Candida sp, Streptococci, Acinetobacter calcoaceticus, Pseudomonas, Serratia, Escherichia coli, Enterobacter, Klebsiella, and Proteus are examples of microorganisms found to cause sepsis.

If sepsis occurs in a hospital setting (nosocomial), it is often very difficult to destroy these organisms with conventional antibiotic therapy because of the resistance developed in these settings.

The best way to prevent sepsis from occurring is through careful aseptic procedures employed to prepare the skin for an injection and to manipulate and inject the sterile device. In-line bacterial retentive filters also help to prevent sepsis although there are other limitations in using these filters such as costs, potential for clogging, and they themselves can be a source of contamination, usually through improper insertional procedures. Also, as discussed in chapter 28, endotoxins resulting from gram-negative bacterial growth will not be removed by sterilizing filters.

With respect to endotoxins, the condition called toxemia results from an inadvertent infusion or injection of a biological toxin such as endotoxin. Endotoxins cause fever, leucopenia, circulatory collapse, capillary hemorrhages, necrosis of tumors, and other cascades of problems that can lead to death if the amount of endotoxin is high. The LD_{50} dose of endotoxin in mice is approximately 150 μg (6). A fatal dose of endotoxin in humans is unknown or not found in the literature, but a threshold pyrogenic dose in humans is 350 endotoxin units (5 EU/kg × 70 kg with 5 EU/kg being the threshold pyrogen dose—see page 428—and 70 kg being the average weight of an adult person). The level of endotoxin is controlled in parenteral drug products and sterile devices through the use of endotoxin limits as discussed in chapter 28. The Limulus Amebocyte Lysate test has proven to be a very sensitive and specific indicator for the presence of endotoxin in amounts much lower than known to cause pyrogenic responses in humans.

THROMBOSIS

Thrombosis is a blood-clotting problem that occurs at the site of injection with either an IV infusion or IV or intra-arterial injection. The thrombus formed may propagate proximally for a distance from the injection site. Complications arising from thrombus formation include emboli formation that may cause pulmonary infarction and secondary infection resulting in septicemia, endocarditis, and/or pneumonia.

Thrombosis occurring in an artery creates a more much serious complication than venous thrombosis. Gangrene of the tissues supplied by the artery could result, especially if collateral circulation around the thrombotic artery is inadequate.

Thrombosis can result from extremes in solution pH, inherent irritating properties of the drug being injected or infused, drug insolubility at the injection site, particulate matter, extremes in osmolality, injecting too much volume of drug product for the blood vessel chosen, reaction with the catheter residing within the vein or artery, and general trauma. Certain people and certain disease states, for example, systemic lupus erythematosis, are prone to react adversely to injections or infusions and the slightest irritation could cause a thrombotic reaction.

SUMMARY

Besides all of these hazards discussed in some detail, parenteral drug administration always is subject to potential serious and specific hazards or complications every time an injection is given. Every parenteral drug injected itself has specific potential side effects associated with its injection. Of course, these are required to be specified in the package insert. Indeed, studying package inserts of drug products administered by injection is the best way to learn and be aware of the potential hazards of injectable drug administration.

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