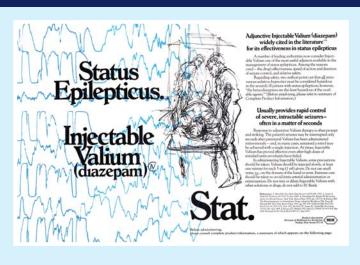
## BENZODIAZEPINES



The benzodiazepines have had a major impact on popular Western society and culture and have entered the folklore of the age (the 'little yellow pills' and 'mother's little helpers' of the famous Beatles song). They fuelled a revolution in biological psychiatry and its social reaction, the antipsychiatry movement of the 1960s. In 1952, the first reports of the clinical effects of chlorpromazine were published, and its obvious

commercial importance and rapid success led the pharmaceutical industry into a race to discover other psychoactive drugs that might have improved properties. Leo Sternbach was a medicinal chemist, who as a Jew had fled the Nazis in 1941, and was employed in the New Jersey research laboratories of the Swiss pharmaceutical giant Roche. He decided in the mid–1950s to investigate the pharmaceutical actions of a group of compounds he had created, which came to be known as the benzodiazepines. Initially no biologic action was found, and his laboratory was then asked to focus on other research areas. In cleaning up, his technician found a few hundred milligrams of some crystallised compounds that were thought to be quinazoline 3–oxides. They decided to

submit these for animal screening. The results were unexpectedly exciting – the drugs had powerful sedative and antiepileptic effects. An intensive pharmacologic programme of work ensued, and in 1960, the first compound was approved and licensed. Valium was licensed in 1963 and in the next 15 years, more than 4,000 related compounds were synthesised and screened, and by 1978, 23 compounds had been licensed worldwide. The value of these drugs in human epilepsy was rapidly recognised. The first reports were in 1960. In 1965 Henri Gastaut weighed in with a laudatory report of the use of Valium in status epilepticus and 6 years later was even more enthusiastic about the new agent clonazepam (Ro 05-4023).



The management of many patients with minor motor seizures has always presented a challenge to physicians responsible for their care. Now, ongoing research into the basic benzodiazepine molecule at Roche Laboratories has resulted in the development of Clonopin... a new and specific oral agent with restent preferences and specific management of the specific oral agent with

development of Clonopin...a new and specific oral agent with potent anticonvulsant properties Clonopin is indicated alom or as an adjunct in the treatment of akinetic, myoclonic and petit mal variant seizures (Lennox-Gastaut syndrome); it may also be useful in petit mal when succinimide therapy has failed. A clinical profile of Clonopin is presented on the following page



fease see last page of this advertisement for complete product information.