

Body and Mind

BY MELVIN KONNER, M.D.

Caffeine High

ABOUT TWO-THIRDS of the way through one of those 36-hour shifts in medical school, I went to the coffee urn — that ubiquitous trough nestled somewhere in or near every known nurses' station — to draw perhaps my 10th cup of the shift. One of the surgical residents — true exemplar of a sarcastic breed — said, "If you sign up now, I'll do your Whipple for you at today's prices." His reference was to an operation on the pancreas that he thought I might someday need; at that time it seemed possible that coffee caused pancreatic cancer. That effect of caffeine, a major ingredient in coffee, has not been proved, but many others are well established: sleeplessness, irritability, anxiety, heart palpitations, increased urination, stomach irritation, fibrocystic disease (benign growths) in the breast, and harm to a developing fetus.

Yet coffee continues to be consumed at a rate of billions of cups a year in the United States alone. Tea, cocoa and many soft drinks contain caffeine as well, and it is sold in many approved over-the-counter drugs for colds, drowsiness and appetite control. It may, in fact, be the most widely used psychoactive drug in the world — despite the frequent carping of health experts. Such a time-honored habit might still be all bad. But before we arrive at that simple conclusion, consider whether all those millions of users might be on to something to which the health experts haven't fully awakened.

Stimulant use is widespread in primitive societies, and has a long tradition in our own. Caffeine is the active ingredient of plants that have been used by native peoples in various parts of the world, from guru nuts chewed by the Sudanese to tea brewed from the leaves of *Thea sinensis*, a bush native to southern China. Caffeine belongs to the class of chemical compounds called methylxanthines (pronounced meth-el-ZAN-theens), and the plants containing them were each discovered independently and used for similar purposes: to stave off fatigue, increase the capacity for work and elevate mood. Coffee itself is extracted from the fruit of *Coffea arabica* and its relatives, which have spread from Arabia throughout the world. Legend has it that shepherds at a monastery in

Arabia saw their goats eat coffee berries and proceed to gambol sleeplessly through the night. The abbot, hearing of these unusually frisky goats, immediately saw the implications for his own long, difficult nights of prayer, and ordered a beverage made from the same berries.

Given how important the stuff has become in getting so many of us through each day, let alone the occasional long night, it is remarkable how little we know about it. Until the last few years, almost nothing was understood about its chemical action. As for psychological effects, some of the best work was done in the 1960's, by Avram Goldstein and his colleagues (mainly Sophia Kaizer) at Stanford University. In a double-blind study — neither the subjects nor the scientists knew who had straight decaf and who had 150 or 300 milligrams of caffeine slipped into their drinks — 20 male medical students described the effects on them after they had the caffeine. At other times, they were asked to describe effects after receiving the placebo. At several points during a three-hour period after drinking the caffeine, they were significantly more likely to use such words as "alert, attentive, observant" and "active, stimulated, energetic" — as well as "jittery, nervous, shaky" — than they were after the placebo.

A follow-up study of "young housewives" extended the findings. Thirty-eight of the housewives who drank five or more cups a day also responded to caffeine with increased rather than a decreased sense of satisfaction, increased rather than slightly increased "pleasant stimulation." The housewives, who were normally heavy users, showed an absence of side effects such as jitteriness and stomach upset.

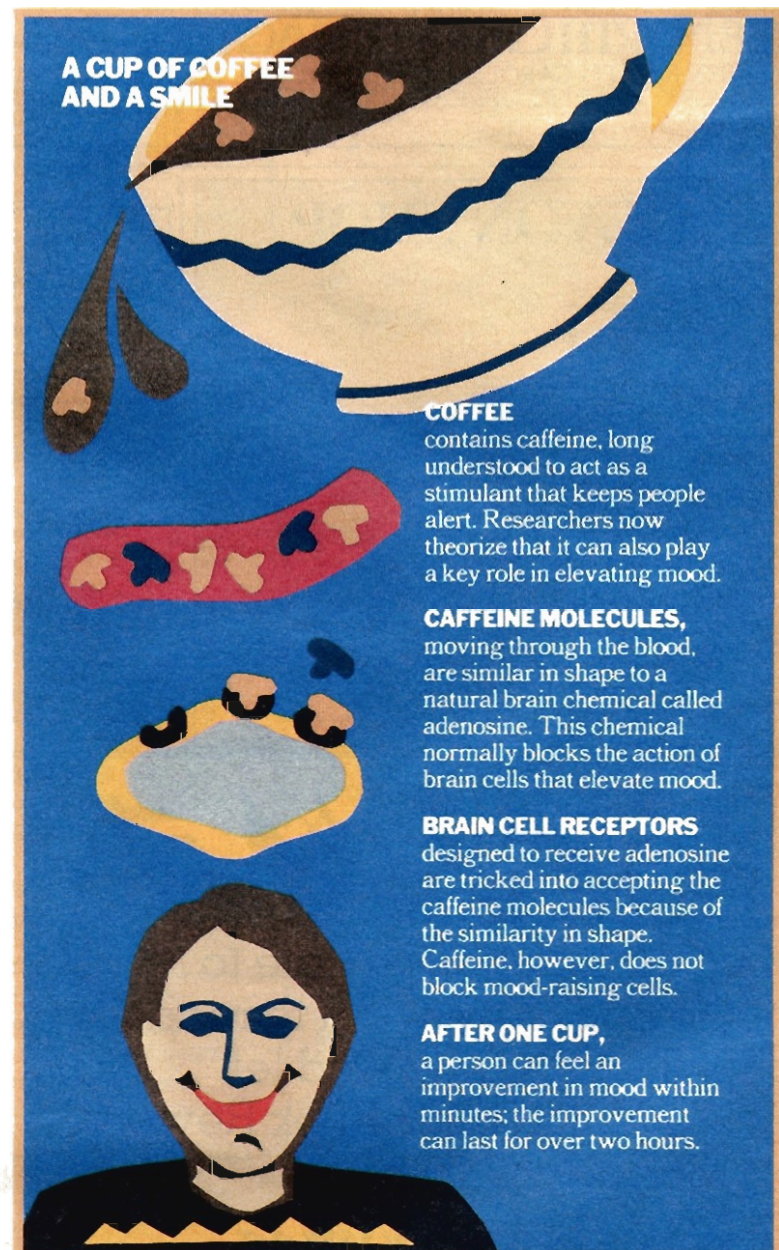
The conclusions of these studies have since been frequently reported. In 1986, research even showed marked effects on the brain's electrical activity, as measured by EEG.

But the most exciting revelations have now come in the field of hard-core brain chemistry. Laboratories such as those of Solomon Snyder at the Johns Hopkins Medical School, in Baltimore, and Bertil Fredholm of the Karolinska Institute, in Stockholm, have shown how caffeine works on brain and body cells — and in the process have discovered important new cell functions. Caffeine and the other commonly used methylxanthines — theophylline and theobromine — acquire the physiological power by their ability to fool the brain and substitute for the natural brain

chemical adenosine (a-DEN-o-seen). The news is that adenosine seems to act like a neurotransmitter, or chemical messenger, and fits highly specific receptors on the surface of some cells. In lock-and-key fashion, this combination of adenosine with its receptor triggers a series of chemical events inside the cell. Caffeine, for its part, looks something like adenosine in molecular structure — enough to trick the receptor. When it meets up with a molecule of caffeine, the key fits and sticks in the lock. But it's the wrong key, and it fails to open the cell door. Meanwhile, adenosine itself is kept away from the cell.

What happens next is more speculative. But it seems likely that in the midst of the morning blahs, or as work becomes tedious in midafter-

Are all those millions of coffee drinkers on to something the experts haven't awakened to?



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noon, or as sleep comes over us in the evening, adenosine suppresses the brain cells that increase alertness and elevate mood. Caffeine, by blocking adenosine's blocking action — a sort of chemical double negative — frees the mood-elevating cells again, and we feel as if we can take on the world.

Until the 1950's, some psychiatrists used stimulant drugs of various kinds to treat depressed patients. In general, they no longer do so. Instead, they use antidepressant drugs, which prolong the effectiveness of mood-elevating cells and their special chemical messenger norepinephrine. It seems not only possible, however, but likely that some of the millions of heavy coffee drinkers are, in fact, using caffeine — consciously or not — to medicate themselves for depression, our most widespread psychiatric condition. Similarly, it is virtually certain that many users and abusers of alcohol rely on it to treat themselves for anxiety.

ESTIMATES OF THE amount of caffeine in one cup of coffee range from 60 to 150 milligrams. If we take 100 milligrams as our estimate, then heavy users may get 500 or 1,000 milligrams a day — well within the range that physicians have found useful in treating certain medical conditions, such as asthma and abnormally low blood pressure, in which caffeine is helpful. In other words, when you get that third, or certainly that fifth cup of coffee, you are in the range of drug therapy.

Now, this is where the physician properly inveighs against the dangers of self-treatment, especially, as here, with a compound whose known adverse effects are by no means trivial. If you are depressed to the point of impairment of function, or if a more moderate but disturbing depression has lasted for months, you should see a psychiatrist and have your treatment supervised, whether it is pharmacological or psychological. If you have a history of heart arrhythmias or stomach ulcers, or a family history of fibrocystic disease, or if you are pregnant, you should certainly not be drinking much coffee. The incidences are rare, but it can even produce a cardiac arrest. Dependence on coffee is common, and withdrawal symptoms include the all-too-familiar headache and even some component of the morning blahs. Such dependence can certainly be self-defeating.

Having said that, I have to say as well that caffeine, as drugs go, is relatively safe. Prescription antidepressants in the most-used category — tricyclics — have a number of undesirable side effects, including dry mouth, fatigue, blurred vision, urinary retention, constipation, impotence and even heart palpitations. They also take weeks to begin working. For these and other reasons there is a renewed interest among psychiatrists in the use of stimulants, such as amphetamines, to treat depression, especially in the elderly, for whom the side effects of tricyclic antidepressants might prove prohibitive, or in patients who must have a prompt response to therapy — because, say, their insurance is about to run out. Stimulants may also be used as an adjunct to more conventional antidepressant therapy.

Meanwhile, the methylxanthines are virtually ignored in this regard. But they must not be. Caffeine's usage as a folk remedy for mild depression is too widespread. Humans have a long tradition of finding simple, effective and safe methods of keeping themselves in good working order. Aspirin and laxatives are other examples of substances that had been proved to work well before the Food and Drug Administration ever came along. Like them, but unlike antidepressant drugs or prescription stimulants, caffeine has been taken billions of times over a period of centuries. There are no prescription drugs for which we have comparable experience, and the absence of clear disaster speaks volumes about its safety, at least in the area of two, three or four cups of coffee a day.

Have we therefore reached the point at which a depressed patient will call a physician and be told: "Take two cups of coffee and call me in the morning"? Clearly not. A person driven to make such a call needs professional help. But more investigation of the antidepressant properties of this well-known drug used appropriately seems essential. And what can be said with certainty now is that physicians need to recognize that some depressed people are already using it — or at least trying to use it — for the purpose of elevating their chronic potentially dysfunctional bad moods. And this practice — alongside its wider use as a weapon against the ordinary blahs — has probably been going on for centuries. ■