orrages, Osler’s nodes, Janeway lesions, and clubbing of the fingers. Neurological examination findings were within normal limits.

Laboratory evaluation revealed the following values: WBC count, 8,600/mm³ (72% neutrophils); hemoglobin level, 9.6 g/dL; platelet count, 436,000/mm³; and erythrocyte sedimentation rate, 95 mm/hour. One of six sets of blood cultures yielded gram-positive rods, subsequently identified as *A. meyeri* by use of the Rapid ANA II system (Innovative Diagnostic Systems, Norcross, GA). The isolate was susceptible to penicillin and clindamycin, but resistant to metronidazole by use of Etest (AB BIODISK, Solna, Sweden). A two-dimensional transthoracic echocardiogram revealed masses (measuring 2.5 cm in diameter) on the mitral valve consistent with vegetations. A transesophageal echocardiogram confirmed a mitral valve vegetation. The patient was treated with ampicillin/sulbactam and the fever promptly subsided. Antibiotic treatment was continued for 6 weeks. The patient was doing well to treatment, without further complication or relapse.

Unlike other *Actinomyces* species, *A. meyeri* seems to have a tendency to disseminate [4]. The sites involved include lungs, bone, skin and soft tissue, breast, liver, and brain [4, 5]. There are no previous reports of endocardial involvement. A review of the literature revealed nine cases of primary actinomycotic endocarditis from 1939 through February 1998 [2, 3]. Among those nine cases, *Actinomyces israelii, Actinomyces bovis* and *Actinomyces viscosus* were implicated in two cases each. The causative species for the remaining three cases could not be determined. There are no distinct clinical features that separate actinomycotic endocarditis from endocarditis due to other bacteria [2]. Our patient had an indolent course and fever was the only clinical manifestation. Given the pathogenesis of actinomycosis, the original site of infection in our patient was probably an undetected periodontal infection.

*Actinomyces* species may be difficult to grow in blood cultures. Among the cases of actinomycotic endocarditis reported previously ~67% were associated with blood cultures positive for *Actinomy-

Hypothyroidism in a Patient Receiving Treatment for Multidrug-Resistant Tuberculosis

Drug-induced hypothyroidism is an infrequent side effect of therapy with either ethionamide or p-aminosalicylic acid (PAS). The frequency of this rarely reported adverse reaction is believed to be increased when ethionamide and PAS are taken together. A MEDLINE search for ethionamide and *p*-aminosalicylic acid–induced hypothyroidism yielded only a few cases. We describe a patient with mild hypothyroidism who was receiving therapy for multidrug-resistant tuberculosis (MDR-TB), tuberculosis that is resistant to at least isoniazid and rifampin, with a regimen that contained both ethionamide and PAS granules.

A 46-year-old man was admitted to a New York City Department of Health Chest Clinic for continuation of directly observed treatment (DOT) for MDR-TB. The patient had been hospitalized at another facility where he had been treated for the past 5 1/2 months with an antituberculous regimen consisting of cycloserine (500 mg at 9 A.M. and 250 mg at 5 P.M.), ethionamide (500 mg at 9 A.M. and 250 mg at 5 P.M.), ofloxacin (400 mg b.i.d.), and PAS granules (4 g t.i.d.). On admission to the chest clinic, the patient complained of nausea and epigastric pain associated with ingestion of the antituberculosis agents. He also complained of a 30-pound weight gain over the past 6 months and constipation that he had had for many years. No abnormalities were evident on physical examination; the patient weighed 254 pounds and his thyroid was not palpable. The results of a complete blood count and blood chemistry panel (including electrolyte, glucose, blood urea nitrogen, creatinine, uric acid, and cholesterol levels, and liver function tests) were all within normal limits.

A thyroid profile performed when the patient was admitted to the chest clinic on 12 December 1997 was notable for several abnormalities: serum thyroid stimulating hormone (TSH) was elevated (28 μU/mL; normal, 0.4–4.2 μU/mL), thyroxine level (T4) was low (3.1 μg/dL; normal, 4.5–12.0 μg/dL), calculated free T₄...
was decreased (0.94 U; normal, 1.75–3.80 U), and the triiodothyronine (T3) uptake was normal at 30%.

The patient continued DOT at the chest clinic; he received ofloxacin (800 mg once daily), cycloserine (500 mg in A.M. and 250 mg in P.M.) and ethionamide (500 mg in A.M. and 250 mg in P.M.). Therapy with the PAS granules was discontinued when the patient was admitted to the chest clinic, since this medication was believed to be the cause of the nausea and epigastric pain. The patient was observed at the clinic ingesting all of his medications on a 5-day-per-week schedule (excluding Saturdays, Sundays, and evening doses). The patient remained 100% adherent with DOT, taking ofloxacin, cycloserine, and ethionamide without experiencing gastrointestinal intolerance or any other difficulties. A thyroid profile that was repeated on 14 January 1998 after 1 month of treatment with the above regimen (excluding the PAS granules) showed the following results: the TSH level was decreased (9.00 μU/mL), the T4 level was normal (6.00 μg/dL), and the calculated free T4 level was normal at 2.23 U. A thyroid profile repeated on 17 March 1998 after 3 months of treatment at the chest clinic showed continued improvement. The TSH level was 4.6 μU/mL, the T4 level was 5.2 μg/dL, and the calculated free T4 was 2.12 U. At no time during treatment did the patient receive thyroid replacement therapy.

Ethionamide and PAS have each been reported as causes of goiter, with or without hypothyroidism in some patients [1–3]. In 1954, Edwards et al. [1] reported studies in patients that showed that the sodium salt of PAS did not interfere with the iodide concentrating mechanism of the thyroid but inhibited the synthesis of thyroid hormone by blocking the organification of iodide in the thyroid.

In 1984, Drucker et al. [2] studied the goitrogenic effect of ethionamide in vitro. They showed that ethionamide inhibited the synthesis of thyroid hormones by blocking both the uptake and the organification of iodine in cultured ovine thyroid cells [2]. Thyroid hormone replacement might prevent the development of PAS and ethionamide-induced goiter [1, 2].

To our knowledge, we have described the first case of hypothyroidism in a patient receiving therapy with both ethionamide and PAS granules that abated after discontinuation of PAS therapy. This would strongly suggest that the PAS granules were the cause of the thyroid abnormalities in this patient. It is suggested that patients who are being treated with PAS or ethionamide may develop hypothyroidism more often than generally recognized and that appropriate tests for hypothyroidism may be indicated for such patients.

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References

Rapid Development of Indinavir-Induced Asymptomatic Crystalluria in a Human Immunodeficiency Virus–Negative Patient

Indinavir-induced crystalluria is a syndrome that has been described recently only in patients with AIDS [1–3]. The syndrome comprises a constellation of symptoms including flank pain, pyuria, transient renal dysfunction, and possible interstitial nephritis. The renal damage appears to be transient and consists mainly of interstitial nephritis and chronic inflammation with transient elevation of serum creatinine levels. The cumulative frequency of flank pain and crystalluria seem to increase as the duration of indinavir therapy increases. Women appear to be affected predominantly, although the number of cases reported so far is small and thus insufficient to draw accurate conclusions [1]. In addition, isolated pyuria in association with indinavir therapy has been described; it seems to disappear when therapy with the agent is discontinued, and it is not associated with urinary tract infections [1]. The onset of this syndrome occurs within a few weeks to months after initiation of indinavir therapy [1, 2]. The crystals have been described as colorless, pointed needles in patterns such as rosettes, fans, and starbursts that are arranged in rectangular plates and sheaves [4]. Indinavir is metabolized primarily in the liver, but 10% of the compound is excreted intact in the urine [5]. In addition, in a recent study [6], the urinary calculi recovered

Figure 1. Light microscopic appearance of indinavir crystals in a fresh urine specimen, obtained from an HIV-negative patient who sustained a needle-stick injury, showing various shapes and sizes of needle-shaped crystals.