infected mothers are at risk of acquiring HIV

• Exclusive Replacement feeding / Exclusive BF along with ARV can reduce transmission significantly

• However top feeding especially bottle not safe in developing countries (diarrhea and LRTI)
INFANT FEEDING : HIV-INFECTED MOTHERS

WHO Recommendations

• Avoid all breastfeeding if replacement feeding is
  • Acceptable
  • Feasible
  • Affordable
  • Sustainable &
  • Safe

• Otherwise, exclusive breastfeeding during the first months of life
INFANT FEEDING - CONCLUSION

INFORMED CHOICE BY MOTHER

• Decision depends on
  – U5MR
  – MMR
  – HIV Prevalence,
  – Demand by the mother
• Exclusive BF or RF
• Exclusive BF & early weaning
• RF- Cow’s milk with spoon
PPTCT PROTOCOLS

• India specific protocols:
  – Initially AZT as per Thai protocol + BF choice
  – Now sdNVP mother & Baby + BF choice
• Modifications required/suggested
  – Mother on ART/In need of ART:
    • Triple drug ART as per National Guidelines: < 2 % trans.
  – Mother not in need of ART:
    • Antenatal: AZT from ≥ 28 wk
    • Intranatal: AZT + 3TC + sdNVP
    • Postnatal: Mother: AZT + 3TC x 1 wk
      Baby: sdNVP + AZT x 1 wk
  Efficacy: < 2 % transmission risk
IF MOTHER COMES LATE

• If antenatal AZT taken for < 4 wk:
  – AZT to baby for 4 wk instead of 1 wk
• If mother comes during labor:
  – Intranatal and postnatal as before except AZT to baby for 4 wk instead of 1 wk
• If mother comes postpartum:
  – Baby given the postnatal component except AZT for 4 wk instead of 1 wk
• Role of drugs for the duration of BF
UN FUTURE GOALS

• Target for decrease in MTCT
  • 25% by 2005
  • 50% by 2010

We can do it
We must do it
We shall do it
POST EXP. PROPHYLAXIS (CDC 1998)

Material infective - Yes

Type of exposure

M.M. /Broken skin

Intact skin

Percutaneous

Volume

Low risk

High risk

Severity

Less severe

More severe

Small

Large

Titer of HIV

Low

High

Basic PEP, Expanded PEP if HIV titer high

Basic PEP

Expanded PEP

No PEP

Offer

Offer

Offer
THANK YOU