The drugging of America: 1971 to 1976

Although they remain the most prescribed group of drugs in the world today, tranquilizers and sleeping pills are being used consistently less often, says a six-year nationwide survey conducted by the National Institute on Drug Abuse.

The recently released report shows a 73 percent decline — from 20 million to 5.5 million — from 1971 to 1976 in prescriptions for barbiturate sleeping pills. Total barbiturate use dropped during the period by 47 percent. NIDA officials attribute the decline to passage of the Controlled Substances Act in 1970 and to the rescheduling of barbiturates in 1973 to a more restrictive drug category, plus "medical education and the availability of other hypnotics [sleeping pills]."

Even the most frequently prescribed drugs in this category — nonbarbiturate tranquilizers such as Valium and Librium — have decreased in use by 7 percent since 1974, when they reached a high of 98 million prescriptions annually.

Nevertheless, 128 million prescriptions for the "sedative-hypnotic" drug group were filled in 1976, including 27 million sleeping prescriptions — an estimated 1 billion doses. And tranquilizers and sleeping pills were implicated in 35 percent of all confirmed drug-related deaths in 1976; barbiturates alone accounted for 18 percent of those deaths, second only to narcotics, which were responsible for about one of four drug-related deaths.

Among nonbarbiturate sleeping pills, only flurazepam (Dalmane) gained in use in each of the six years. Dalmane is the only such hypnotic experimentally proved effective for up to 14 days, according to NIDA. Nonbarbiturates in general appear to be longer-lasting and have fewer side effects, the study concludes.

The report goes on to note that the vast majority of people get their drugs on an outpatient basis, rather than in the hospital. Pharmaceutical sales to drug stores exceeded sales to hospitals by 10 to 1 in 1975. The prescription of such drugs is dominated by three medical specialties: family/general practice, internal medicine and psychiatry/neurology. And some sedative-hypnotic drugs seem particularly popular with each specialty. For instance, although family doctors and GPs constitute 25 percent of all office-based physicians, they account for 42 percent of all outpatient prescriptions for sodium pentobarbital (Nembutal). And though psychiatrists and neurologists represent just 7 percent of office-based doctors, they prescribe 42 percent of all outpatient methyprylon (Nodular).

NIDA investigators also found that the belief that physicians overprescribe hypnotic drugs "was not supported. While almost two-thirds of those receiving the most common hypnotic drugs are females, two-thirds of the entire patient population are female," the report states. "In fact, the greatest users proportionately of sedative-hypnotic drugs are males over age 65."

Nonmedical use and abuse is found primarily in the 18-to-25-year-old age group, NIDA officials say. Males use such drugs nonmedically more frequently than females, and sedatives are taken more often than tranquilizers. According to the data, three of four admissions for barbiturate abuse are persons under age 25; of those admissions, 28 percent reported daily use and another 37 percent at least weekly use.

Even though barbiturates remain a constant factor in emergency room admissions (about 10,000 related admissions a year), barbiturate-related deaths have decreased by approximately 50 percent. This contrasts to the overall increase in drug-connected deaths and suicides from 1971 to 1976. Still, the risk of death or injury is far greater for barbiturates than for other sedative-hypnotics. □

Studies in purple link light to pump

A bucket-brigade model for pumping hydrogens across a membrane has been proposed to explain how the purple protein of a salt water bacterium *(Halobacterium halobium)* stores energy from light. Walter Stoekenius of the University of California at San Francisco described his model and the underlying wealth of detailed measurements on the pigment, called bacteriorhodopsin, at the recent conference on the Molecular Basis of Cell-Cell Interaction in San Diego (SN: 2/18/77, p. 105). Manfred Sumper of the Institut für Biochemie der Universität in Würzburg, Germany, also reported on how the purple membrane is formed.

The purple membrane, with its single protein, is probably the natural membrane best characterized in function and structure. It is the simplest biological energy-transducing and active transport mechanism encountered thus far, Stoekenius says. A crystalline array of protein in a membrane comprised of two lipids absorbs light and pumps protons (hydrogen nuclei) from the inside of the cell to the outside (SN: 3/6/76, p. 149).

Stoekenius proposes a model for how the simple membrane can pump protons. Extensive studies have given no evidence of a pore in the membrane or a binding molecule that could swing ions from one side to the other. Therefore, he postulates a molecular bucket brigade, which passes protons from the cytoplasm to the surrounding medium. The bacteriorhodopsin would provide the route. The protein, in closely packed alpha helices, winds back and forth across the membrane. Other studies have shown that a network of hydrogen bonds, as between the interlocking helices, can shuttle protons efficiently. Stoekenius points out that the bucket brigade, estimated to contain 10 to 12 members, must include a gap; otherwise the protons could transfer in both directions and short circuit the gradient. He suggests retinal, the light-absorbing portion of the pigment, is the controlling segment.

The retinal group of bacteriorhodopsin gives up and accepts a proton as part of its response to light. The pigment also changes shape. Therefore, Stoekenius hypothesizes that, during the conformational change, a slight movement of the retinal group lines it up with one part of the hydrogen bond network. The proton released from retinal is transferred along the helices to the outside medium. The retinal group then shifts back to its other position, where it recharges with a proton delivered from the cytoplasmic side of the membrane. "The small movement provides the barrier," Stoekenius explains. A fuller understanding of the pumping mechanism, he says, awaits more data on the amino acid sequence of bacteriorhodopsin (at least two laboratories are currently analyzing that sequence), a finer map of the pigment's position in the membrane and the details of its chemical response to light.

External oxygen levels control the number of purple patches in the membrane. The bacteria have little purple membrane when oxygen is abundant. A shortage of oxygen induces production of purple patches until they comprise up to 50 percent of the cell surface. Sumper reports that synthesis of two out of the three components of the purple membrane is under strict control.

Limited oxygen directly induces synthesis of opsin, the protein portion of the pigment molecule. Presence of extra opsin, in turn, initiates synthesis of retinal, the light-absorbing portion of the pigment, Sumper finds. The lipids of the membrane, in contrast, are taken from a pre-existing pool, so they need not be synthesized during purple membrane production. Exactly how the protein is inserted into the purple membrane is not yet known. In other systems, large precursors to proteins may contain specific "instruction" regions (SN: 7/30/77, p. 73). Sumper now has the first hint of a protein precursor in the purple membrane system. Bacteria stripped of their outer walls make no opsin, but instead produce several related proteins, two of which are larger than opsin. Finally, Sumper finds that organization of the bacteriorhodopsin into its crystalline lattice, after insertion in the membrane, requires energy from the proton gradient. □