serve only for metabolic conversion of exogenous chemicals. On the contrary, MFO enzymes are also involved in important endogenous functions (*22*), and it may be some of these that are more truly indicative of the ancestral activities of the system. But secondary plant substances are ubiquitous and of broad potential offensiveness, and, in the world of today, they may be the major group of hazardous substances against which the MFO enzymes of herbivores must operate.

A point of further evolutionary interest is that the MFO systems of animals are not "foolproof." Being programmed primarily to effect lipophile-hydrophile conversions rather than detoxifications per se, MFO enzymes sometimes transform substances that are initially relatively innocuous into ones that are actually toxic. Substances thus "bioactivated" include not only certain synthetic compounds (*23*), but also some familiar natural products (*24*). Among the latter are the so-called pyrrolizidine alkaloids, a group of widely distributed plant substances converted by mammalian MFO activity into hepatotoxic pyrroles (*25*). Plants that produce such bioactivatable compounds may, in effect, have succeeded in overcoming the biochemical defenses of their herbivorous enemies.

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Asymptomatic Gonorrhea in Men: Caused by Gonococci with Unique Nutritional Requirements

Abstract. *In a retrospective case-control study, gonococci with nutritional requirements for arginine, hypoxanthine, and uracil were recovered from 24 of 25 men with asymptomatic gonorrhea and 10 of 25 men with symptomatic gonorrhea (P = .0001). These strains represent a smaller proportion of gonococcal isolates from blacks than from whites. Asymptomatic urethral infection is important in the epidemiology of gonorrhea, particularly among whites.*

The proportion of heterosexual men with gonorrhea who lack signs or symptoms of urethritis is low among men who voluntarily seek care in venereal disease clinics (*1*), but is high among infected men brought to treatment because they were named as sex contacts of women with gonorrhea. No signs or symptoms were noted in 44 percent of culture-positive sex partners of women with acute pelvic inflammatory disease (*2*), in 57 percent of infected sex partners of women with disseminated gonococcal infection (DGI) (*3*), and 39 to 56 percent of infected sex partners of infected women detected by routine screening in a family planning clinic (*4*). Thus men with asymptomatic infection are important as transmitters of gonorrhea.

It has not been determined whether it is the characteristic of the host or the organism, or a combination of both, which determine whether urethral gonococcal infection produces urethritis. However, it is known that many men with DGI have asymptomatic urethral infection as the apparent primary focus from which their bacteremia arises (*5*), and most gonococci which cause DGI are uniquely susceptible to penicillin G (*6*), and resistant to the complement-dependent bactericidal action of normal human serum (*7*). In some areas of the United States, isolates from patients with DGI also have unique nutritional requirements for arginine, hypoxanthine, and uracil on chemically defined media. For example, in Seattle, gonococci whose nutritional requirements include arginine, hypoxanthine, and uracil ($Arg^-Hyx^-Ura^-$) were recovered from 89 percent of patients with DGI, and only 38 percent of patients with uncomplicated gonococcal urethritis (*8*).

Our case-control study was undertaken to determine whether Arg^-Hyx^-

Ura⁻ was also associated with asymptomatic gonorrhea in men who did not have DGI, and were not sex partners of patients with DGI. The asymptomatic cases consisted of 20 white and 5 black asymptomatic heterosexual men who were examined because they had other venereal diseases, or because they were named as contacts of women with gonorrhea. All 25 denied recent or current symptoms of urethritis, and no urethral exudate was detected by urethral stripping. None had had sexual exposure during the 7 days prior to treatment, and thus all were beyond the usual incubation period of gonorrhea. *Neisseria gonorrhoeae* was isolated from the urethra of each case. Each asymptomatic case was matched by age and race with another heterosexual male control with symptomatic gonococcal urethritis treated at the same clinical facility within 30 days of the case with which they were matched.

Specimens were obtained for culture from both the asymptomatic cases and the symptomatic controls by inserting a urethrogenital swab into the urethra. The swabs were inoculated onto a selective medium, consisting of 1 percent V-C-N Inhibitor (Baltimore Biological Laboratory, BBL), 1 percent IsoVitaleX (BBL), 5 percent "chocolatized" sheep blood, in gonococcal (GC) base agar (BBL), and incubated at 36°C in candle jars. All isolates were identified by Gram stain, oxidase reaction, colonial morphology, and sugar degradation reaction. All isolates were tested for nutritional requirements for arginine, hypoxanthine, uracil, methionine, and proline, as described (*8*), except that agarose was used instead of methanol-extracted agar to give better growth of the Arg⁻Hyx⁻Ura⁻ strains.

Arg⁻Hyx⁻Ura⁻ strains were recovered from 96 percent (24/25) of the asymptomatic men and from 40 percent (10/25) of the symptomatic controls ($P < .0001$, Fisher's exact test). The reason why Arg⁻Hyx⁻Ura⁻ strains are more likely than other strains to cause asymptomatic infection is not known. These nutritional requirements per se might limit the intracellular or extracellular growth of these strains. Alternatively, it is possible that these phenotypic markers are coincidentally linked to another determinant responsible for the failure to cause inflammation.

The results were analyzed by race; Arg⁻Hyx⁻Ura⁻ strains were isolated from 95 percent (19/20) of the asymptomatic white men, 100 percent (5/5) of the asymptomatic black men, 45 percent (9/20) of the symptomatic white men, but from only 20 percent (1/5) of the symptomatic black men. The difference between symptomatic black and white men is not significant in this small sample, but in a study of 214 gonococcal isolates collected by Thornesberry and Wiesner from men in nine U.S. cities participating in the CDC (Communicable Disease Center) Cooperative Gonorrhea Therapy Study, the proportion of isolates which was Arg⁻Hyx⁻Ura⁻ was five times higher for whites than for blacks ($P < .001$) (*9*).

These data may help explain reported racial differences in the incidence of gonorrhea. Age-specific case rates of gonorrhea were reported separately for whites and nonwhites in the United States until 1970. In that year, for the peak age group 20 to 24, the reported incidence of gonorrhea per 100,000 population was 1013 for white men, and 14,061 for nonwhite men (*10*).

Our studies suggest that the higher incidence of gonorrhea among nonwhites is attributable to the symptom-producing strains other than Arg⁻Hyx⁻Ura⁻, perhaps because the symptom-producing strains are being transmitted more efficiently or eliminated less efficiently among nonwhite than among white populations. Some evidence supports the second possibility. Darrow found that 28 percent of black men delayed 15 or more days after the onset of symptoms of gonorrhea before seeking treatment, but only 11 percent of white men delayed this long (*11*). The reason for the differences in illness behavior is not apparent, and may relate to socioeconomic status, differences in the availability or acceptability of health care, or attitudes towards illness. In a white population, perhaps infections with symptom-producing strains tend to be treated promptly, and hence eliminated from the population, whereas the Arg⁻Hyx⁻Ura⁻ strains are allowed to persist because they produce no symptoms. However, in nonwhite populations, infections with symptom-producing strains may have a better chance of transmission because they are treated after a longer duration of symptoms.

Our findings are of considerable public health significance. The data suggest that the control of gonorrhea among nonwhites may rest on identification and earlier treatment of men with ignored symptoms of gonorrhea. Conversely, the further control of gonorrhea among whites depends to a greater extent upon a reduction in the reservoir of strains which persist because of their ability to cause asymptomatic infection.

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Aspergillus oryzae (NRRL Strain 1988)

The technical comment "*Aspergillus oryzae* (NRRL strain 1988): A clarification" by Fennell (*1*) apparently requires further clarification, since Morse has expressed the opinion that "the question remains open" (*2*).

We offer the following additional information that may help settle the question of contaminant versus variant. Our laboratory was one to which Morse sent a subculture of their NRRL 1988 "variant." We confirmed its capability for producing aflatoxins and characterized the mold as typical of *Aspergillus parasiticus*. Since El-Hag and Morse had reported receiving a similar variant from the American Type Culture Collection subculture (ATCC 9362) of the same strain of *A. oryzae* they had received from the USDA Northern Regional Research Laboratory (NRRL), we obtained ATCC 9362 directly from ATCC. This subculture did not produce aflatoxin on any of the substrates usually employed for this purpose, and its culture characteristics were typical of *A. oryzae*. The "variant" was therefore not