STI case management

Francis Ndowa - GFMER
Theodora Wi - WHO
Session outline

- STI case management
- STI syndromic case management
  - Algorithm development
  - Implementation
  - Algorithm evaluation
- STI laboratory diagnosis
- Screening
Objectives of an STI programme

- to interrupt the transmission of sexually transmitted infections
- to prevent development of disease complications and sequelae
- to reduce the risk of HIV infections
Objectives of STI case management

- to provide appropriate antimicrobial therapy in order to:
  - obtain cure of infection
  - decrease infectiousness
- to limit or prevent high risk behaviour
- to ensure that sexual partners are treated in order to interrupt the chain of transmission
STI case management: Requirements

- Accurate diagnosis
- Treat at first encounter
- Rapid cure with effective drugs
- Simple
- Integrated approach
- Condom promotion
- Education/Counselling
- Partner notification
Components of Comprehensive STI case management

- History taking (symptoms and risk assessment)
- Examination (signs)
- Treatment
  - Patient and sexual partners
- Counselling for STIs and HIV testing
- Condom promotion
STI Case Management

- Infected
- Asymptomatic
- Symptomatic
- Partner Treatment

• Screening
• Presumptive treatment
• Partner management

• Communications:
  - Symptom recognition
  - STI treatment seeking behavior
  • Acceptable, accessible and quality services

• Syndromic Management
• Etiologic Management

Effective treatment
Diagnostic approaches

Disadvantages

• Low sensitivity and specificity

• Mixed infections cannot be detected

• Simple tests not available

• Cost: existing rapid tests expensive (except for syphilis)

• Delay: results are not readily available

• Cost of over-treatment

• Side-effects of antimicrobials treatment

• clinical

• laboratory

• syndromic
Operating principles (Factors that influence patients’ choice of health facility)

- Accessible
  - Location
  - Convenient opening hours
  - Affordable
- Acceptable
  - Non-stigmatizing
  - Non-judgmental staff
  - Linked to other services
- Confidential

- Quality of services
  - Efficiency of service delivery
  - Effective services / therapy
  - Available drugs and other resources
  - In line with standard guidelines
  - Informed consent
STI syndromic case management

- **Syndromic diagnosis:**
  - Identification of consistent group of symptoms and easily recognized signs (syndromes)

- **Syndromic treatment:**
  - Treat the main organisms responsible for causing the syndrome

- **Through a series of flowcharts:**
  - Guides the health-care worker through the correct identification and treatment of an STI-associated syndrome
  - Offers a package of comprehensive care from history taking, examination, to counselling/education on risk reduction and partner notification and treatment
Urethral discharge

Patient complains of urethral discharge or dysuria

- Take history and examine
- Milk urethra if necessary

Discharge confirmed?

No

Any other genital condition?

No

- Educate and counsel
- Promote condom use and provide condoms
- Offer HIV counselling and testing
- Review if symptoms persist

Yes

Use appropriate flowchart and/or treat appropriately

Yes

TREAT FOR GONORRHOEA* AND CHLAMYDIA

- Educate and counsel
- Promote condom use and provide condoms
- Offer HIV counselling and testing
- Manage and treat partner
- Advise to return in 7 days if symptoms persist

*If microscopy is available, do Gram stain smear of urethral exudates. If no intra-cellular Gram-negative diplococci are seen, treatment for chlamydial infection only may be considered.
**Test-of-Cure for N. gonorrhoeae**

1. **ASYMPTOMATIC but**
   - Test-of-Cure positive for *N. gonorrhoeae* by Gram stain, culture or NAATs OR
   - sex partner of person with cephalosporin-resistant *N. gonorrhoeae*

   **Take history and examine to exclude other infections or conditions**

2. **MANAGE AS CEPhALOSPORIN-RESISTANT N. GONORRHOEAE**
   - Collect specimen for microscopy, culture and susceptibility tests or NAATs and genotyping (subject to availability of resources and laboratory capacity)
   - Treat immediately with higher dose of ceftriaxone IM (500mg-1gm)*
   - REVIEW AFTER 72 HOURS OR
   - REVIEW AFTER 7 DAYS IF ONLY NAAT TESTING IS AVAILABLE

3. **PERFORM TEST-OF-CURE**
   Collect specimen for bacteriological culture or NAATs and genotyping (if possible)

4. **MANAGE AS TREATMENT FAILURE**
   1. Laboratory-guided treatment in consultation with an infectious disease expert
   2. Dual therapy (2gm Azithromycin + Gentamicin 240mg or Spectinomycin 2gm) OR
   3. Either Gentamicin 240mg or Spectinomycin 2gm)
   4. Notify national health authorities and GASP Networks
   5. Review and perform another test-of-cure
   6. FOLLOW UP UNTIL CURED MICROBIOLOGICALLY

**Test-of-Cure negative?**

- Yes: Educate and counsel
- No: Promote/provide condoms
- Test-of-Cure negative?

- Yes: Educate and counsel
- No: Promote/provide condoms
- Ensure treatment of sex partner(s)
Flowchart for the management of cephalosporin treatment failure for urogenital infections – symptomatic patients

N.B. This flowchart assumes that the patient has received and taken effective therapy for gonorrhoea and chlamydia prior to this consultation OR Chlamydial infection has been reliably excluded by appropriate laboratory tests.

Patient presents with persistent genital discharge following treatment with a recommended cephalosporin regimen

- Collect appropriate (urethral, cervical or rectal) specimen for microscopy, culture and susceptibility testing;
  - NAATs & genotyping, if resources permit;
  - Treat immediately with higher dose of ceftriaxone IM (500mg-1gm)
  - Treat for TV, Mycoplasma genitalium (based on local epidemiological information);
  - Notify National Reference laboratory.

- Educate and counsel
- Offer HIV testing and counselling
- Promote/provide condoms
- Ensure treatment of sex partner(s) with high dose ceftriaxone IM (500mg-1gm)
- Review in 3 days

Clinically cured?

- Educate and counsel
- Promote/provide condoms
- Ensure treatment of sex partner
- Follow up patient, if indicated

Discharge confirmed?

- Take history and examine
- Milk urethra, if necessary

Any other genital condition?

Use appropriate flowchart and treat appropriately

- Educate and counsel
- Promote/provide condoms
- Ensure treatment of sex partner(s)
- Review if necessary with advice not to pass urine for about 1 hr before attendance

Clinically cured?

- Educate and counsel
- Promote/provide condoms
- Ensure treatment of sex partner
- Follow up patient, if indicated

Discharge confirmed?

- Educate and counsel
- Promote/provide condoms
- Ensure treatment of sex partner(s)
- Review if necessary with advice not to pass urine for about 1 hr before attendance

Use appropriate flowchart and treat appropriately

MANAGE AS TREATMENT FAILURE DUE TO AMR

1. Refer for laboratory guided treatment in consultation with an infectious disease expert
2. Notify national health authorities and GASP Networks

PATIENT AND SEX PARTNERS TO BE FOLLOWED UP AND MANAGED UNTIL CURED MICROBIOLOGICALLY
Genital ulcer disease

Patient complains of a genital sore or ulcer

Take history and examine

Only vesicles present? Yes

No

TREAT FOR HSV-2. TREAT FOR SYPHILIS IF INDICATED

• Educate and counsel
• Promote condom use and provide condoms
• Offer HIV counselling and testing

Ulcer healed? Yes

No

• Educate and counsel on risk reduction
• Promote condom use and provide condoms
• Offer HIV counselling and testing

Ulcer improving? Yes

No

Refer to higher level of care

TREAT FOR SYPHILIS AND CHANCROID. TREAT FOR HSV-2

• Educate and counsel on risk reduction
• Promote condom use and provide condoms
• Offer HIV counselling and testing

• Manage sexual partners
• Review in 1 week

Ulcer healed? Yes

No

• Educate and counsel on risk reduction
• Promote condom use and provide condoms
• Consolidate counselling for HIV and HSV-2
• Manage and treat partner

Continue treatment for a further 7 days

1 Indications for syphilis treatment:
- RPR positive or equivalent test; and
- Patient has not been treated for syphilis recently.
Agents causing genital ulcer disease (GUD) by region until 1990’s
Botswana
Changes in the aetiology of GUD
1993 - 2002

*In 1993 a study was done by the National AIDS Control Program in Botswana in collaboration with the STD Research Unit, South African Institute for Medical Research, Johannesburg among 108 GUD patients.

Source: M. Rahman. ISSTDR. Ottawa 2003
Botswana: Aetiology of genital ulcer disease 2002

- HSV2: 59%
- No organism identified: 39%
- T. Pallidum: 2%
- H. ducreyi: 1%
- TPHA/RPR: 15%
- HIV: 30%

N=137

Source: M. Rahman, ISSTDR, Ottawa 2003
Current genital ulcer algorithm in Botswana

Complaint sores/ulcer on genitals

- Vesicles, blisters or history of recurrence
  - Yes: Soak in warm water, educate, condoms
  - No: Ulcer found on genitals

- Ulcer found on genitals
  - Yes: Treat for syphilis and chancroid
    - Yes: Treat
    - No: Educate
    - Yes: Review in 7 days
  - No: Other STD?
    - Yes: Treat
    - No: Ulcer healed

Sensitivity: 33%
Specificity: 45%
Over treatment rate: 99%
Infections missed: 67%
Cost per infection Tx.: $88.0
Piloted genital ulcer algorithm in Botswana

Complaint of sores/ulcer on genitals

- Only vesicles present? Yes → Treat for herpes return in 7 days if symptoms persist
  - No → Ulcer found on genitals
    - Yes → Treat for syphilis, chancroid and herpes Ask patient to return in 7 days
    - No → Other STI?

- Ulcer healed Yes → Other STI?
  - No → Ulcer improved but not healed continue therapy for 7 days and return
  - Ulcer not improved REFER

Sensitivity 99%
Specificity 13%
Over treatment rate 36%
Infections missed 1%
Cost per infection Tx. $4.5
Prevalence of selected STIs among female populations in Africa in the 1980’s and 1990’s
Vaginal discharge syndrome

VAGINITIS

- Most common causes
- Easy to diagnose
  - Lab tests
  - Clinically

- Serious complications (?)
  - Adverse outcome of Pregnancy
  - Endometritis, PID
  - BV and HIV

CERVICITIS

- uncommon cause
- Not easy to diagnose
  - No simple tests

- Complications are severe
  - PID
  - Ectopic pregnancy
  - Infertility
Patient complains of vaginal discharge, vulval itching or burning

Take history, examine patient and assess risk\(^1\)

Is there abnormal discharge or vulval erythema?

Yes

Lower abdominal tenderness?

Yes

Use flowchart for lower abdominal pain

No

Use appropriate flowchart for additional treatment

No

Is there abnormal discharge or vulval erythema?

Any other genital disease?

Yes

Use appropriate flowchart for additional treatment

No

TREAT FOR BACTERIAL VAGINOSIS AND TRICHOMONAS VAGINALIS

Vulval edema/curd like discharge, erythema, excoriations present?

Yes

TREAT FOR CANDIDA ALBICANS

No

• Educate and counsel
• Promote condom use and provide condoms
• Offer HIV counselling and testing

TREAT FOR CHLAMYDIA TRACHOMATIS, GONOCOCCAL INFECTION, BACTERIAL VAGINOSIS AND TRICHOMONAS VAGINALIS

High GC/CT prevalence setting\(^2\) or risk assessment positive?

Yes

• Educate and counsel
• Promote condom use and provide condoms
• Offer HIV counselling and testing

No

\(^1\) Risk factors need adaptation to local social, behavioural and epidemiological situation.

\(^2\) The determination of high prevalence levels needs to be made locally.
Patient complains of vaginal discharge, vulval itching or burning

Take history, examine patient (external, speculum and bimanual) and assess risk

Lower abdominal tenderness or cervical motion tenderness present?

No

Cervical mucopus or erosions or high GC/CT prevalence setting or risk assessment positive?

Yes

Perform wet mount/Gram stain microscopy of vaginal specimen

Motile trichomonads?

TREAT FOR TRICHOMONAS VAGINALIS

Clue cells seen plus pH>4.5? KOH positive?

TREAT FOR BACTERIAL VAGINOSIS

Budding yeasts or pseudohyphae seen?

TREAT FOR CANDIDA ALBICANS

No abnormal findings?

TREAT FOR CHLAMYDIA TRACHOMATIS AND GONOCOCCAL INFECTION plus vaginal infection according to speculum and microscope examination findings

Use flowchart for lower abdominal ainf

Lower abdominal tenderness or cervical motion tenderness present?

Yes

Motile trichomonads?

TREAT FOR TRICHOMONAS VAGINALIS

Clue cells seen plus pH>4.5? KOH positive?

TREAT FOR BACTERIAL VAGINOSIS

Budding yeasts or pseudohyphae seen?

TREAT FOR CANDIDA ALBICANS

No abnormal findings?

Educate and counsel; promote condom use and provide condoms; manage and treat partner and, offer HIV counselling and testing; ask patient to return if necessary

1Risk factors need adaptation to local social, behavioural and epidemiological situation.

2The determination of high prevalence levels needs to be made locally.
Due to its low sensitivity, microscopy is not recommended in the management of ano-rectal infections.

**RISK ASSESSMENT**
- Unprotected sex in last 6 months? **plus**
- Partner with STI? or
- Multiple sex partners?

**Anal discharge?**
- YES
  - **Anal and/or perineal pain?**
    - YES
      - TREAT FOR GONORRHOEA AND CHLAMYDIA
      - Educate & counsel
    - NO
      - Follow up after 1 week.
      - If symptoms persist:
        - **TREAT FOR LGV**
        - OR
        - Refer for other gastrointestinal assessments
  - NO
    - TREAT FOR HSV-2
    - plus GONORRHOEA AND CHLAMYDIA
    - Educate & counsel
- NO
  - Other management needed?
    - Educate and counsel

**ANO-RECTAL ULCER?**
- YES
  - TREAT FOR HSV-2
  - plus GONORRHOEA AND CHLAMYDIA
  - Educate & counsel
- NO
  - Take history and do physical examination

**Patient with passive/receptive anal sex in last 6 months and/or anal symptoms**

Follow up after 1 week.

If symptoms persist:
- **TREAT FOR LGV**
- OR
- Refer for other gastrointestinal assessments
Implementation: Pre-requisite information

- Prevalence of STIs
- STI treatment-seeking behaviour
- Treatment practices & counselling (PI6 & PI7)
- Level of (and capacity for) training of implementers
- Drug policy, ordering and distribution system
- Stakeholders involvement
- Review of literature (need ‘evidence criteria’)
Implementation con’t

- Conduct or analyze etiological studies
  - Genital ulcer syndrome
  - Male genital discharge syndrome
  - Female genital discharge (+/- risk-assessment)
  - Resistance patterns
- Assess if there is need to depart from WHO or existing national/regional algorithms
- Adaptation for high/low risk environment
  - high/low prevalence area
  - high risk/low risk populations
Implementation con’t

- Determine the role of the laboratory
  - for case management (and monitoring as ‘test of cure’)
  - for screening and case finding
  - for supporting research
  - for antimicrobial susceptibility studies

- Determine levels of use/capacity
  - will influence flowchart design & need pre-testing
  - will influence choice of drugs
  - depends on referral patterns
Implementation: drug selection

- Criteria for the choice of drugs (WHO, 2003)
  - efficacy (cure at least 95% of those infected)
  - safety
  - cost
  - compliance and acceptability
  - availability (e.g. at primary health care level)
  - use in pregnancy
  - broad spectrum (can cover co-existing infections)
  - resistance unlikely to occur rapidly
Implementation con’t

- Printing and distribution (and translation) of flowcharts
- Training
  - post-service institutional training
  - on-the-job training
  - pre-service training
  - what cadres to train
- Drug procurement and distribution
Implementation: Monitoring and Supervision

- **WHAT?**
  - clinical outcomes on returnees and non-returnees
  - cured/ improved/ treatment failures
  - referral/ no follow-up
  - *Neisseria gonorrhoeae* susceptibility
  - etiological surveys
  - quality of care (PI6, PI7)

- **HOW (universal? sentinel sites? Standardised protocols? consensual workshops)**

- **WHEN?**
Evaluation of algorithms

- Validity: sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV)
- Feasibility: infrastructure, personnel
- Cost: direct and indirect costs, cost/effectiveness
- Acceptability: health care provider, STI patient, programme manager
### Validity of an algorithm

- **Comparison between:**
  - Outcome of algorithm – simultaneous studies, real outcome in field conditions
  - Gold standard diagnosis – laboratory tests

### Gold standard test

<table>
<thead>
<tr>
<th>Algorithm</th>
<th>+</th>
<th>-</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>A: (true positive) Correctly treated</td>
<td>B: (false positive) Over-treated</td>
</tr>
<tr>
<td>-</td>
<td>C: (false positive) Missed infections</td>
<td>D: (true negative) Correctly diagnosed as negative</td>
</tr>
<tr>
<td>Total infected</td>
<td>Total not infected</td>
<td></td>
</tr>
</tbody>
</table>

- Sensitivity: \( \frac{A}{A + C} \)
- Specificity: \( \frac{D}{B + D} \)
- Positive Predictive Value: \( \frac{A}{A + B} \)
- Negative Predictive Value: \( \frac{D}{C + D} \)
Cost per case cured

Total cost of all diagnoses and treatment

\[
\text{Number of cases cured}
\]

Cost per case cured decreases if:

- Prevalence increases
- Specificity of flowchart increases
Implementation Cycle

- Evaluate programme and interventions
- Train and supervise
- Strengthen STI programme management and intervention activities
- Assess the epidemic and the response
- Advocate for STI inclusion in the health-care agenda
- Adopt and adapt evidence-based interventions
Screening for STI (Asymptomatic STIs)

- Asymptomatic STIs are major concern

- Population to screen
  - SW (HIV guidelines)
  - MSM/TG (HIV guidelines)
  - Pregnant women
  - FP clients
  - Sexually active adolescents (??)
  - Patients diagnosed with other STIs

- STIs to screen
  - Syphilis
  - Gonorrhoea
  - Chlamydia
  - Trichomonas
  - HIV

**Important Considerations:**

Which population should be targeted for screening?

What STIs to screen? Which STI to screen when + for one, when HIV+?

When to screen? Re-screening

How to screen?
  - What tests including rapid test?
  - How frequent?
  - What methodology?

What treatment? E.g. GC+ CT
## Screening

<table>
<thead>
<tr>
<th>Populations</th>
<th>STIs</th>
<th>Laboratory Test</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex workers, men having sex with men and transgender</td>
<td>Syphilis</td>
<td>RPR/ TPHA Rapid Test</td>
<td>Pro-active screening</td>
</tr>
<tr>
<td></td>
<td>Gonorrhoea</td>
<td>GC culture NAAT Gram stain (men)</td>
<td>Usually not available in low resource settings</td>
</tr>
<tr>
<td></td>
<td>Chlamydia</td>
<td>NAAT</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HIV testing</td>
<td>HIV rapid test</td>
<td>Ensure pre and post test counseling</td>
</tr>
</tbody>
</table>
## Screening

<table>
<thead>
<tr>
<th>Populations</th>
<th>STIs</th>
<th>Laboratory Test</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant women</td>
<td>Syphilis</td>
<td>RPR/ TPHA Rapid Test</td>
<td>First trimester</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gonorrhoea</td>
<td>GC culture NAAT</td>
<td>(ideal, based on resources)</td>
</tr>
<tr>
<td></td>
<td>Chlamydia</td>
<td>NAAT</td>
<td></td>
</tr>
<tr>
<td>HIV testing</td>
<td></td>
<td>HIV rapid test</td>
<td>Ensure pre and post test counseling</td>
</tr>
<tr>
<td>Populations</td>
<td>STIs</td>
<td>Laboratory Test</td>
<td>Comments</td>
</tr>
<tr>
<td>------------------------------</td>
<td>----------</td>
<td>-----------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td>Adolescent – below 26 years</td>
<td>Syphilis</td>
<td>RPR/TPHA Rapid Test</td>
<td>Pro-active screening</td>
</tr>
<tr>
<td></td>
<td>Gonorrhoea</td>
<td>GC culture</td>
<td>NAAT Gram stain (men)</td>
</tr>
<tr>
<td></td>
<td>Chlamydia</td>
<td>NAAT</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HIV testing</td>
<td>HIV rapid test</td>
<td>Ensure pre and post test counseling</td>
</tr>
</tbody>
</table>
Laboratory Diagnosis of STIs

Choosing tests for STIs
(Numerous STIs and large variety of tests)

- Decide on:
  - Which and how many STIs to invest in testing?
  - Who to test?
  - What purpose?

- Prioritize base on the following:
  - Infection prevalence
  - Impact of the infections and complication on individuals and populations
  - Test performance characteristics
  - Cost of the tests
  - Reasons for testing
Factor influencing choice of the test

- Test specific consideration
  - Performance (sensitivity, specificity, predictive value)
  - Specimen collection and transport requirements
  - Prevalence
  - Associated morbidity
  - Resources (financial, personal, infrastructure)
  - Relative importance

- Purpose of testing
  - Surveillance
  - Quality assurance
  - Evaluation of syndromic diagnosis
  - Diagnosis
  - Screening
  - Antimicrobial susceptibility testing
# Laboratory test for syphilis at different level of care

<table>
<thead>
<tr>
<th>Disease</th>
<th>Laboratory test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>P</th>
<th>S</th>
<th>T</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syphilis</td>
<td>Dark Field Microscopy</td>
<td>85-95</td>
<td>100</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>VDRL</td>
<td>71-100</td>
<td>79-98</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>RPR cards</td>
<td>73-100</td>
<td>79-98</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>FTA-ABS</td>
<td>85-100</td>
<td>95-100</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>TPPA / TPHA</td>
<td>70-100</td>
<td>96-100</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Rapid test – (treponemal test)</td>
<td>70-100</td>
<td>96-100</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Direct FA</td>
<td>90-95</td>
<td>&gt; 98</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PCR</td>
<td>&gt;95</td>
<td>&gt;99</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Level of care: P = primary; S = secondary; T = tertiary
Partner Management

- **Issues:**
  - Context specific – index case and gender issues
  - STI discordant partners
  - Partner violence – tools to assess and prevent
  - Increase coverage for partner notification and management

- **Approaches:**
  - Patient referral – contact cards, concurrent patient-partner therapy (CPPT) or bring in your own partner (BYOP)
  - Patient delivered partner therapy (PDPT) - evidence of decreased re-infection
    
    *Studies have shown that provision of medication to partners has shown to be more effective than just providing prescription to the partners*
  - Provider initiated