in rats (*12*), and in patients having hepatic insufficiency from alcoholic hepatitis (*13*). Hypertrophic, hypoactive smooth ER is frequently associated with hyperplasia, or increased formation of new cells. The relation between the two phenomena needs elucidation.

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Sulfadiazine-Resistant Group A Neisseria meningitidis

Abstract: *A meningitis epidemic due to Group A meningococci was unusual in that most of the strains isolated from patients were generally resistant to sulfadiazine. This is the first report of sulfonamide resistance in an epidemic strain of* Neisseria meningitidis *Group A.*

The etiologic agent of a meningitis epidemic in Meknes, Morocco, which was part of a more general epidemic involving several Moroccan cities was *Neisseria meningitidis* Group A. Such epidemics have been common in Africa, but this particular epidemic was somewhat unusual because it occurred outside the "meningitis belt," that area north of the equator and south of the Sahara (*1*). As the epidemic progressed, some of the strains isolated from cerebrospinal fluid of patients seemed to be resistant to sulfonamide drugs. This impression was subsequently confirmed. Thus, the epidemiologic situation more closely resembled that reported by Millar *et al.* (*2*), with epidemics due to sulfadiazine-resistant Group B meningococci, than the more classic epidemics caused by Group A strains. This was apparently the first meningococcal meningitis epidemic studied in which *N. meningitidis* Group A was sulfadiazine-resistant.

The Meknes epidemic lasted several months and involved several thousand cases. At its peak, approximately 20 new hospital admissions were seen each day. Of these about 75 percent were confirmed by laboratory diagnosis through culture or examination of spinal fluid. Strains of meningococci were identified by typical butyrous or viscid, grey to yellowish, colonial growth. Colonies were oxidase-positive. Typical Gram-negative diplococci were observed microscopically. Acid was produced from dextrose and maltose, and no acid was produced from levulose or sucrose. Identity was established by specific agglutination in monovalent antiserum to meningococcus.

Resistance to sulfadiazine was determined by plate-dilution technique and disc-sensitivity tests. For plate-dilution tests, measured amounts of the sodium salt of sulfadiazine were added to Mueller-Hinton agar to yield concentrations of 1, 5, 10, 20, and 40 mg per 100 ml in the medium. Petri dishes of these agars were inoculated to yield isolated colony growth. Ninety-one isolates from cerebrospinal fluid obtained during the peak period of the epidemic were tested satisfactorily by the plate-dilution technique. Disc-sensitivity tests were performed on 370 Group A meningococcal isolates obtained from the cerebrospinal fluid or blood of patients.

The sensitivity tests by both techniques revealed that many of the isolates were resistant to sulfadiazine. By the disc test, 55 percent demonstrated some degree of resistance; 38 percent were completely resistant, while 17 percent were slightly sensitive.

In the plate-dilution tests, isolates also exhibited different degrees of sulfadiazine resistance. Ninety percent of the strains were resistant to 1 mg of sulfadiazine per 100 ml. Resistance to 5 mg of sulfadiazine per 100 ml was observed in 49 percent of the isolates. Growth of 10 percent of the strains was not inhibited by sulfadiazine concentrations of 10 mg per 100 ml or greater. It has been reported that over 96 percent of Group A meningococcus cerebrospinal fluid isolates were inhibited in vitro by 0.5 mg of sulfadiazine per 100 ml (*3*). Furthermore, in tests of Group B meningococci isolated since 1963, 51 percent grew on Mueller-Hinton plates containing 5 mg of sodium sulfadiazine per 100 ml (*4*). Therefore, sulfadiazine resistance was demonstrated in many isolates from this Group A meningococcal meningitis epidemic.

Important medical and epidemiologic significance may accompany this discovery of sulfadiazine-resistant Group A meningococci. This is especially true because such strains have appeared in epidemic meningitis form. Sulfadiazine and perhaps other sulfa drugs may no longer be automatically relied on for treatment or prophylaxis of meningococcal disease. We are now faced with the same problems with Group A strains as those presented to us by the Group B sulfa-resistant meningococcus strains since 1963. For example, the carrier state cannot be eliminated from the nasopharynx of an individual by treatment with sulfadiazine when the strain encountered is resistant in vitro to more than 0.1 mg of sulfadiazine per 100 ml (*5*). Even more important, because Group A meningococci are common agents in individual meningitis cases, clinicians must now be alert to the presence of sulfa-resistant Group A meningococci in the population. Alternate choices of antibiotic drug therapy for meningitis patients should be considered.

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