of violence with mental illness. Their analysis of the records of 1241 men remanded in Brixton prison showed that in the group charged with homicide just over a third were psychiatrically abnormal; five (11%) of those convicted were schizophrenic. Despite the risk of undercounting this was a disproportionately large group in relation to expectations from epidemiological data, and the number of schizophrenic patients who had been violent towards others without resulting fatality exceeded expectations by over 22 times.

In 1939 Lionel Penrose showed a negative correlation between the prison population, the homicide rate, and the availability of mental hospital beds. Since 1954 the number of patients in mental hospitals in England and Wales has declined by 67 000, but only 3010 expatients are supported by local authorities.[27] These figures suggest one explanation for the discrepancy between the current findings of Taylor and Gunn and those of several previous studies,[28–30] all of which failed to find any appreciable excess of schizophrenic patients prosecuted for violent crimes. As a society we have been failing in our care of schizophrenics. Their difficulties in obtaining psychiatric treatment,[27 31] their high suicide rates after discharge from hospital,[32] and the prevalence of serious mental illness among the destitute and in prison,[33 34] are further indictments of "community care" policies.[35–37] The links between violence in our society and the neglect of mental illness by successive governments need wide publicity —and the government should not be allowed to remain silent on this issue.

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Rifampicin in non-tuberculous infections

A recent review of the use of rifampicin in non-tuberculous infection in North America raises the question of current practice in Britain.[1] Should rifampicin be used more widely? Or should it be reserved for a few specific indications?

Rifampicin was synthesised in 1965 and rapidly recognised as having bacterial activity against *Mycobacterium tuberculosis*. It also has a broad antimicrobial spectrum against Gram positive and Gram negative organisms and can penetrate most tissues because it is lipid soluble. Despite these attributes, however, it has been little used in non-tuberculous infections owing to fears of the development of resistance by *M tuberculosis* and other bacteria. Rifampicin is also relatively expensive—though considerably cheaper than many of the more recent cephalosporins—and potentially toxic.

One problem encountered early in clinical experience was the rapid development of bacterial resistance when rifampicin was used alone. Rifampicin's antibacterial activity depends on its ability to bind and inactivate bacterial DNA dependent RNA polymerase. Resistant strains occur during monotherapy by a modification altering the binding of rifampicin to this target enzyme. This mechanism of resistance is specific to rifampicin.

Rifampicin is said to be the most potent antistaphylococcal agent available, but it must be used with another agent to avoid resistance.[2] One report described synergy between rifampicin and oxacillin, which was influenced by both the concentration of the antibiotics and the bacterial inoculum used in laboratory studies—but these did not necessarily predict the clinical outcome.[3] In clinical practice rifampicin is a valuable reserve drug for use in refractory *Staphylococcus aureus* infections, including endocarditis, and is effective for staphylococcal infections in patients with chronic granulomatous disease because of its effective penetration of neutrophils.[4] Rifampicin is usually active against *Staph aureus* resistant to methicillin and might be considered for use in individual patients infected with a resistant strain, but experience shows that its use on a large scale would inevitably be associated with the appearance of rifampicin resistant *Staph aureus*.[5] *Staph epidermidis* has a less predictable sensitivity pattern than *Staph aureus*: it is often multiresistant, though usually sensitive to rifampicin. Rifampicin has been recommended as an initial choice of treatment for endocarditis due to *Staph epidermidis*,[6] and also in infections of cerebrospinal fluid shunts due to this organism.[7]

The intracellular penetration of rifampicin suggests that it should be effective in infections caused by typically intracellular organisms such as *Chlamydia* spp and *Brucella* spp. Rifampicin is the most active agent available against *C trachomatis* but may rapidly develop resistance in vitro.[8] Rifampicin and chlortetracycline ointments were found to be equally effective in sexually transmitted *C trachomatis* infection of the eye,[9] and rifampicin has also been reported effective in endocarditis due to *C psittaci*.[10] Because of the combination of the rapid development of resistance and the availability of other effective agents such as tetracyclines or erythromycin rifampicin should not be used routinely in chlamydial infection, but it is valuable in deep seated infection. Rifampicin has also been used in combination with erythromycin to treat serious infections due to

Legionella pneumophila when erythromycin alone has not eradicated the infection.[11]

In North America rifampicin has been used since 1971 for prophylaxis of close contacts of meningococcal meningitis. Around one quarter of strains of *Neisseria meningitidis* isolated from serious infections in Britain are now resistant to sulphonamides, and many centres use rifampicin for prophylaxis. There have been no reports from Britain of *N meningitidis* resistant to rifampicin after prophylaxis, though there have been from America.[12,13] Widespread resistance of meningococci to rifampicin is more likely to occur in closed communities than in the general population, and it would be prudent to use another agent (for example, trimethoprim) with rifampicin for prophylaxis of closed communities such as boarding schools.[14] American workers now believe that prophylactic agents should be given to contacts of patients with meningitis caused by *Haemophilus influenzae*,[15] and there have been several reports on the use of rifampicin: Cox *et al* found that a dose of 20 mg/kg was effective in eradicating *H influenzae* from the nasopharynx of carriers,[16] but Daum *et al* found little benefit in prophylaxis with a dose of 10 mg/kg, particularly in children under 5, the group for whom protection is most required.[17] Serious infection with *H influenzae* after contact with an index case is rare in Britain, and more information is needed on both carriage and transmission of *H influenzae* before prophylaxis is shown to be required. Infections with *H influenzae* resistant to rifampicin after prophylaxis have been reported from the United States, including one case of secondary meningitis.[18] Rifampicin has been combined with erythromycin or fusidic acid to eradicate nasal carriage of *Streptococcus pneumoniae* resistant to penicillin in South Africa, but resistance to rifampicin appeared with use of the latter combination, probably owing to poor penetration of fusidic acid into respiratory secretions.[19]

The combined antimicrobial activity and pharmacokinetics of rifampicin and trimethoprim have been investigated with a view to using the combination to treat urinary infection.[20,21] Both agents have a long serum half life and are lipid soluble, so they seem suitable for use together. The risk of side effects from the use of rifampicin is well recognised, however, and this combined with the ready availability of several other effective antimicrobial agents for the treatment of urinary infections has made the combination unnecessary for uncomplicated infections. The treatment of chronic bacterial prostatitis is more difficult: rifampicin and trimethoprim both penetrate prostatic fluid well, and the combination may be more effective than the current standard treatment with co-trimoxazole. The combination of rifampicin and minocycline should also be evaluated. Giamarellou *et al* reported the successful use of rifampicin and trimethoprim in the treatment of chronic bacterial prostatitis due mainly to *Staph aureus*.[22]

The main argument against the routine use of rifampicin for non-tuberculous infection remains the risk of resistance developing in *M tuberculosis*, though a survey comparing the countries where rifampicin was restricted and those where it was freely available for non-tuberculous infections found no difference in the incidence of resistance of *M tuberculosis* to rifampicin.[23] Furthermore, the side effects reported with the use of rifampicin are sufficient to make its use in minor infections unacceptable. The side effects on the liver are well known,[24] but gastrointestinal upsets and an influenza like syndrome have also been associated with intermittent treatment. Major side effects—which are rare—include thrombocytopenia and haemolytic anaemia from antibodies to rifampicin.[1]

Rifampicin also accelerates the metabolism of some other drugs by induction of hepatic microsomal enzymes. McAllister *et al* described an interaction between rifampicin and prednisolone resulting in the reduction of the bioavailability of prednisolone.[25] A similar interaction between rifampicin and oral contraceptives might cause considerable problems if rifampicin was used widely. Dosages of these drugs should be increased when rifampicin is used concomitantly. In common with virtually all antibiotics the use of rifampicin has been associated with the development of pseudomembranous colitis.[26]

Nevertheless, rifampicin has great potential for use as a prophylactic and therapeutic agent. The potential problems of toxicity and development of resistance are sufficient to preclude its use routinely in non-tuberculous infections, and when it is used care should be taken to use another agent with similar pharmacological and antibacterial properties.

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