detection markers. Some estimate glomerular filtration rate (cystatin C), some reflect on renal injury (actin, kidney injury molecule-1, Na^+/H^+ exchanger isoform-3), and others show inflammation associated with acute renal failure (interleukins 6, 8, and 18).[12–16] For NGAL, the next steps are evident. Once the results of Mishra and colleagues have been confirmed, an automated robust assay besides ELISA is needed. To be acceptable clinically, the assay should measure NGAL rapidly, day or night. All proposed markers for early detection of acute renal failure require vigorous prospective evaluation in large populations. Initial performance must be reproduced at multiple study sites. Once valid biomarkers for early detection have been identified, we should evaluate them in combination. Why limit ourselves to one marker? As shown in cardiology, haematology, and hepatology, we may extend our information to differentiate causes, stages, or subpopulations of patients with acute renal failure by a combination of markers. This combination of markers could eventually lead to differentiated preventive and therapeutic approaches. For the present, we still have to content ourselves with available inadequate markers that do not permit early detection. However, the data for NGAL and other biomarkers encourage optimism that better markers are on the horizon that might affect patients' management and outcome. As with NGAL, such marker(s) might not only be an early sign of acute renal failure but also a mediator of repair mechanisms, which would further enhance its value. Exciting times lie ahead of us.

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I have received fees for speaking from DadeBehring, Marburg, Germany.

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Can DOTS control multidrug-resistant tuberculosis?

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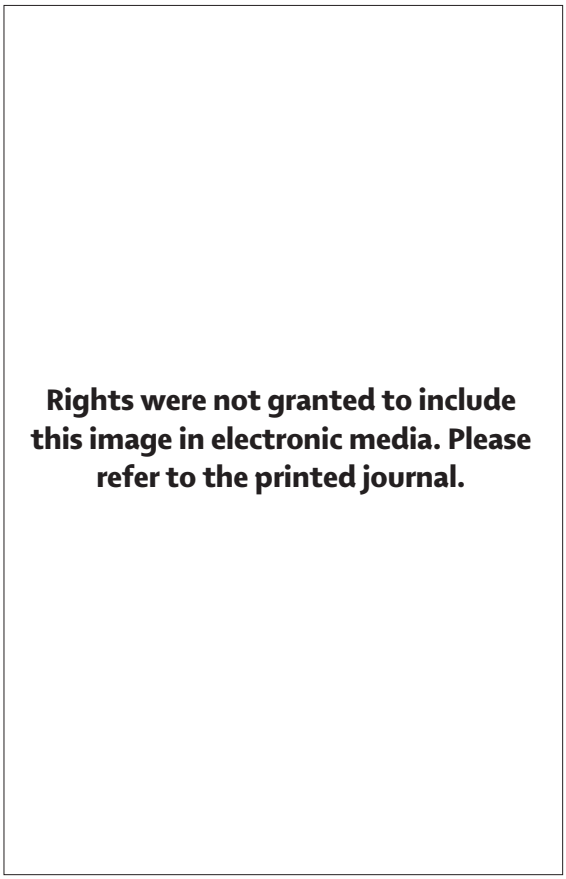
WHO's strategy for DOTS is the main weapon against the global tuberculosis epidemic. DOTS was originally an acronym to emphasise directly-observed treatment and short-course chemotherapy with combinations of first-line drugs. It is now better thought of as the brand name of a broader public-health strategy, including diagnosis by sputum-smear microscopy, mechanisms for supporting patients over 6–8 months of treatment, systems for the maintenance of drug supplies, and for recording and reporting. There is abundant evidence that, when all the recommended procedures are in place, chemotherapy under DOTS can achieve cure rates of 90% or more, and prevent the emergence of resistance to first-line drugs. However, it is equally clear that, in populations where resistance has already spread because therapy has been inadequate in the past, first-line drug regimens are associated with higher rates of treatment failure and death.[1]

The probability of failure is especially high for patients carrying *Mycobacterium tuberculosis* resistant to both isoniazid and rifampin (ie, multidrug-resistant

tuberculosis. Treating patients with multidrug-resistant tuberculosis with first-line drugs can prolong an episode of illness, and thereby increase transmission. It has long been understood that a strain of drug-resistant *M tuberculosis* can spread through a population or die out, depending on both the intrinsic biological fitness of the strain and on the quality of treatment available to patients.[2,3] Although some recent theoretical work has reaffirmed the principles,[4,5] the scientific literature is desperately short of quantitative studies that specify the conditions under which multidrug-resistant tuberculosis will propagate or be eliminated in real control programmes. The national tuberculosis programmes in Hong Kong[6] and South Korea,[7] among others, have shown that they can reduce the number and proportion of patients carrying drug-resistant strains, but their success might not be due entirely to DOTS because these programmes also relied, to some degree, on second-line drugs.

In this context, the work of Kathryn DeRiemer and colleagues, in this issue of *The Lancet*, provides important new evidence that a DOTS programme with only first-line drugs can reduce the transmission of drug-resistant tuberculosis, especially multidrug-resistant tuberculosis. In a population-based prospective study of 436 patients in Orizaba Health Jurisdiction in southern Mexico, these investigators found that the incidence of previously untreated, drug-resistant cases fell from 9·4 to 1·5 per 100 000 people per year between 1996 and 2000. The incidence of patients presenting for retreatment dropped from 11·1 to 3·5 per 100 000 per year over the same period. At the outset, 22% of previously untreated patients with pulmonary tuberculosis were carrying drug-resistant strains, and 6·7% were patients with multidrug-resistant tuberculosis. In the final year of the study, only 7·8% of new patients were carrying drug-resistant strains, and there were no cases of multidrug-resistant tuberculosis. These data add to an earlier study by the same research group,[8–10] and these encouraging results suggest that the net genetic fitness of the multidrug-resistant strains circulating in this part of Mexico is less than that of the drug-susceptible strains, and too low for the multidrug-resistant strains to be maintained.

Together, these data tell a compelling story about the control of multidrug-resistant tuberculosis by a good basic DOTS programme. There are, however, some outstanding questions about the interpretation of the findings. The first is whether it is possible in DeRiemer and colleagues' study clearly to distinguish the different effects of DOTS on the prevalence and incidence of drug-resistant tuberculosis. Conspicuously, the numbers of new and retreatment cases that were drug-resistant, and in the proportion of cases that were part of genotypic clusters, fell mostly during the first year of the study. This is what would be expected if the first effect of the DOTS programme in 1996 was simply to clean up the backlog of chronic (prevalent) and previously undiscovered cases. DeRiemer argues that is not the main effect because the number of cases detected in the first year of the DOTS programme was no higher than in the preceding 3 years. However, prevalence can be reduced by improving the quality of treatment, as well as by increasing the rate of case detection. The cure rate under DOTS did improve between 1995 and 2000,



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DOTS at Navrongo Hospital, Ghana

and it was presumably better during this period than in preceding years.

The effect of DOTS on the incidence rate of tuberculosis also presents a puzzle. Incidence fell by 54% over the 5-year period, but 44% of the reduction happened in the final year of the study. Annual rates of reduction in tuberculosis incidence as high as 44% are extremely rare because, even if transmission is stopped instantly, new cases of tuberculosis continue to be generated from a reservoir of latent infections. The explanation for the sudden fall might lie partly in the random fluctuations of small numbers: during 1999–2000, only 38 new cases were discovered in the 300 000 people living in Orizaba. Nonetheless, a study of incidence rates in the years since 2000 should be illuminating.

Despite these anomalies, it seems clear that the DOTS programme in Orizaba has improved the quality of treatment and cut the transmission of *M tuberculosis*, including drug-resistant strains. This is not to conclude, however, that DOTS is enough. Even with the best possible application of first-line treatment, patients with multidrug-resistant tuberculosis still have a lower chance of being cured and of surviving an episode of illness in this part of Mexico and elsewhere.

As DOTS programmes around the world become robust enough to manage the majority of patients who carry drug-sensitive strains,[11,12] programme managers can begin to provide a better service for the drug-resistant minority. In an ideal world, every patient with multidrug-resistant tuberculosis would be identified by drug-sensitivity testing, and given a combination of first-line and second-line drugs that is individually tailored to the pattern of resistance. In practice, adapting treatment to the needs of each patient is prohibitively costly in many settings, even with the lower prices of drugs procured through the Green Light Committee of the Stop TB Partnership.[13] Because some of the drugs are toxic and administered by injection, individualised treatment requires a high level of medical expertise. The few ambitious programmes that have taken this approach have achieved high rates of cure for patients with multidrug-resistant tuberculosis, as expected, but only on a small scale.[14,15]

Tuberculosis-control programmes in high-burden countries will often have to opt for something less than individualised testing and treatment. One way to improve on the basic package of care is to offer, to patients that have failed their first course of treatment, a fixed retreatment regimen containing second-line drugs. In Peru and Bangladesh, this approach has yielded higher cure rates for patients undergoing retreatment at not much extra cost.[16,17]

As the evidence base develops, for example through the DOTS-Plus programme for resistance management,[18,19] the choices facing programme managers will become clearer. In the meantime, the Orizaba study provides some reassurance that the introduction of DOTS will usually improve the standard of care for patients and reduce transmission, rather than fanning the flames of an epidemic of multidrug-resistant tuberculosis.

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We declare that we have no conflict of interest.

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Ethnicity in sexually transmitted infections and sexual behaviour research

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Ethnicity has been a contentious issue in sexually transmitted infection and HIV research, partly because it contributes to the mythology of beliefs that might add to discrimination, and partly because it is an apparently potent marker of risk. A study by Kevin Fenton and colleagues in today's *Lancet* is a welcome addition to the evidence, and provides more light than heat. These investigators provide a comprehensive view of sexual behaviour across ethnic groups in Britain, including solid information about differences in sexual behaviour. However, sexual behaviour (the zero-order variable underlying the risk of sexually transmitted infection) might also be subject to other ethnocultural variables, including religion, gender, and social class, that are at present captured as ethnicity.

Religion appears to be protective for some of the ethnic groups, particularly in women, perhaps because it often prescribes different sex-related norms such as the importance of virginity before marriage for women. For example, the differences and their direction in cohabiting between men and women from Pakistani and Indian backgrounds (who might otherwise be referred to collectively as Asian)[1] is probably based on traditional Muslim and Hindu religious values and interacting gender, education and class prescriptions (education frequently modifies traditional gender and class prescriptions for both male and female behaviour). In addition to religious background, ethnic culture may also influence gender roles and provides norms and sanctions that regulate sexual risk-taking and other risk behaviours.[2] Social class might also be a marker for cultural differences not captured by existing social-class classifications. The values and beliefs conferred by social class and status in one country might not be equivalent to the classification system for social class of another—eg, in some Indian populations, caste-class interactions, particularly where class is socioeconomically determined. Fenton and colleagues point to a possible social desirability effect on some of the sexual behaviour questions. Gender roles conferred by ethnocultural background might be differently influencing the responses of men and women.[3]

Fenton and colleagues' study strongly suggests that gender roles and norms might influence the behaviour of men and women, and that they might exacerbate differences in sexual behaviour within specific ethnic groups. However, the overall pattern that emerges indicates that the expectations about the sexual behaviour of men and women might also transcend group differences. Sometimes it is the interactions between ethnicity and gender that contribute to sexually transmitted infection rates. Further, Fenton alerts us to the fact that discrimination and stigmatisation secondary to race and ethnicity also need to be considered as potentially having direct and indirect effects on sexual behaviour and the seeking of treatment.

Ethnicity requires the self-identification of survey participants, which is often constrained by ethnic categories provided in survey interviews. Black African or black Caribbean appear to designate geographic regions more than ethnic categories, and it is important to clarify where racial definitions are (or are not) ethnic ones. Grouping individuals according to categories that do not map to the social characteristics which influence sexual behaviour might mask important differences that more specific categories would be able to reveal. Ethnic group homogeneity can be tested as an empirical