HISTORY AND PREPARATION OF INTRAVENOUS SOLUTIONS.*

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Intravenous medication, as the name indicates, is a direct, exact and efficacious method of administering medicine, and is employed quite extensively in medical practice with drugs of known and proven therapeutic value, also in an experimental way on animals.

Not only is intravenous medication the most direct, but it is also well known that many patients are unable to take certain medicines when given orally, for example, salicylates, iodides, mercury and iron salts, which cause unpleasant digestive disturbances and form chemical compounds with the contents of the stomach, thereby entirely defeating the purpose for which the medicine is given. This constitutes one of the reasons why intravenous and hypodermatic forms of medication are holding such an important place in the practice of medicine to-day.

One would be led to believe, from the knowledge of the extensive use of hypodermatics, that these antedated intravenous medication. However, this is not the case, as intravenous injections of drugs were administered several centuries before medicines were given hypodermatically.

If we consider the transfusion of blood under intravenous injections, then that procedure goes back to the remote antiquity. The Egyptians are said to have practised it. The earliest method of intravenous medication dates as far back as 1492, when it was recommended for the treatment of Pope Innocent VIII. If we confine ourselves strictly to the subject of the injection of drugs, the first experiment of that character was performed in England by Christopher Wren, Professor of Astronomy at Oxford, who first tried the bold experiment of injecting drugs into the veins of animals. In 1656 he injected opium and crocus mettalorum, using dogs as his subjects of experiment. His injection apparatus consisted of a quill attached to a small bladder, and not the hypodermic syringe, as we have to-day. The opium stupefied the dogs, but did not kill them; while the crocus caused violent vomiting.

The first injection to man was given by Wren in 1657. It appears that a certain foreign ambassador at the court of St. James became interested in Wren's experiments and offered a delinquent servant of his as a subject for experiment. In 1662 J. D. Major, an English physician, and Escholtz made several successful injections on human beings.

Altogether the experiments at this first and early period of intravenous injections were discouraging in their results, and for that reason the practice fell into disrepute, and was not revived until about the end of the eighteenth century. The reason for this was that the preparations were applied indiscriminately in all kinds of cases, and, perhaps, the preparations were not compounded properly. At the same time they paved the way to our present rational intravenous therapy based on careful pathologic, pharmacologic and chemical research, and to-day the drugs used for intravenous injection are increasing rapidly.

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In preparing intravenous solutions there are certain critical points to be considered; for instance, precipitation, contamination, sterilization and compatibility with the blood stream. I am unable to go into detail in this matter, because in numerous cases each drug or chemical requires special preparation before being made compatible with the blood stream. However, there are others that need very little treatment and the solution is all that is required of it for intravenous use.

The ampoule is the preferred form of marketing and dispensing intravenous solutions because it is free from contamination, more exact and more permanent. In preparing the ampoules they are washed with a special apparatus made for this purpose, or by other means, such as boiling in distilled water and cooling quickly, whereupon water enters the ampoule and is rinsed out. This is repeated several times, and in some instances the ampoules are first prepared by washing in acid and rinsing them thoroughly before the preceding process is carried out. When this procedure is completed the ampoule is sterilized, which is usually done in a sterilizing oven at about 125°C., or in an autoclave.

The sterilized ampoules are then filled by one of several methods, namely, the vacuum, gravity or pressure, the vacuum being preferred when it can be used, or when a large number is to be filled. In the vacuum method the ampoules are put in a crystallizing dish bottom up, or put on a special plate and a crystallizing dish placed over them and both inverted; hence, the ampoule is bottom up and ready to be put in the desiccator made for the purpose. A little in excess of the calculated amount of the preparation to fill the ampoule is poured in the crystallizing dish. The crystallizing dish, containing the ampoules, is then put into the desiccator. The desiccator is closed and the air exhausted by the vacuum, and by gradually allowing it to re-enter, the atmospheric pressure forces the liquid into the ampoule. In the gravity method of filling ampoules the burette or special graduated tubes made for the purpose are found the most convenient; while in the pressure method the hypodermatic syringe cannot be surpassed.

The filled ampoule is then ready for sealing. In most cases it is done in large quantities by means of a blast, but they may also be sealed by means of a Bunsen flame. The hermetically sealed ampoules are then tested by touching or drawing over a blotter, or by boiling in colored water, and in case of leakage after the water has cooled the colored solution will be found inside of the ampoule. The sealed ampoule is now ready for sterilization, the heat, of course, depending upon the nature of the compound, and often requires a considerable amount of research work.

Because of the favorable view the medical profession has taken on intravenous medication, and because of the constant increasing demand from all parts of the country for all kinds of preparations, it is necessary that pharmacists should be prepared for such dispensing. The most important point to be considered is, to see that the preparation is free from contamination and precipitation, is properly sterilized, and is compatible with the blood stream. Certain drugs require special preparation before making them compatible with the blood stream, and unless the pharmacist has the time to devote to experimental work and to testing the finished product, both chemically and physiologically, it is safer not to attempt to prepare intravenous solutions. It has been our experience that seemingly harmless chemicals or drugs, as well as the more potent ones, have given severe reaction or anaphylaxis, and in some instances have proven fatal to animals.

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