EVOLUTION OF MEDICAL APPLICATION OF SYRINGE

Basic concept of syringe is not new. It is however not easy to trace back in the history to pin point when syringe was invented and by whom. Early men knew to use blow-pipes and darts to introduce substances into the body. Medical historians suggest that ancient Babylonian and Egyptian medicine men employed injections for soothing irritations and clearing bowels and other body cavities. They generally used to employ animal bladders attached to wooden or bamboo or ivory hollow tubes for infusing fluid in the body cavity (see Fig. 1A). Egyptian embalmers probably used some prototypes of piston type syringes to clear and embalm dead men’s skulls in the process of mumification. However, there is no direct evidence to suggest that piston syringe was in vogue for medical purposes even in the time of Hippocrates (460–377 BC) and Galen (129–200 AD) although both of them have recommended use of clysters and enemas. The prototype of modern day piston syringe was improvised sometime late in the fifteenth century and gradually became popular in clinical use mainly for giving enemas. In his textbook, named Chirurgia published in 1497, an Alsatian surgeon Hieronymus Brunswig (1450–1533?) showed a piston syringe as a surgical tool. In 1580, famous French surgeon named Ambroise Pare (1510–1590) mentioned the syringe as a common surgical tool. Interestingly, its use in modern medical purposes like intravenous, intramuscular and subcutaneous injections however began rather recently, around the second half of the seventeenth century.

In 1628, William Harvey (1578–1657) published his book, Exercitatio Anatomica de Motu Cordis Sanguinis Animalibus (An Anatomical Exercise on the Motion of the Heart and Blood in Animals) and described the circulation of blood. Christopher Wren (1632–1723) who was then the Savilian Professor of Astronomy at Oxford understood that blood circulation could be used to carry liquid medicine to different parts of the body, thus giving rise to a revolutionary idea of injecting medicine towards systemic level rather than simply at the local level. Wren is probably the first person recorded to have used intravenous injection in Britain. In 1657, Wren with the help from Robert Boyle and John Wilkins constructed a simple syringe and started injecting medicinal substances in experimental animals. Sir Christopher Wren initially performed experiments in which he infused substances like wine and ales into the venous circulation of dogs with not unexpected results. Boyle therefore proposed a human trial of intravenous injection, but it turned out to be a failure1. Throughout their experiments, Wren, Boyle and other investigators primarily used bladder based pump type syringe and unit gravity
When oral route could not be approached. For the time being, the interest of biomedical experimentalists for syringe and syringe-based infusion of fluid into human body took a back seat, it was practiced mainly in form of fixing the dead corpses, in animal experiments and veterinary infirmary. In the early part of nineteenth century, consistent attempts were made to improve syringe based injection approach by quite a few investigators that included English physiologist James Blundell, famous French physiologist Francois Magendie and young Bostonian physician Hale. The contribution of Thomas Latta from Edinburgh in this connection was noteworthy. In 1807, The Edinburgh Medical and Surgical Dictionary clearly defined a syringe as 'a well known instrument, serving to imbibe or suck in a quantity of fluid and afterwards expel the same with violence', and further 'a syringe is used for transmitting injections into cavities and canals'. In 1843, Charles Sage received the patent for his model of syringe (see Fig. 1C).

At the beginning of the nineteenth century, several experimentalists were attempting to devise methods of administering substances into the body through other routes besides oral and venal routes. Taking clue from Magendie's report in 1809, A.J. Lasieur described a method of administering substances via skin, applying them directly to blisters on the skin. In 1836, G.V. Lafargue used a vaccination lancet to introduce morphine under the skin. A drip-type hollow needle was developed by F. Rynd in 1844. In 1853, Alexander Wood (1817–1884) used a modified model of Ferguson type syringe (see Fig. 1D) to treat one of his lady patients who could not take opium feeding of liquid through a quill into blood vessels, generally veins (see Fig. 1B). In 1661, Dr. John Elsholz, a physician to the King of Prussia began a series of experiments on animals and human subjects and wrote a book on injection, Clysmatica Nova in which he described 'how to administer a medicine through an opened blood vessel so that it has the same effect as if it had been taken orally'. In 1667, Johann Daniel Major who was a Professor in Physics in Kiel wrote a book on injections entitled Chirurgia Infusoria. It contains probably the earliest illustration of an intravenous injection and suggestion of blood transfusion through venous route. However, Major probably did not perform any experiment himself. In 1668, famous Dutch physician and anatomist Regnier de Graaf (1641–1673) wrote a short book on clysters, in which he described a syringe with a metal barrel directly attached to a curved pipe. He proposed to use it to trace blood vessels of corpses.

Just after these developments, progress in the idea of syringe and injection was dismayed following serious dispute centering around the process of blood transfusion (Fig. 2). This is not surprising because in many cases animal blood was transfused into humans, resulting in severe reactions and deaths. There were also many cases of failure in the attempts of intravenous injection, primarily from the lack of notion of sterility. The antipathy was clear. In a report given by a famous German surgeon, Lorenz Heister (1683–1758) in 1750, he stated that 'frequently the event turns out worse than the disease', despite the fact that he had profound experience in intravenous injection and he suggested it as a measure when oral route could not be approached. For the time being, the interest of biomedical experimentalists for syringe and syringe-based infusion of fluid into human body took a back seat, it was practiced mainly in form of fixing the dead corpses, in animal experiments and veterinary infirmary. In the early part of nineteenth century, consistent attempts were made to improve syringe based injection approach by quite a few investigators that included English physiologist James Blundell, famous French physiologist Francois Magendie and young Bostonian physician Hale. The contribution of Thomas Latta from Edinburgh in this connection was noteworthy. In 1807, The Edinburgh Medical and Surgical Dictionary clearly defined a syringe as 'a well known instrument, serving to imbibe or suck in a quantity of fluid and afterwards expel the same with violence', and further 'a syringe is used for transmitting injections into cavities and canals'. In 1843, Charles Sage received the patent for his model of syringe (see Fig. 1C).
Fig. 1: Evolution of syringe in the history of medicine. A, A model of primitive enema syringe. The pressure bulb used to be made from animal bladder and the quill from ivory or bamboo. Much later, in the seventeenth century, elastic bulb and bottle made from rubber gum replaced the use of animal bladder. B, A model of the seventeenth century syringe. Wren used a similar type of syringe for his experiments of intravenous injections. C, A model of the nineteenth century syringe. Charles Sage received patent on January 10, 1843 for the model shown. D, A model of early hypodermic syringe. A similar type of syringe was used by Alexander Wood. E, A watch chain syringe (graduated) used mainly for subcutaneous injection in the late nineteenth century. Marketed by Messrs. Joseph Wood & Co. F, Multipurpose syringe of Pavez with different types of canulae.
a French physician named Charles Gabriel Pravez (1791–1853) used metal syringe with hollow needle to inject coagulants into blood vessels in animals to treat aneurysms (see Fig. 1F). Later, Wood justified the use of syringe based injection of drugs in different kinds of remedies. Alexander Wood however believed that the action of the opiate given subcutaneously was principally local and he therefore was very careful in delivering the medicine near to a nerve so that effective relief of pain could be given to the patient. Scottish-Canadian physician Charles Hunter (1873–1955) however remarked that it also demonstrated systemic action. There is some evidence that this difference in opinion led to an “acrimonious debate” between Wood and Hunter. It has been suggested that Wood’s fundamental mistake that the effect of hypodermic injection of a substance was primarily local implicating that drug dependence was very unlikely by hypodermic injection of opiates actually paved the path for emergence of a huge number of patients morbidly dependent upon morphine, so-called ‘morphinists’ of the nineteenth century. In 1869, Paul Viktor von Bruns (1812–1883) published in Germany a text on hypodermic medication and illustrated glass and metal syringes with graduated barrel and a plunger with locking device. This is called Luer-lock type syringe and was originally designed by a German named Luer. His syringe remained popular in modified form until recently.

The syringe-based injection of medication was sensed as a great boon since Harvey’s time. Yet undoubtedly there were some serious problems like infection, shock, embolism, and abscesses associated with syringe-based medication and these were
consistently reported since the time of Lorenz Heister in 1750 and later by Kane in 1880. The major objection to the use of the hypodermic syringe was the frequent occurrence of abscesses at the site of injection. By 1885, the danger of addiction (contrary to Alexander Wood’s conviction) was widely recognized. Nevertheless, other investigators found newer uses for the syringe. In 1874, Pierre Cyprian Ore experimentally used intravenous injection of chloral hydrate for inducing anesthesia. In 1890s, Guido Baccelli used quinine to treat malaria, and mercuric chloride to treat syphilis, and carbolic acid to treat tetanus. In 1920s, a series of effective intravenous anesthetic agents came into practice: Amytal, Nembutal, Evipan and Pentothal.

An understanding of the Germ Theory of diseases and thus medical importance of using sterile and disposable needles and syringes in syringe based medication became quite apparent following the gigantic contributions of Louise Pasteur, Joseph Lister and Robert Koch. Following this, the necessity of using disposable and sterile syringe and needle was firmly established in the medical practice. In 1950, a U.S. patent for disposable syringe was received by Arthur Smith. In 1954, Becton, Dickinson and Company came up with mass production of disposable glass syringe and needle to meet the need of mass administration of polio vaccine for American children under the leadership of Dr. Jonas Salk (1914–1995). Plastic disposable hypodermic syringe, named Monject, was introduced by the Roehr Products in 1955. This reduced the cost and increased safety further. Although there is now a serious global concern about its use in narcotic abuse and associated infections, the syringe based injection method for medical purposes doubtlessly saves lives and gives comfort directly and indirectly to a large number of sufferers everyday.

**Additional notes**

1. This human trial was arranged so that Sir Christopher Wren injected a dose of *crocus metallorum* into the vein of an unruly servant of an Aristocrat. As soon as the injection was given, the man fell into a swoon and the master immediately called off the test for he felt the test was dangerous.

2. In the early nineteenth century, various veterinary hospitals across the world were using no other method to administer medicine than intravenous route for prompt response and requirement of lesser amount of drugs.

3. James Blundell (1770–1868) was a noted English physiologist from the Guy’s Hospital in London. He presented in 1818 his findings associated with the transfusion of whole blood by means of the syringe in dogs and in humans. [Blundell J. Experiments on the transfusion of blood by the syringe. Medicochir Trans 1818; 9: 56–92.]

4. Francois Magendie (1783–1855) administered a Javanese arrow poison to dogs by means of pointed wooden barbs thrust into the rump. The effect was lethal and the poison later was found to be strychnine. He reported this experiment in 1809. Later he attempted to manage a mad dog by infusing warm water into veins. In 1823, he injected two pints of
water into a vein of a man who was dying of hydrophobia. The subject recovered dramatically but died of septicemia.

5. Hale (1797–1861) who was a young physician from Boston injected half an ounce of warm castor oil into a vein of his left arm in 1824. Shortly afterwards, he noticed an oily taste in his mouth and the felt nauseous. Later he suffered severe bowel disturbances as if he had taken a purgative and he became ill. After a month or so, he however recovered completely.

6. Based on a report that Russian soldiers had received treatment of intravenous opium with good results, WB O'Shaughnessy suggested during 1831–1832 that intravenous injection of 'tep id water holding a solution of the normal salts of the blood' could be an effective treatment of cholera; the cause of cholera was not known at that time [Source: Review of book in Lancet 1832; ii: 926–929]. Thomas Latta who was a physician in Leith, Scotland, read this report and attempted to rescue a number of cholera victims by intravenous infusion of water containing salts and saved many lives [Latta T. Malignant cholera. Lancet 1832; ii: 274–277].

7. Dr. Wood published his results in a paper entitled “New method of treating neuralgia by the direct application of opiate to the painful points” published in Edinburgh Medical and Surgical Journal in 1855. In 1885, he wrote, ‘in all probability what is true in regard to narcotics will be found to be equally true in regard to other classes of remedies.’

8. Morphine was developed in 1820s. Throughout nineteenth century morphine was widely used for medical treatment of various disease conditions. The first recorded fatality from hypodermic syringe induced overdose of morphine was Dr. Wood’s wife, she had been injecting morphine to excess. In the American Civil War (1861–1865), an estimated four hundred thousand soldiers became addicted to opiates after liberal use of morphine injections.

9. Medicine operations or representation of all methods of the manual application of medicine materials (Tubingen 1869).

Sources: