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principle 

Although there is an abundance of re-
cently published results from controlled
clinical trials for the newer macrolides (as
reviewed by Lynch and Martinez [8]), the
new fluoroquinolones, and a combination
of β-lactams with or without macrolides,
reports of recent data on doxycycline are
very limited. A recent review that included
a MEDLINE search for the evaluation of
doxycycline in the treatment of CAP re-
vealed only 2 studies published since 1990,
only 1 of which was performed after 1995,
when the prevalence of penicillin-resistant
S. pneumoniae (PRSP) was relatively high
(>10%) [9]. In this latter study, only 43
patients were treated with doxycycline; of
these, only 8 patients had documented in-
fecion due to S. pneumoniae (none with
PRSP) [10].

We agree with Dr. Johnson [1] that
doxycycline represents a potentially inex-
pensive, fluoroquinolone-sparing alter-
native for the treatment of CAP and that
effective options for therapy that take the
pressure off use of fluoroquinolones is im-
portant. Although doxycycline is included
as an option in the recent practice guide-
lines, it is rarely used. In a review of an-
timicrobial use by >2000 patients with
CAP who were treated as outpatients, Gil-
bert et al. [11] found that, although 73.4%
of outpatients received a macrolide agent,
only 3.5% received doxycycline. Since
doxycycline is generic, there is no cor-
porate advantage for promotion of the
drug or for sponsoring a clinical trial. We
agree with Dr. Johnson that a well-con-
trolled clinical trial is indicated, and we
echo his call for alternative sources for
sponsoring such a study. Use of doxycy-
ccline should prove to be a cost-effective
therapy for the treatment of CAP and is
an important therapy option that deserves
more use and study.

Fernando J. Martinez, Joseph P. Lynch III, and Thomas M. File, Jr.

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Schizophrenia after Prenatal Exposure to Toxoplasma gondii?

Sirs—Recently, Clinical Infectious Diseases published a study about a possible association between Toxoplasma gondii infection and schizophrenia [1]. Individuals with first-episode schizophrenia were found to have significantly increased levels of IgG-, IgM-, and IgA-class antibodies to Toxoplasma, compared with healthy control subjects. However, because of the cross-sectional nature of the study, questions remained concerning the timing of the infection. Other studies in this field have included attempts to link schizo-
phrenia to infections that occur during pregnancy—in particular, influenza and rubella. The initial findings of an association between schizophrenia and influ-

Because infection with T. gondii is one of the most common infections to occur during pregnancy, we examined the relation-
ship between congenital toxoplasmosis and schizophrenia. We conducted a 30-year psychiatric follow-up study of 13
persons known to have congenital toxoplasmosis. These patients were members of a cohort who had been recruited during a prospective study of 1821 pregnancies in Amsterdam during the period 1964–1965. Although these persons were asymptomatic at birth, a 20-year follow-up study showed that 9 of them developed signs of chorioretinitis [5]. We attempted to approach all 13 subjects for a series of investigations, including an interview about psychiatric characteristics that was based on the Comprehensive Assessment of Symptoms and History (CASH) [6] and the Schedule for Affective Disorders and Schizophrenia–Lifetime version (SADS-L) [7]. Appropriate informed consent was obtained, and the study was performed in accordance with the standards of the Human Ethics Committee of the University Medical Center in Utrecht (The Netherlands).

Seven of the 13 subjects (age, 31–32 years) were examined. Five subjects refused to collaborate, and 1 person, who had been adopted as a child, could not be examined because he had committed suicide at the age of 20 years. The latter subject had been aggressive in school, and he was found guilty of arson on many occasions. A psychiatrist had made a diagnosis of antisocial personality disorder.

Five persons (1 man and 4 women) from the group of 7 examined subjects did not report having any psychiatric abnormalities and were considered to be healthy. One male patient reported having had a major episode of depression at the age of 30 years and a long-standing cannabis dependence. One patient was known to have had a gender-identity disorder and had undergone male-to-female surgical reassignment. In utero, this subject had been exposed to diphantoin, and there is evidence to suggest that exposure to this agent may lead to gender-identity disorder [8].

The results of Sabin-Feldman tests were positive for 6 patients, with titers ranging from 1:2 to 1:128. For 1 male subject, the result of a Sabin-Feldman test was negative, although all previous test results had been positive (in 1984 and 1986, the titers were 1:128). MRI of the brains of the 7 examined subjects revealed no clinical abnormalities.

To our knowledge, this is the first cohort-based psychiatric follow-up examination of adult patients with congenital toxoplasmosis. The results show that persons with congenital toxoplasmosis do not necessarily develop schizophrenia during early adulthood, but the small number of subjects precludes the drawing of any conclusions about a normal or possibly elevated risk of developing schizophrenia.

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References

Malnutrition and Pulmonary Tuberculosis

Sir—We read with interest the article by Oursler et al. [1] in which the authors concluded that comorbid illnesses and conditions, such as diabetes mellitus, renal failure, chronic obstructive pulmonary disease, and immunosuppression, are important predictors of mortality among patients with pulmonary tuberculosis (TB). These observations confirm the findings of earlier reports [2, 3] and provide additional evidence that pulmonary TB continues to have a significant associated mortality rate, even in industrialized nations where advanced medical technology is available. The authors also found that the clustering of pulmonary TB infections, as determined by DNA fingerprinting, was not an independent factor associated with death.

Although the investigators made an effort to obtain a history of weight loss, little attention was given to this factor as a possible predictor of mortality. In a study of hospitalized patients, malnutrition (defined as a body mass index of <90% of ideal body weight or considerable recent weight loss, as recorded by the evaluating clinician) was an important risk factor for a poor outcome [4]. It has also been observed that the mortality rate was 60% for patients with pulmonary TB who had respiratory failure necessitating mechanical ventilation, despite the administration of appropriate 4-drug anti-TB therapy. Nutritional status, as measured by serum albumin concentration and hemoglobin level, was an important predictor of survival [5].

Drug therapy and nutritional balance are 2 interconnected aspects of therapy for TB infection that are within the control of the physician. Other variables, such as the pa-