Monkeys With a Man on Their Backs

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It's 7:00 a. m. - still dark - the wind is howling outside. MI turns to his mates.

"These jitters are getting real bad, I can't take it any longer."

"Cool it, man," says M2, "you just have to learn to control yourself, besides, he'll be here any minute now."

7:05 a. m., the lights come on, the door opens, a large man, in a brown uniform, strides in carrying a needle and syringe in one hand, a bottle in the other. The bottle is labelled MORPHINE. The man fills the syringe with the clear fluid, opens the latch on the cage door and the first monkey comes out to receive his scheduled "fix".

Like Clockwork, every 6 hours, day in, day out, a group of 80 to 100 monkeys in the Department of Pharmacology at the University of Michigan (U. of M.), Ann Arbor, receive a fixed dose of narcotic.

About thirty years ago a group of research chemists started an immense project to synthesize compounds with potential analgesic potency in order to find one as analgesic as morphine, but which did not possess morphine's main side effect - addiction.

At this time, Dr. Maurice H. Seevers, now Chairman of Michigan's Pharmacology Department, suggested to the Committee on Narcotics and Drug Addiction that it would be invaluable to have a means by which these synthetic agents could be quickly screened for their addicting liability. The Committee agreed with his suggestions and the colony of "junky-monkeys" was formed at the U. of M.

The unsuspecting animals (the common Rhesus-Macacca Mulatta) are imported from India, placed into quarantine for one month, then trained to receive an injection of saline on a schedule of one injection every six hours. When the monkey is completely trained to this schedule, morphine is substituted for the saline and the monkey is started on the "hooking" schedule. At the end of one month the monkey has become completely dependent on his "fix".

Years of investigation in man and monkey have shown the close parallelism of both species in their reaction to the narcotics analgesics. When morphine is withheld from the monkey who has become dependent on his "fix" he goes "cold turkey" and demonstrates all of the symptoms that man does under similar circumstances. The monkey enters what is termed the "abstinence syndrome". The systems of the body somehow adapt to the constant presence of morphine in such a manner that the body comes to rely on the morphine to maintain a normal state of equilibrium. Removal of the morphine disrupts this abnormally-produced homeostatic state - hence "abstinence".

The animal suffers from nausea, vomiting, "goose flesh" (pilo-erection), cramps, muscular weakness and tenderness, excessive chattering and crying ("screaming meamies") among the many which comprise the total syndrome. One injection of morphine at this point, will reverse all of the symptoms and revert the monkey to his "abnormally-normal" state of existence.

Another similarity exists between the addict and the addicted monkey who has to rely on "the man" to inject his fix for him. The addict prowls the night to obtain his fix. He also has to rely on the man ("pusher") for his fix.

Although only a very small percentage of the total addicted population become "hooked" through the clinical usage of the narcotic analgesics (to overcome pathologic



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or post-operative pain), the existence of a potent, non-addicting analgesic might, in time, do away with the illicit "drug-trafficking" since their potential usage would gradually diminish. This is only one of the reasons, among many, that such an agent is searched for.

A morphine injection will reverse the "abstinence syndrome". All of the semi-synthetic narcotic analgesics ("opiates", heroin, dilaudid, metopon, etc.) and the synthetics ("opiods", demerol, methadone, levorphan, etc.) will also reverse the "abstinence syndrome". In fact, the greater majority of agents with properties similar to morphine produce this reversal. Years of investigation and comparison have shown that all of the agents that have the capacity to reverse the abstinence syndrome or that can substitute for morphine in the addict, so that he does not go "cold turkey", have addicting liability. This means that if they are abused in a manner similar to morphine they will produce the addiction of the narcotic analgesics.

All of the industrially synthesized potential analgesics are submitted to the U. of M. through the Drug Addiction Committee at Washington. At the U. of M., they are injected into addicted monkeys to determine if they are able to substitute for morphine and prevent "abstinence".

In this manner, agents can be classified as to whether they have high, intermediate, low, or addicting liability. These are further defined as:

HIGH. An agent which will reverse all of the symptoms of the abstinence syndrome in a dose which does not produce any toxic side effects.

INTERMEDIATE. An agent which will suppress all of the abstinence signs, but only with doses which elicit undesirable effects such as stupor, tremors, ataxia.

LOW. When an agent only produces minor suppression of some of the signs of abstinence and attempts to produce more or complete suppression with larger doses is prevented by the intervention of toxic effects such as coma or convulsions.

NO. When an agent fails to produce any specific suppression of the morphine abstinence signs.

Agents that show no, or only mild, addicting liability under these conditions are submitted for further trial in man at the United States Public Health Service Hospital at Lexington, Kentucky. If, after extensive testing in man, an agent shows that it has no potentially "abusive" properties (will not be abused for the effects it produces), it might become the analgesic of choice - provided that it possessed no other "ill-effects" (mainly respiratory depression).

The group of compounds of current interest are the narcotic antagonists. These are agents which are capable of preventing or reversing the activity of the narcotic analgesics. However, when given alone, some of these have been shown to be quite potent analgesics. Monkey-testing has shown that they possess little, if any addicting liability, but in man they produce hallucinations and psychotic states.

Only time will tell if the ideal agent will be produced..... meanwhile.....
"Hey, mate, feel that juice running through your veins — great, man. What's going to happen to us if they find this ideal, non-addicting compound?"

"Man, its going to be rough going for a while."

"Let's wait it out"

"It's 7:00 a.m. - still dark

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