

Trichomonas vaginalis



Global
Antibiotic
Resistance
Partnership

100
1908 - 2008



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Trichomonas vaginalis

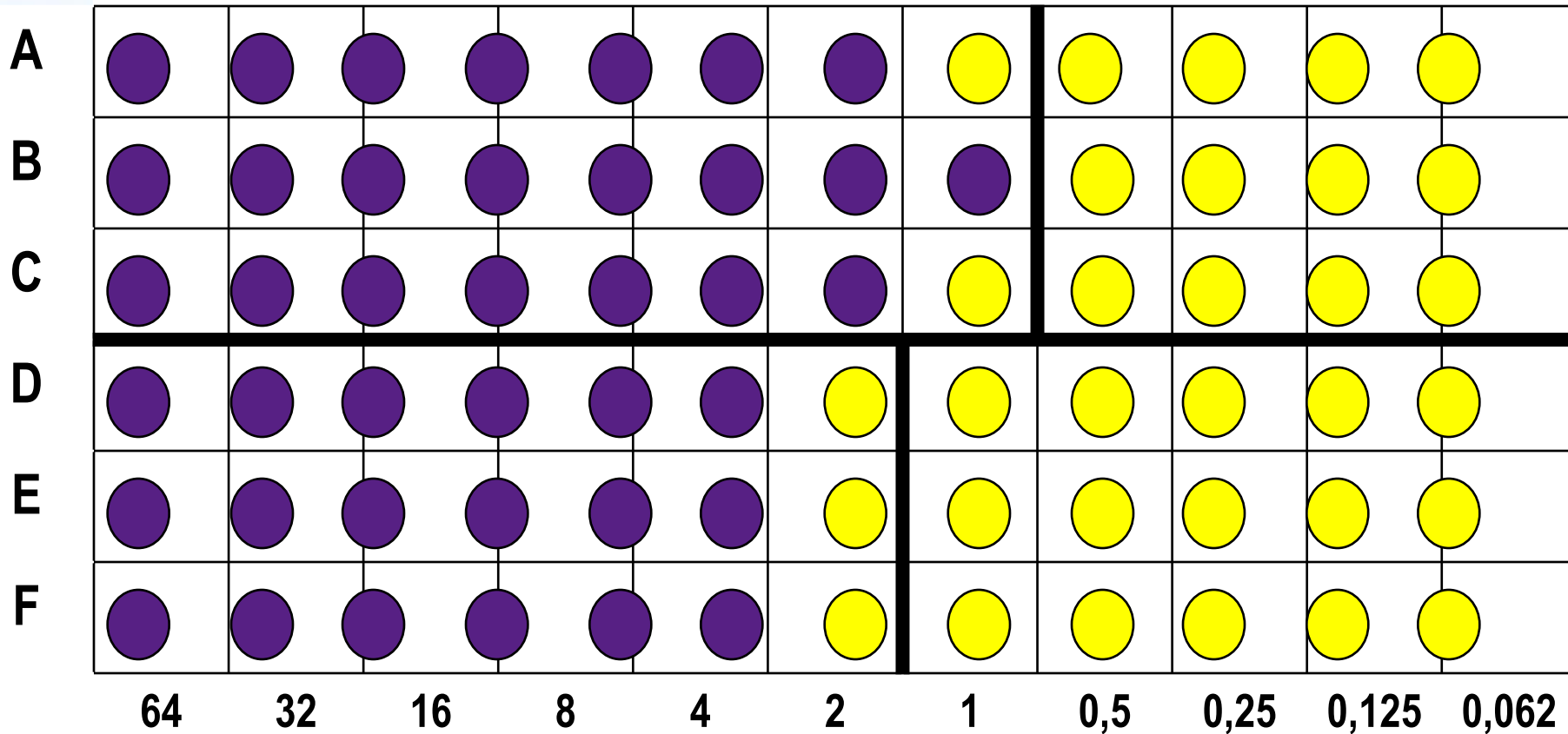
- **Non-bacterial, non-viral sexually transmitted protozoan**
- **±180 million new infections occurring worldwide every year**
- **WHO estimates incidence in sub-Saharan Africa at 32 million**
- **In South Africa:**
 - **prevalence average 30%**
 - **incidence from 20% to 56%**
- **Most common, curable STI in the world**
- **Metronidazole drug of choice since 1959**
- **Possibility of resistance has been repeatedly suggested and dismissed**
- **Published data have confirmed the increase of metronidazole resistant isolates**
- **In South Africa, 10-20% of field isolates (unpublished data)* had high levels of resistance *in vitro***

Trichomonas vaginalis

Susceptibility testing

- **To perform serial two-fold dilutions of metronidazole in micro-titre plates**
- **To determine Minimum Inhibitory Concentration (MIC) & Minimum Lethal Concentration (MLC) endpoints of metronidazole considering the following variables:**
 - **Environmental conditions influencing susceptibility (aerobic compared to anaerobic)**
 - **Incubation period (24 hours compared to 48 hours)**
 - **Endpoint determinations (visual compared to microscopic)**

DIAGRAMMATIC PRESENTATION OF RESULTS FOR SUSCEPTIBILITY TESTING



Results for Minimum Inhibitory Concentration (N=36)

AEROBIC

	MIC ₅₀	MIC ₉₀	RANGE
Microscope 24 h	0.9 µg/ml	2.7 µg/ml	0.25-8.0 µg/ml
Microscope 48 h	1.2 µg/ml	2.9 µg/ml	0.2-8.0 µg/ml
Visual 48 h	0.5 µg/ml	1.7 µg/ml	0.125 – 6.25 µg/ml

ANAEROBIC

	MIC ₅₀	MIC ₉₀	RANGE
Microscope 24 h	0.9 µg/ml	1.9 µg/ml	0.2-4.0 µg/ml
Microscope 48 h	1.2 µg/ml	3.7 µg/ml	0.25-8.0 µg/ml
Visual 48 h	0.7 µg/ml	1.9 µg/ml	0.2- 6.25 µg/ml

Results for Minimum Lethal Concentration (N=36)

AEROBIC

**7 Days
incubation**

MLC ₅₀	MLC ₉₀	RANGE
1.4 µg/ml	3.4 µg/ml	0.4 -12.5 µg/ml

ANAEROBIC

**7 Days
incubation**

MLC ₅₀	MLC ₉₀	RANGE
1.1 µg/ml	3.6 µg/ml	0.25-12.5 µg/ml

Trichomonas vaginalis

CONCLUSIONS

- For MIC & MLC: All isolates tested were considered to be susceptible (CLSI guidelines: MIC \leq 32 $\mu\text{g/ml}$, MLC \leq 50 $\mu\text{g/ml}$)
- Visual endpoint values were slightly lower than endpoints obtained by microscope - not enough acid produced
- Generally values obtained under aerobic conditions were similar to values obtained anaerobically - differences observed were minimal
- Metronidazole remains an appropriate agent for treatment of trichomoniasis

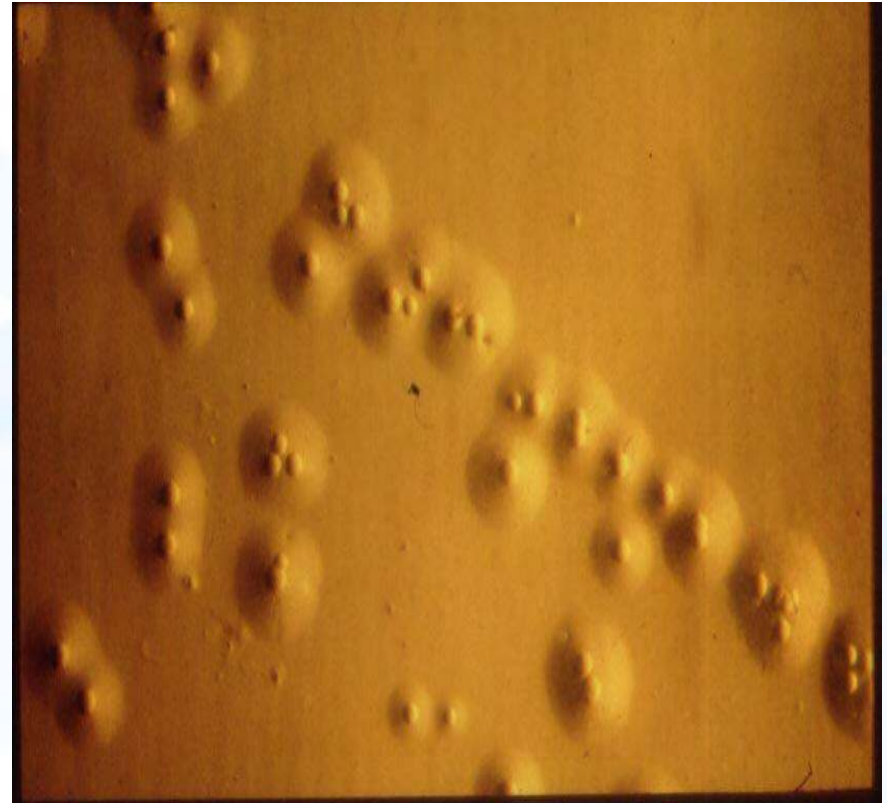
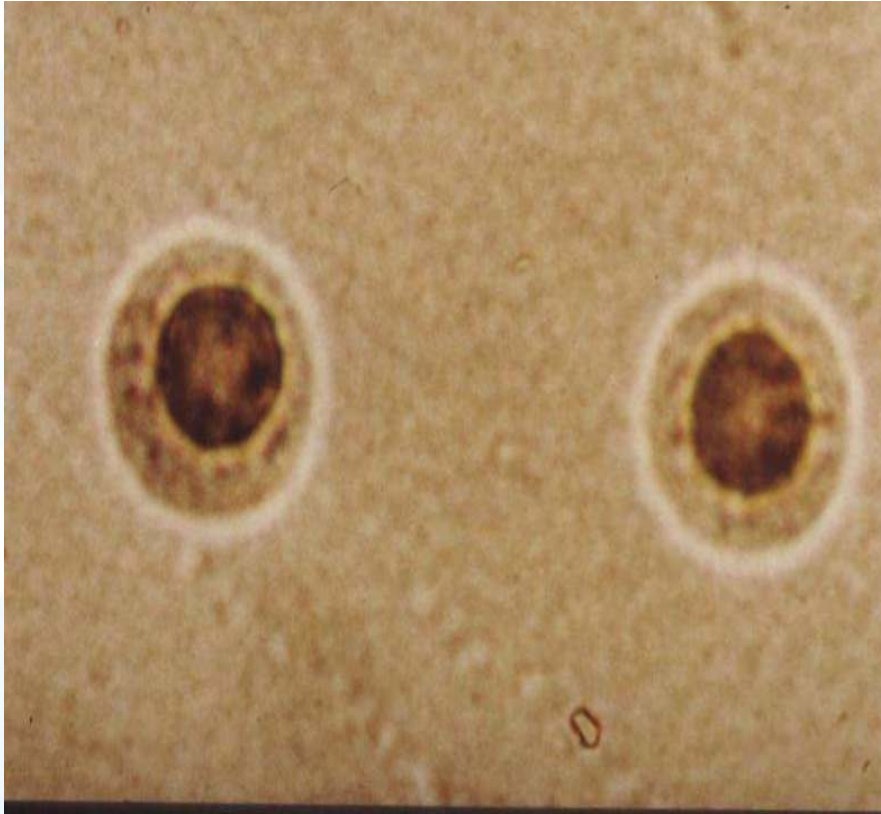
LIMITATIONS

- Did not record the number of subcultures performed - can induce resistance in the laboratory
- No reference ATCC strain with known MIC or MLC was available

CONSIDERATIONS

- *In vitro* values of metronidazole susceptibility are only indicators of the degree of sensitivity or resistance of a specific trichomonad isolate under fixed laboratory conditions
- Not possible to extrapolate MIC and MLC values to the tissue levels that are necessary to cure an infection

GENITAL MYCOPLASMAS



Mycoplasma genitalium

- **Smallest self-replicating prokaryote**
- **Lacks cell wall**
- **Genome of only 580 kilobase pairs**
- **Characteristic pear/flask shaped morphology with terminal tip organelle for attachment**
- **Role in disease difficult to establish – difficult to grow in culture, long duration, low yield**
- **Molecular assays – led to number of studies (qualitative & quantitative)**
- **Studies – developed countries show an association between *M genitalium* and male urethritis**

Mycoplasma genitalium

LOCAL STUDIES

- Sexually transmitted pathogens in men – detected in 43% of symptomatic men vs 9% of asymptomatic men ($p=0.04$). Applied modified Koch's postulates
- Patients with urethritis – bacterial load – conc higher in men with urethritis vs asymptomatic men ($p=0.02$)
- Greater number of organisms = greater severity of symptoms

Mycoplasma genitalium

TREATMENT

- Lacks cell wall - beta-lactams inherent resistance
- Susceptible to those that inhibit protein synthesis
- CDC guidelines - macrolides, tetracyclines & flouroquinolones
- Cannot determine MIC – because not easy to culture & intra-cellular location
- Clinical trials – test of cure by detection of organism, bacterial load

Mycoplasma genitalium

TREATMENT

- **Hannan 1998** – in-vitro study showed susceptibility to azithromycin but not doxycycline & ciprofloxacin
- **Falk 2003**, Swedish study where patients were re-tested after 4-5 weeks – tetracycline did not eradicate *M genitalium* & azithromycin was more active
- **CDC 2006** guidelines recommends 1g zithromycin single dose or doxycycline 100mg BD for 7 days
- **Bradshaw et al 2006**, Australian study reported significant treatment failure with single dose Azithromycin (resistance to macrolides) & infection cleared with 400mg moxifloxacin for 10 days.
- **Bjournalius et al 2008** recommend 500mg Azithromycin first day followed by 250mg for 4 days for treatment failures

CHALLENGES WITH DRUG RESISTANT STIs

- **Diverse aetiological agents – bacteria, viruses, protozoan**
- **Some organisms cannot be cultured/difficult to culture on artificial media**
- **Intracellular location**
- **Mixed infections in high-risk behaviour populations**
- **Impact of HIV**
- **Management strategies such as syndromic management**
- **Commensal flora that can cause disease**

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