Firstly, when T/2 values are as little as 1.5–2.5 days, the time between baseline venesection and first therapy must be recorded accurately as delays of initial dose by only a few hours may produce 10–20% errors in any calculation. Secondly, assumptions made in these models do not allow for sudden biological changes in viral load at or near the time of onset of treatment, and we find such events do occur in up to 10% of patients studied and will totally invalidate the subsequent analysis.

Nevertheless, we believe there is a place for this simple model and have already used it to assist in the early prediction (within 1 month) of the relative efficacies of different antiretroviral therapies in HIV-1 disease. Such "screening" procedures in small patient groups (10–20 patients/group), receiving different combination therapies, using virological endpoints will allow the selection of superior drug combinations that can go forward into longer, more expensive clinical trials.

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Failure of itraconazole to prevent Enteroxotozoon bieneusi infection

Microsporidia are obligate intracellular parasites which have been increasingly recognised as a significant cause of morbidity in AIDS patients. A variety of drugs have been used in attempts to treat the most frequently identified microsporidial agents (Enteroxotozoon bieneusi, Enteroxotozoon cuniculi, Enteroxotozoon hellem, Septata intestinalis). Blinded, placebo-controlled studies, however, are lacking. Preliminary clinical results have shown fumagillin to be promising for treatment of keratoconjunctivitis due to Enteroxotozoon hellem, and albendazole to have activity against S intestinalis. Currently, there is no proven effective treatment for Enteroxotozoon bieneusi, the most prevalent microsporidian which is capable of causing debilitating diarrhoea and wasting syndrome in AIDS patients. Albendazole may mitigate enterocytozoon-associated diarrhoea but fails to eradicate the parasite. Because E bieneusi has not yet been maintained in long-term tissue culture, it has not been possible to evaluate the effects of therapeutic regimens on this microsporidium owing to the lack of an appropriate in vitro testing system. Recent studies, however, have suggested that the polar tubule apparatus contained within the microsporidium spore may be a useful target for chemotherapeutic intervention. This structure, characteristic of all microsporidian species, consists of a tightly coiled, hollow, polar tubule which upon appropriate environmental stimulation undergoes extrusion from the spore to attach to a suitable host cell. Subsequently the infectious sporoplasm is passed through the polar tubule into the target cell where a new generation of microsporidian organisms is produced. Recently Leitch et al investigated the capability of different agents to interfere with polar tubule extrusion. They used an in vitro assay utilising Enteroxotozoon hellem cultured from an AIDS patient. Four agents were found to inhibit polar tubule extrusion: Cytochalasin D, demecoline, nifedipine and itraconazole. One of these agents, itraconazole, has been used to treat microsporidiosis of invertebrates, and there has been anecdotal experience that it has activity in the treatment of human ocular microsporidiosis due to encephalitozoon. Although it was suggested that itraconazole may have activity against other species of pathogenic microsporidia, its efficacy against E bieneusi has not been investigated. We report the case of an AIDS patient who developed intestinal E bieneusi infection while on high-dose itraconazole for secondary prophylaxis against histoplasmosis.

A 41 year old homosexual patient was diagnosed HIV-positive in 1985. He remained asymptomatic until 1993 when he presented with fever, unproductive cough, dyspnoea and an elevated serum lactic dehydrogenase (LDH). Histoplasma capsulatum was cultured from bone marrow specimens. With amphotericin B therapy the patient recovered. Four weeks later, when LDH and histoplasma polysaccharide antigen titre had normalised, therapy was switched to itraconazole 200 mg bid. Nine months later while still receiving 200 mg bid he started to complain of watery diarrhoea five to 15 times a day accompanied by a weight loss of 1-3 kg. His CD4 cell count at that time was 60 cells/μl. E bieneusi was detected in multiple stool specimens and in a
small bowel biopsy specimen. No other pathogens were found. At the time of diagnosis the serum drug level of itraconazole was 7.9 µg/ml (levels above 2.0 µg/ml are considered therapeutic). Albendazole and metronidazole were ineffective in ameliorating the patient's diarrhoea. Symptomatic therapy with tinctura opii and loperamide resulted in a decrease of the stool frequency to two to five bowel movements per day. The patient continues to excrete *E. bieneusi* in his stool.

Although a single report can provide only limited evidence, in this patient high dose itraconazole failed to protect against the development of *E. bieneusi* infection. Further studies are necessary to establish firmly the drug sensitivity pattern of this microsporidium. Because albendazole may provide some palliation and preliminary evidence is available that atovaquone may also have efficacy against *E. bieneusi* [D Schwartz, personal communication], we recommend that itraconazole should currently not be considered as a first-line drug for use in *E. bieneusi* infections in persons with AIDS.

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**Letters to the Editor**

**Chlamydia trachomatis in gynaecological infections in Luanda, Angola**

*C. trachomatis* infection is today one of the most widespread sexually transmitted diseases (STDs) in the world. The major chlamydial affections in man are non-gonococcal urethritis and sterility caused by epididymitis and deferentitis. In females both gynaecological and obstetrical infections such as endocervicitis and pelvic inflammatory disease (PID) are reported, sometimes with severe complications.

The purpose of this study was to evaluate the incidence and the clinical picture of chlamydial infection in females in an African country, as a marker of gynaecological health state.

This study was conducted in 1992 at the Maternity Hospital *Lucrecia Paim*, Luanda, Angola. The sample population was 400 women (age ranging from 14 to 60 years) showing vaginal discharge and/or other symptoms related to the genital area. For the identification of *C. trachomatis* on cervical swabs, the indirect immunofluorescence (IFA) with monoclonal antibodies (Microtrak Syva Co., USA) was used. In addition serum was collected and tested for IgG and IgA content by ELISA Chlamydia (Sclavo).

In the cervical swabs of 111 patients, corresponding to 27.75% of the study population, *C. trachomatis* was evident. Of these, 68 patients presented single or multiple coinfections with *Candida albicans*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis* (data not shown). The distribution of the symptoms in the 111 patients was hyperaemia 57.6%, cervicitis 51.5%, pelvic pain 41.1%, dyspareunia 36.4%, dysuria 28.8%. Single or associated clinical symptoms, observed in 43 patients positive only for chlamydia, are shown in the table. The incidence of endocervical infection appears higher (25.2%) in the age group 20–24 years.

Different methods of contraception were used by the positive patients: six used condom, 24 oral contraceptives, 31 IUD, while 50 did not use contraceptives.

In 80 positive and in 10 negative IFA cases, we have measured the prevalence of anti-*C. trachomatis* IgG and IgA in the serum. Only 32 were positive for both IgA/IgG, while 51 were positive for IgG alone confirming the greater sensitivity of this Ig class.

This is the first study on the incidence of *C. trachomatis* in Angola and very few studies have reported the frequency of this disease in Southern Africa. The prevalence of 27-75% in females referring to the gynaecological hospital with signs of STD can be considered rather elevated in comparison with other countries of the area. Reports vary from 4.7% in South Africa2 to 23% in Mozambique.
Failure of itraconazole to prevent Enterocytozoon bieneusi infection.

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