

Table 1-2 Summary of the History of Sterile Drug Technology

1656	First experimental injection by C. Wren in dogs (first container was an animal bladder and first needle was a feather quill)
1662	First injection (opium) in man
1796	E. Jenner used intradermal injections of cowpox virus to inoculate children against smallpox
1831	Introduction of IV therapy treatment of cholera with salt, bicarbonate, water
1855	First use of hypodermic syringe for subcutaneous injection
1860s	Pasteur/Lister/Koch all contributed to discovery of germ theory of disease, concerns for sterility and development of sterilization methods (but not accepted for decades)
1884	Use of first autoclave for sterilization
1890s	Crude filters (asbestos) used for filtering drugs
1923	Florence Siebert discovered cause of pyrogenic reactions
1938	Food, Drug, Cosmetic Act passed by Congress (after sulfanilamide disaster). Ethylene oxide sterilization introduced
1940s	Penicillin started being used
1941	Freeze-drying introduced
1961	HEPA filters, laminar airflow introduced in pharmaceutical industry
1963	Clean room standards introduced, FDA first published proposed GMP regulations
1965	Parenteral nutrition introduced
1970s	Emergence of biotechnology, LAL test for endotoxins
1980s	Introduction of controlled IV devices, controlled delivery, home health care First drug product (Humulin®) from recombinant DNA technology approved by FDA
1987	First publication of FDA Aseptic Processing Guidelines and Guidelines for Process Validation
1990s	Barrier isolator technology, aseptic process validation, process validation, pre-approval inspections, biotechnology growth
1992	<i>The International Conference on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use</i> Established
1996	European Union published Guidance on Manufacture of the Finished Dosage Form issued
1997	First human monoclonal antibody approved (Rituxan®, rituximab to treat cancer)
2000s	Monoclonal antibodies, impact of genomics and proteomics on new parenteral drug therapy, Quality by Design, disposable technologies
2004	FDA publishes revision to Aseptic Processing Guidelines.
2010	Possibilities include vast new numbers of biosimilar products approved, more advances in aseptic processing to the point that parametric release of products produced by aseptic processing can be done, advances in on-line 100% measurement of quality parameters, oral delivery of proteins, complete automation of filling, stoppering and sealing processes, most product manufacturing outsourced; the possibilities are as many as can be imagined.

in Figure 1-1. The drug injected was opium. While the poor human receiving this injection may have had his pain alleviated, he likely was going to die, eventually from microbial and pyrogenic contamination introduced using this crude means of injection. Other drugs injected into humans during those early days were jalap resins, arsenic, snail water, and purging agents. It is improbable that the initial pioneers of injectable therapy had much appreciation about the needs for cleanliness and purity when injecting these medications. After 1662, injecting drug solutions into humans was not commonly practiced until late in the 18th century.

Intravenous (IV) therapy was first applied around 1831 when cholera was treated by the IV injection of a solution containing sodium chloride and sodium bicarbonate in water. Normal saline was used by Thom Latts to treat diarrhea in cholera patients using intravenous infusions. Intravenous feeding was first tried in 1843, when Claude Bernard used sugar solutions, milk, and egg whites to feed animals. By the end of the 19th century, the intravenous route of administration was a widely accepted practice. Injections of emulsified fat in humans were first accomplished by Yamakawa in 1920 although, not surprisingly, major problems existed in formulating and stabilizing fatty emulsions.

It is conjecture who really was the first person to invent and use a syringe. According to medhelpnet.com, a French surgeon, Charles Gabriel Pravaz (Fig. 1-2), and a Scottish physician, Alexander Wood, independently invented the hypodermic syringe in the mid-1850s. Other references credit G. V. LaFargue for inventing the first syringe used for subcutaneous injections in 1836 with wood, using it to inject morphine. Charles Hunter first used the word "hypodermic"