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Treating Onychomycosis: A Head-to-Head Comparison of Terbinafine and Itraconazole

ABSTRACT & COMMENTARY

Synopsis: *Terbinafine had higher cure rates and lower relapse rates than itraconazole at 5 years.*

Source: Sigurgeirsson B, et al. Long-term effectiveness of treatment with terbinafine vs itraconazole in onychomycosis. *Arch Dermatol*. 2002;138:353-357.

THIS STUDY FOLLOWS UP THE LAMISIL VS. ITRACONAZOLE IN Onychomycosis (LION) study whose results were published in 1999. Briefly, the LION study demonstrated that continuous terbinafine (Lamisil®) had higher mycological and clinical cure rates than itraconazole (Sporanox®). The original cohort of patients was multinational. The trial was prospective, randomized, double-blind, and double-dummy and analysis was intention-to-treat. The doses given were terbinafine 250 mg/d for 12 or 16 weeks and itraconazole 400 mg/d for 1 week every 4 for 12 or 16 weeks. The patients were followed for 18 months.

The current study (the LION Icelandic Extension Study) examined the 144 patients enrolled in the 3 Icelandic centers. The study had 2 parts. The first part sought to determine what happened to the patients over a course of 5 years. The second part took patients who had relapsed under either treatment and treated them with terbinafine for additional 12-week courses, whenever they had clinical signs of infection or when fungal cultures became positive after initial clearing.

Sigurgeirsson and colleagues had 3 definitions of "cure." First, there was mycological cure, which was the primary end point. It was defined as negative culture and no dermatophytes seen on microscopy. Second, there was clinical cure: 100% normal-looking toenail. Finally, there was complete cure, a combination of mycological and clinical. Relapses could also be mycological or clinical and were defined as you might expect, except that mycological was

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INSIDE

determined at 12 months and clinical at 18 months. The difference allowed toenails that were mycologically cured, but clinically abnormal, to grow out.

The patients were followed for an average of 54 months with visits every 6 months. Both groups were similar. They averaged 48 years old and were two-thirds male. The offending organism in 97% of cases was *Trichophyton rubrum*. The patients had onychomycosis for little better than 12 years with an average of 5.5 toenails infected.

After 18 months, 46% of terbinafine patients and 13% of itraconazole patients had a mycological cure without need of a second intervention. The clinical cure rates were 42% and 18%, respectively. Complete cure rates were 35% and 14%, respectively.

At the 18-month check, 5 of 57 (9%) terbinafine patients who were mycologically cured at 12 months had relapsed. The corresponding relapse rate among itraconazole patients was 7 of 32 (22%). At the end of the study, 13 of 57 (23%) terbinafine and 17 of 32 (53%) itraconazole patients had a mycological relapse. The clinical relapse rates were similar, 21% and 48%, respectively.

Seventy-two patients, who at 18 months had clinical signs of onychomycosis, accepted an offer of continued treatment with terbinafine. There were 25 patients from the terbinafine group and 47 patients who had taken itraconazole. At the end of the study, 23 (92%) of the terbinafine group and 40 (85%) of the itraconazole group were mycologically cured. Clinical cure rates were 76% and 77%, respectively.

COMMENT BY ALLAN J. WILKE, MD

In this head-to-head study, terbinafine had better clinical and mycological cure rates when compared to itraconazole. Additionally, most patients, who had failed initial treatment with either drug, responded to repeat courses of terbinafine. This may be explained by the fact that terbinafine is *fungicidal* and itraconazole is *fungistatic*. This study did not evaluate itraconazole performance after treatment failure.

Apparently, there is money to be made in foot fungus. No doubt, you have seen the direct-to-consumer advertisements that Janssen and Novartis run, emphasizing the cosmetic improvements achievable with their drugs. Indeed, both companies host web sites (http://www.sporanox.com/ and http://www.lamisil.com/fsite/html/ symptomatic.htm) that offer information about the disease, the medications, and coupons for the first prescription. This is not to play down the serious nature of onychomycosis, which can lead to more severe disease and affect quality of life, but to highlight the competition for our patients' attention and dollars.

One of the criticisms leveled at LION, which the LION Extension Study aimed to answer, was the length of follow-up. Since toenails typically take 12-18 months to grow out, there was concern that the 18-month follow-up was too short. Five years seems long enough.

The cost of therapy was not addressed. A 12-week course of itraconazole 400 mg/d for a week (84 100-mg capsules) would retail around $500. Terbinafine 250 mg/d for the same length of time (also 84 tablets) is about $550. This does not include the cost of physician visits or liver function testing for terbinafine. Because itraconazole has many drug interactions (cyclosporine, digoxin, quinidine, and phenytoin, for instance), there may be additional expense if you monitor those drugs. The dose of itraconazole is not the one that appears in the product information insert. Janssen recommends 200 mg/d for 12 weeks (168 capsules!).

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Not for the faint hearted or light of wallet!

There are other therapies for onychomycosis. Griseofulvin is cheaper, but less effective. Ciclopirox (Penlac®, which also has a web site http://www.dermik.com/prod/ penlac/penlac.html) is available as a lacquer that is applied once daily for 48 weeks. It costs $180, but its complete cure rate is less than 10% and after 12 weeks of stopping therapy, 40% of patients had relapsed.[1]

My one caveat is that Novartis funded this study. I will allow the reader to discover which drug Novartis manufactures. ■

Dr. Wilke is Assistant Professor, Family Medicine, Medical College of Ohio, Toledo.

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1. *Med Lett Drugs Ther.* 2000;42:51-52.

Changing Patterns of New Tuberculosis Infections

ABSTRACT & COMMENTARY

Synopsis: *Although the incidence of tuberculosis has declined in the United States in the last decade, new cases have actually risen among foreign-born residents. Molecular and epidemiological analyses of tuberculosis case isolates in New York City suggest that reactivation of latent infection is responsible for the rise, while declining rates of acute transmission account for most new cases in US-born residents.*

Source: Geng E, et al. Changes in the transmission of tuberculosis in New York City from 1990 to 1999. *N Engl J Med.* 2002;346:1453-1458.

Starting with 812 new cases of tuberculosis (TB) diagnosed between 1990-1999 at Columbia Presbyterian Medical Center in northern Manhattan, and eliminating 29 who were not local residents, 575 isolates (77%) were able to be "DNA fingerprinted" using restriction-fragment-length polymorphism. This enabled clusters of cases from recent transmission to be distinguished from unique cases, and further information on clinical, social, and demographic variables could then be linked from records at the Tuberculosis Control Program in the New York City Department of Health.

Unique TB isolates were found in 52% of the cases, while the remaining 48% were part of clusters, with matching of at least one other in the cohort, implying they were caused by recent transmission. However, this pattern changed with time over the 10-year study period, such that clustered isolates initially accounted for 63% but declined to 31% by 1999. By the end of the decade, most new cases of TB in this area were caused by unique strains.

Population characteristics associated with recent clustered transmission were (in descending order) injection-drug use, homelessness, black race, pulmonary source of isolate, HIV infection, and male sex. For unique isolates presumably arising from latent reactivation, the most likely characteristics were Hispanic ethnic background, diagnosis after 1993, non-US birth, white race, age older than 60 years, and Asian race.

Using a multivariate analysis, the strongest independent association for reactivation of latent infection was non-US birth with Hispanic ethnic background, diagnosis after 1993, age > 60 years, and other non-US births. The other characteristics found associated with recent transmission did not identify any greater risks in the non-US-born group, except for HIV infection that increased the risk of a clustered or recently transmitted infection rather than a latent reactivation.

COMMENT BY MARY ELINA FERRIS, MD

These results have important implications for TB control programs in areas of recent immigration. The extremely high rate of new TB cases in this New York City neighborhood at > 125 cases/100,000 persons was far higher than the city-wide rate of 50/100,000, and much higher than the US overall rate of 10.5/100,000 in 1992. With one of the highest concentrations of recent immigrants in Manhattan (40% non-US born, mostly from the Dominican Republic), Geng and colleagues hypothesized that this foreign-born population was either not being reached by TB control efforts or else had different sources of infection. The hospital also served an adjacent area of US-born African-Americans that could be used as a comparison group.

Control of TB in New York City was remarkably successful from 1992-2000, resulting in a decline of 65% in new cases. Improvements were attributed to directly observed therapy, infection control, and standardization of initial drug treatment regimens.[1] However, it soon became apparent that new cases at the end of the decade were predominantly in non-US born residents. This study shows that most of these more recent infections resulted from reactivation of latent TB, which would not necessarily be affected by the measures that reduced new acute transmissions of TB.

New immigrants to the United States are required to be free of active TB on chest x-ray, but there are current-

ly no specific requirements for skin testing that could detect latent disease. TB remains a serious problem worldwide, accounting for 2-3 million deaths annually, and in countries with limited health facilities, up to a 36% infection rate. The Institute of Medicine recommended intensified interest in latent TB 2 years ago,[2] predicting that soon the majority of new cases of TB in the United States would occur in foreign-born persons coming from nations with high rates of the disease. Mexican immigrants, for example, currently account for nearly 25% of all new cases in the United States

Clinicians should be aware that the risk of reactivating latent TB for immigrants is highest during the first 5 years after arrival; of those who develop the disease, a third do so within 1 year. Current guidelines from the CDC and others encourage skin testing of recent immigrants, and 9 months of isoniazid treatment for latent infection, for persons from countries of high tuberculosis prevalence.[3,4] Until Immigration regulations and public health efforts change to target these populations, the burden for detection of these new tuberculosis cases remains in our own primary care offices. ■

Dr. Ferris is Clinical Associate Professor, University of Southern California, Los Angeles, Calif.

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Disappearance of Pathogenic *H pylori*?

ABSTRACT & COMMENTARY

Synopsis: *Pathogenic cagA+ strains of H pylori seem to be vanishing, changing our expectations regarding H pylori and human disease.*

Source: Perez-Perez GI, et al. *Gut*. 2002;50:295-298.

Gastric colonization by *Helicobacter pylori* is probably as old as mankind. Most adults in developing countries are positive for this organism, while its prevalence is far lower in developed countries. In all settings, *H pylori* is more common in the elderly. The cagA+ strains of *H pylori* are associated with such unfavorable outcomes as peptic ulcers and gastric cancer, but they may also be correlated with decreased risk of esophageal diseases (eg, GERD). This study is from large numbers of Finnish subjects between 1973 and 1994 during which both cagA+ and cagA- prevalence fell. However, the prevalence of cagA+ strains fell more dramatically in subjects < 45 years of age (34% to 8%) than cagA- strains (falling from 12% to 6%). It was concluded that there is declining acquisition of cagA+ *H pylori* in younger subjects and that *H pylori* acquisition occurs primarily during childhood although low rates of adult acquisition do occur as well.

COMMENT BY MALCOLM ROBINSON MD, FACP, FACG

There seem to be many misconceptions about the significance and management of *H pylori* infections in our patients. Although there has been a statistical correlation between this organism and some nasty diseases, most people with gastric colonization by *H pylori* are asymptomatic and totally unaffected. This work suggests that infections with pathogenic *H pylori* are destined to become even less frequent than is currently the case. A recent article confirmed that most newly acquired *H pylori* infections happen before age 10,[1] suggesting that treatment and prevention strategies should be directed at that age group. One should assess adult patients for *H pylori* only in the presence of peptic ulcer. The likelihood of any association between *H pylori* and disease will only get smaller as the years pass by. ■

Dr. Robinson is Medical Director, Oklahoma Foundation for Digestive Research; Clinical Professor of Medicine, University of Oklahoma College of Medicine, Oklahoma City, Okla.

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Special Feature

Rapid Malaria Diagnosis

By Mary-Louise Scully, MD

A previously healthy 6-year-old boy who recently immigrated to the United States from Hon-

duras presented with a history of fever, abdominal pain, and headache. Although initially afebrile, while in the emergency department his axillary temperature reached 41.6°C and he vomited 3 times. His physical exam was remarkable for a palpable spleen tip and a liver that extended 1 cm below the right costal margin. A routine white blood cell (WBC) count was performed by use of the Cell-Dyn 4000 automated blood-cell analyzer (Abbott) giving the scattergram shown in Figure 1.

In the process of obtaining a routine WBC count, red blood cells (RBCs) are lysed and free malarial parasites were then detected as a distinct population on the basis of light-scattering traits, such as cytoplasmic and nuclear optical characteristics (ie, size, granularity, lobularity, and complexity). The malaria organisms in Figure 1 appear as a population that is slightly smaller than lymphocytes with a low angle of scatter (1'- 3') but greater granularity and surface complexity as shown by the pattern of orthogonal scatter (90'). *P vivax* malaria was confirmed in this patient by examination of Wright-Giemsa-stained slides.

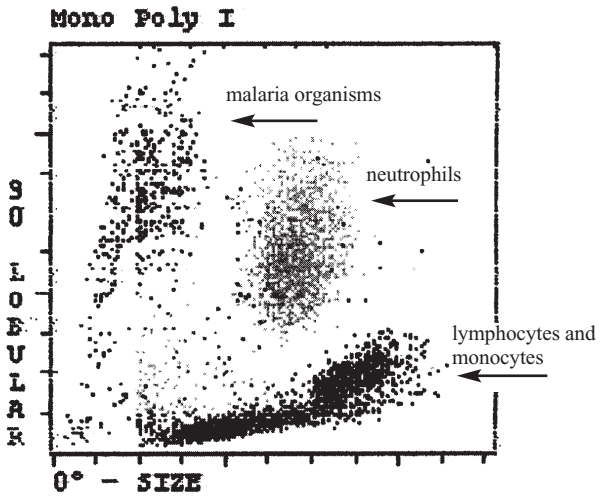
■ COMMENT BY MARY-LOUISE SCULLY, MD

Automated blood cell analyzers can contribute to the detection of malaria, especially in cases when there is no clinical suspicion. The Abbott, CD 3500 blood-cell analyzer has been reported to detect levels of parasitemia as low as 1500 parasites/µl. However, an experienced pathologist can detect as few as 5-20 parasites/µl of blood using light microscopy of Giemsa-stained blood films. Therefore, it should be emphasized that the automated blood cell analyzer is not an appropriate screening test for malaria, but may play a role in situations where malaria is not suspected.

The careful examination by a trained microscopist of a well-prepared stained blood film remains the "gold standard"of malaria diagnosis having excellent sensitivity, the ability to characterize all 4 *Plasmodium* species as well as being used to quantify parasitemia. The disadvantages of the Giemsa-stained thick blood films (G-TBF) are that it is labor-intensive, and its success depends on having well trained microscopists. PCR has even greater sensitivity than the G-TBF as shown by several authors who reviewed PCR positive/G-TBF negatives and confirmed that "false"positives were in fact true positives.[1] Some experts now question if indeed the G-TBF is still the proper yardstick by which to measure all other tests.

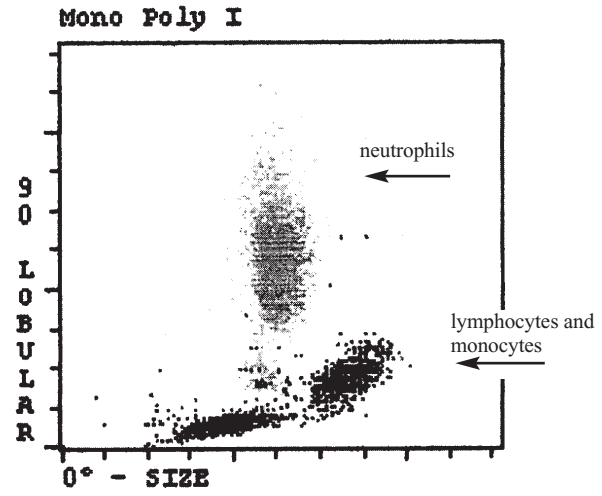
In a recent review, Moody defines a rapid diagnostic test for malaria as a method that requires 1 hour or less.[2] Fluorescent dyes such as acridine orange (AO) and benzothiocarboxypurine (BCP) have affinity for the nucleic acid in the parasites' nucleus. Which will exhibit an apple green or yellow fluorescence when excited by UV light at a wavelength of 490 nm. The centrifugal quantitative buffy coat or QBC II (QBC, Becton Dickinson) combines an AO-coated capillary tube and an internal float to separate layers of granulocytes and platelets using centrifugation. Parasites usually concentrate in the granulocyte-erythrocyte interface and can be viewed using a long-focal-length objective (paralens) with a fluorescent microscope. Results of experimental and field

Figure 1



Scattergram generated by an automated blood-cell analyzer for the patient with *Plasmodium vivax* malaria. Compare with Figure 2 below.

Figure 2



Scattergram generated by an automated blood-cell analyzer for a person without malaria. Adapted from: *Clin Infect Dis*. 2001;33:1944-1945.

Table

Immunochromatographic Malaria Tests

Test	Target Antigen	Species detected
Parasite F	HRP-II	*P falciparum*
ICT Pf	HRP-II	*P falciparum*
Path Falciparum Malaria IC	HRP-II	*P falciparum*
Optimal	pLDH	*P falciparum* and *P vivax*
ICT Pf/Pv	Aldolase/HRP-II	*P falciparum* and *P vivax*

studies to assess the sensitivity of QBC have varied, but the majority show sensitivities of more than 90%. The largest study of 18,845 blood samples showed a positivity rate of 25% for QBC (100% sensitivity) and 18% for G-TBF.[3]

The major advantage of the QBC is its speed and relative ease of interpretation. The disadvantages would be the need for electricity, the cost of capillary tubes and equipment, and the difficulty in species identification and quantification. An added benefit of the QBC may lie in its ability to diagnose other diseases in the febrile patient such as relapsing fever, African trypanosomiasis, and filariasis.[4-6] The QBC also gives the clinician in the field a simultaneous hematocrit and platelet count. These are extremely useful data since anemia and thrombocytopenia are important indicators of severe illness.

Another fluorescent microscopy technique is the Kawamoto technique in which a fluorescent microscope is fitted with an interference filter and AO is used to stain thin blood films. Expertise is needed to distinguish parasites from the Howell-Jolly bodies since they will stain with AO as well. Another fluorochrome technique using a solution of benzothiocarboxypurine (BCP) applied to an unfixed, dry, thick blood film has a reported sensitivity and specificity of greater than 95% for *P falciparum*. This method overcomes the necessity for rapid examination that is often needed in other fluorescence techniques.

PCR, although strictly not a rapid method, is certainly going to play an important future role in malaria diagnosis, perhaps even modifying our "gold standard." The value of PCR lies in its excellent sensitivity (able to detect ≤ 5 parasites/µl of blood) and its ability to detect all species of *Plasmodium* in nested or multiplex assays. PCR-based methods are useful for malaria studies on strain variation, mutations, and the study of parasite genes involved in drug resistance. As PCR technology improves, this technique may be able to be performed fast enough to be more useful to the clinician.

A recent congress of the World Health Organization produced a document entitled *New Perspectives in Malaria Diagnosis*. In this document, the term rapid diagnostic tests (RDTs) was restricted to immunochromatographic methods to detect *Plasmodium*-specific antigens in a fingerprick blood sample.[7] These tests can be performed in about 15 minutes by persons with minimal training and require no electricity or special equipment. These tests often have a test strip or dipstick bearing monoclonal antibodies directed against the target parasite antigen (*see Table*).

One antigen targeted is the histidine-rich protein II (HRP-II), a water-soluble protein produced by trophozoites and young (not mature) gametocytes of *P falciparum*. Three commercially available HRP-II antigen dipstick tests with significant published data are the **Parasite F, ICT *Pf***, and the **Path Falciparum Malaria IC** tests. Sensitivities of these kits are generally more than 90% at parasite densities greater than 100 parasites/µl of blood. Below this level, sensitivities fall. False negatives may be due to a gene deletion for the production of HRP-II. Therefore, a strong positive with a test such as ICT *Pf* is highly predictive of *P falciparum* parasitemia, but a negative test should not exclude the diagnosis of malaria.[8]

These 3 RDTs using HRP-II will not detect nonfalciparum malaria. False positives with rheumatoid factor may occur, though less frequently with the monoclonal IgM antibodies used in the **ICT *Pf*** and **Path Falciparum Malaria** tests. A major disadvantage of RDTs using HRP-II antigens is that in many patients the tests remain positive for 7-14 days following treatment—results that may be confused with drug resistance or treatment failure.

Parasite lactate dehydrogenase (pLDH) is a soluble glycolytic enzyme produced by asexual and sexual stages (gametocytes) of all 4 species of malaria parasites. The OptiMAL tests for *P vivax* and *P falciparum* uses 3 monoclonal antibodies that can bind to active pLDH. Two of the antibodies are panspecific, recognizing all 4 malaria species while the other detects only for *P falciparum*. These monoclonal antibodies do not seem to cross-react with LDH from other

organisms such as pathogenic bacteria, fungi, *Leishmania*, or *Babesia* spp. In one series, the sensitivity of the OptiMAL for *P falciparum* was 88% and for *P vivax* 94%.[9] Lower sensitivities are found at levels of parasitemia less than 100 parasites/µl or for *P ovale* and *P malariae*. In the future, a more sensitive monoclonal antibody may help improve detection of *P ovale* and *P malariae*.

Clearance of parasites from the blood during therapy for malaria correlates with a fall in pLDH levels that can be detected with the OptiMAL test. Therefore, tests to detect or measure pLDH might play a future role in monitoring response to therapy, especially in areas where blood films are not easily available.

Aldolase is another enzyme in the glycolytic cycle of the malaria parasite. In the **ICT *Pf/Pv*** test, panspecific monoclonal antibodies against *Plasmodium* aldolase are combined in a test with HRP-II to detect *P vivax* and *P falciparum*. Results for *P vivax* have been disappointing at lower levels of parasitemia. The **ICT *Pf/Pv*** had 96% sensitivity for *P vivax* if there were more than 500 parasites/µl of blood but had only 29% sensitivity for parasite levels less than 500 parasites/µl.[10]

According to the WHO document, an ideal RDT for malaria should 1) detect all 4 species of malaria at least as accurately as microscopy; 2) have a sensitivity of 100% for levels of 100 parasites/µl (0.002% parasitemia); 3) have a specificity of at least 90% for all species; and 4) provide quantitative information on parasite density. Also these test kits should not require refrigeration, be reliable in extreme heat, and have a shelf life of 1-2 years. Further testing in the field and technical improvements are still needed, but someday these test kits may even play a role in the self-diagnosis of malaria in travelers to remote areas. ■

Dr. Scully is a member of the Group Health Cooperative of Puget Sound, Seattle, Wash.

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Oral Care in Nursing Homes Reduces Pneumonia

ABSTRACT & COMMENTARY

Synopsis: *With oral brushing after every meal and weekly dental care, elderly nursing home residents had half as many febrile days and one third as many pneumonias, a difference that persisted whether they needed help with feeding.*

Source: Yoneyama T, et al. *J Am Geriatr Soc.* 2002;50: 430-433.

ELEVEN NURSING HOMES IN JAPAN WERE USED FOR THIS 2-year study, enrolling 417 residents with a mean age of 82 years. Only residents who were without acute disorders for the preceding 3 months were selected, and no subjects had any pre-existing pulmonary disease or required feeding tubes. No dentist had been in charge of the homes before the study began, and the majority had neglected oral care with plaque, periodontal disease, and caries.

Every study participant received a physical exam and

baseline chest x-Ray, and then were randomized to a program of oral care or control group. The oral care group received 5 minutes of oral brushing of the gums, palate and tongue (without dentures present) after every meal, and some needed further scrubbing with povidone iodine 1%. They also received plaque and calculus control weekly from dentists or dental hygienists as needed. The control group performed some toothbrushing irregularly themselves but none from caregivers. Dentures were used by 45% of the total group, and these were all brushed daily and cleaned weekly.

New pneumonias were diagnosed in 11% of the patients receiving the oral care program and 19% of the control group, a statistically significant difference. The oral care group also had less febrile days (15%) vs. the control group (29%). More pneumonias were seen in the subset of patients who needed feeding assistance, but the ones who received oral care were less likely to develop pneumonia than the control group. Death rates from the pneumonias that developed were also less in the oral care group (7%) than the control group (16%), giving a relative risk of death from pneumonia for those who did not receive oral care of 2.4.

The effect of oral care on mental status and activity was measured every 6 months by Mini Mental Status Examinations (MMSE) and Activities of Daily Living (ADL) scales. Although both showed a tendency to improve from baseline in the oral care group, only the MMSE had a significant difference at the end of the 2- year study.

■ COMMENT BY MARY ELINA FERRIS, MD

This article provides a strong case for more attention to oral care for the elderly. Besides the obvious benefits of a cleaner-feeling mouth, less periodontal disease, possibly better chewing ability and social interaction, there is now an association of less pulmonary infections with conscientious mouth care. An accompanying editorial in this journal calls it "cost-effective to maintain but costly to ignore."[1] Since pneumonia is the leading cause of death and hospitalizations in nursing homes, even a 10% decrease would save more than $800 million in the United States annually. This could easily justify a full-time aide solely for oral care at each of our nation's 19,000 nursing homes (at an estimated cost of < $500 million/year).

While the study might be criticized as starting with a neglected group of elderly at baseline, actually other studies have confirmed the poor state of oral care in institutions.[2] Regulations and enforcement have not emphasized oral care in the past, and minimal training is provided to the nursing aides who generally implement the care. This study provided weekly dental professional care, which may not be feasible in many settings, so it remains to be demonstrated what effect a more modest improvement in oral care would produce.

The connection between oral pathogens and pneumonia, acquired through routine aspiration, has been suggested in epidemiological studies,[3] and anerobic bacteria from the mouth have been demonstrated in transtracheal aspirates.[4] Although this study does not prove that oral flora are the source of pulmonary infections, it lends support to greater emphasis on this often neglected aspect of nursing home care. ■

References

1. Terpenning M, et al. *J Am Geriatr Soc.* 2002;50: 584-585.
2. Mojon P, et al. *Gerodontology.* 1997;14:9-16.
3. Terpenning M, et al. *J Am Geriatr Soc.* 2001;49: 557-563.
4. Finegold SM. *Rev Infect Dis.* 1991;13:S737-S742.

CME Questions

9. Which of the following is correct?

a. Automated blood analyzers (eg, Abbott CD3500) have greater sensitivity in the detection of malaria parasites in peripheral blood than does light microscopy.
b. Automated blood analyzers (eg, Abbott CD3500) cannot detect *P falciparum* in peripheral blood.
c. Acridine orange stains the endoplasmic reticulum of malaria parasites.
d. The QBC test, using acridine orange staining, can detect, in addition to Plasmodia, Borrelia, trypanosomes and filaria in peripheral blood.

10. Which of the following is correct with regard to the treatment of onychomycosis in the LION and the LION Icelandic Extension Studies?

a. Itraconazole was superior to terbinafine at 18 months.
b. At the end of a mean follow-up of 54 months, terbinafine was superior to itraconazole.
c. Terbinafine is more likely than itraconazole to be associated with drug-drug pharmacokinetic interactions.
d. Itraconazole, in contrast to terbinafine, does not have a potential interaction with phenytoin.

In Future Issues:

Approach to the Patient with Chronic Hepatitis C Infection