

verage toxicological dose of an article like opium, for instance, gives no adequate or intelligent notion of what the continued or frequent dose of the same drug is; nor does it give any adequate or intelligent notion of the physiological action and consequent therapeutical power of its continued or its frequent dose.

Let us consider first the *continued dose*. By this is meant the administration of a drug in such a way that the elimination of one dose shall not be completed before the absorption of the following dose has commenced.

The single dose is an appropriate quantity given once or oftener, without keeping it continually in the blood. The therapeutical value of these doses and the physiological difference between them are of great importance.

Let us look at some illustrations of this difference and value.

Ammonia and its salts "readily enter the blood, and must to some extent increase its alkaline reaction; but from their volatility and high diffusion power they are rapidly eliminated, and hence their action on the blood and the organs of the body is a very transient one." The elimination of a single dose of carbonate of ammonia is practically completed in an hour or two after it is administered. Its physiological action is correctly stated by the United States Dispensary to be "stimulant, diaphoretic, antispasmodic, powerfully antacid, and in large doses emetic." In consequence of this action, it is largely used in depressed conditions of the vital powers. This is the well-known action of a single dose or of a few doses given near together, after which the system is freed by elimination from the drug. No change is produced in the quality of the blood. If a continued dose of ammonia is given, that is, if it is given so often, say every hour for several days, that the blood is continuously charged with it, a very different set of phenomena from those just described appear. "When ammonia or its carbonate is administered"—in this way—"for some time to animals or man, the effect is to modify the blood-corpuscles; they become easily soluble, crenate at the edge, many-sided, colorless, transparent, collapsed, and loosely agglomerated, but not in rolls, and the blood when drawn, or after death is absolutely fluid or loosely coagulated."\* These phenomena were observed by Dr. B. W. Richardson, of London. They closely resemble the changes in the blood which occur in patients suffering from typhoid and typhus fevers. Hence it appears that the single dose of ammonia produces rapid and effectual stimulation of the heart, while the continued dose of the same article alters the quality of the blood, and notably of the blood-corpuscles. The single dose exerts a therapeutic, the continued dose a toxic action on the economy. It is unnecessary in this presence to dwell upon the obvious therapeutic inferences that follow from these data, at least so far as ammonia is concerned.

Gallic acid is another illustration of the difference between the single and the continued dose. This acid is rapidly eliminated. Physiologists tell us that a couple of hours after it has been swallowed, it has practically left the system, by way of the kidneys, to such an extent that it exerts no appreciable action upon the blood after that length of time. Gallic acid has a well-deserved reputation for controlling certain forms of hemorrhage. Suppose it is given in single doses of ten grains, more or less, three times a day, which Dr. Clarke apprehends is the usual method of administration, the blood will be subjected to the restraining action of the acid only about six hours out of the twenty-four; not long enough to hold steadily in check a hemorrhagic disposition. Suppose now, that instead of the single, the continued dose is administered, by which the ratio of elimination to absorption is constantly regarded, and the blood kept continuously charged with gallic acid; the result will be a continuous action upon the blood not an intermittent one. It is needless to point out the fact that continuity of action is very sure to give rise to phenomena that will not follow intermittence.

No drug exhibits in a more striking light both the physiological and the therapeutical differences between single and continued doses than alcohol. The partial, confused, and incomplete recognition of these differences by various observers and experimenters, who have examined and described the physiological action of alcohol, goes a great way toward explaining the various and often discordant results at which they have arrived. We learn from the experiments of Messrs. Lallemand, Perrin, and Duroy, as well as from those of Drs. Anstie, Parkes, Smith, Binz, and others, that the disappearance of a single dose of alcohol from the system, either by elimination from it or combustion in it, or by both processes, practically takes place in about six or eight hours after its ingestion. Traces of alcohol may be found in the blood and in the excreta for a much longer period than this; but so much of it leaves the system within eight hours, that what remains of any single dose beyond this length of time has no real physiological value. A person who takes a dose of alcohol, in the shape of wine or other alcoholic liquid, once in each twenty-four hours, subjects his organism to the action of alcohol about one-third of that time, and leaves it free from that action about two-thirds of the same period. A person who takes what is known in non-scientific language as an "eye-opener" in the morning, wine with his dinner or lunch, a digester in the afternoon, and a "night-cap" on retiring, takes the continued dose of alcohol. His blood is continuously charged with alcohol to a greater or less degree. There are phthisical patients who imitate this method of ingesting alcohol, and take a daily continued dose of it, keeping their blood charged with it more than two-thirds of the time.

Alcohol taken in a single daily dose, by which the blood is practically free from it more than two-thirds of the time, and alcohol taken in a daily continued dose, by which the blood is practically charged with it more than two-thirds of the time, are sub-

\* Practicable Therapeutics. By Edward John Waring. American edition, p. 61.