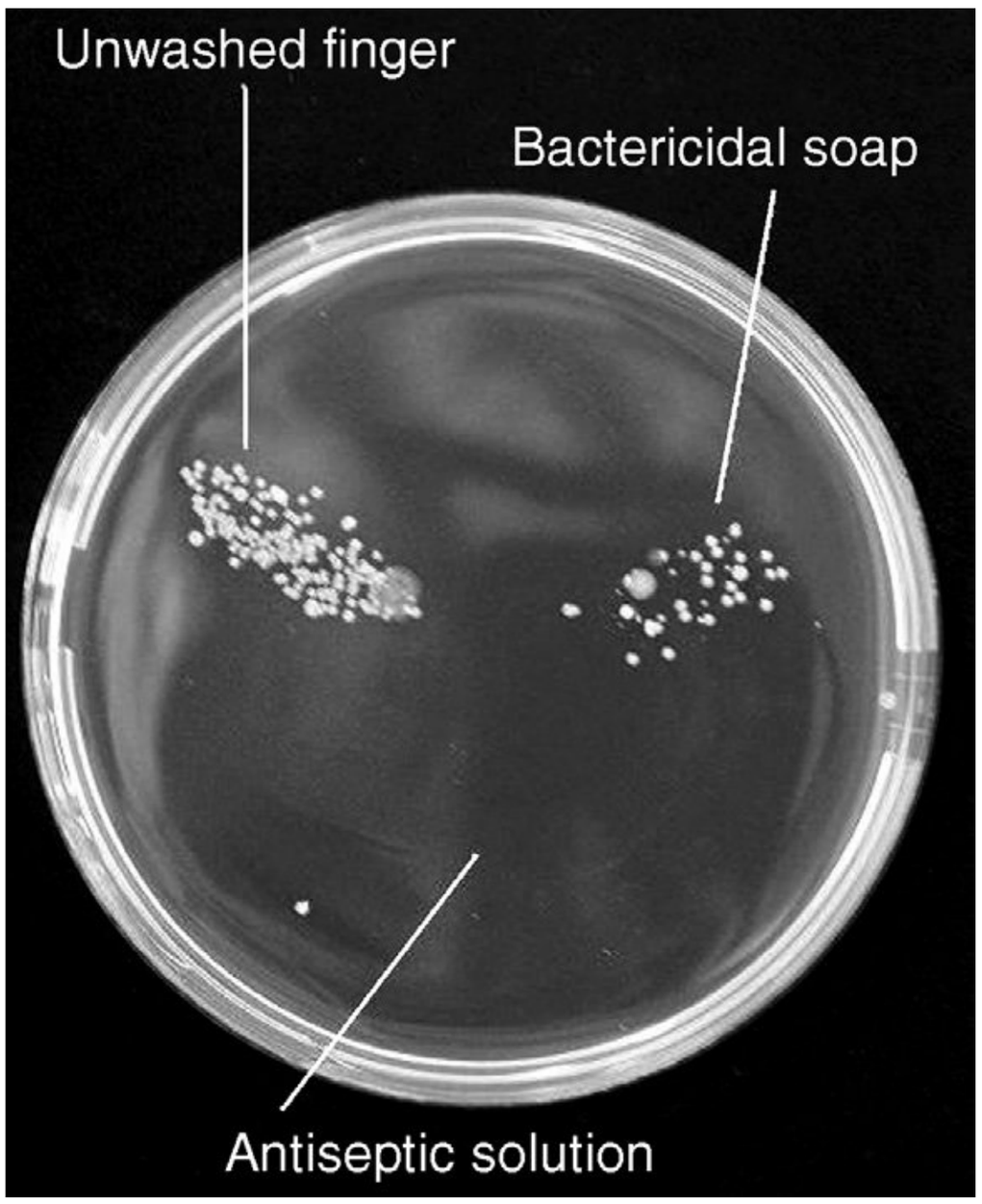

Fig. 50.1 • Colonies of bacteria resulting from 'fnger dabs' onto agar. Top left: bacteria from unwashed fnger; top right: a fnger washed with 'bactericidal' soap; bottom sector: no colonies arising from a fnger swabbed with antiseptic solution.

relied upon to eliminate contamination, but a recognized antiseptic is far more effective.

The methods and equipment used for monitoring levels of contaminants arising from water, raw materials and the environment are described in Chapter 14.

Factors influencing the growth of spoilage organisms

In addition to water activity that was considered earlier in this chapter, factors influencing the rate and extent of growth of a contaminant within a pharmaceutical raw material or manufactured medicine include:

- nutrient availability
- temperature
- pH
- redox potential
- the presence and concentration of antimicrobial chemicals.

Microorganisms differ enormously in their metabolic capabilities. Some, like *E. coli, Pseudomonas aeruginosa* and several *Bacillus* species, can synthesize all the amino acids and vitamins they need from a variety of simple carbon and nitrogen sources. The minerals that they require are often present in sufficient concentration as impurities in the ingredients of the medicine. Thus, in the absence of antimicrobial chemicals, organisms of this type may grow to concentrations of 10^4 per mL or gram, or even higher in products like syrups, linctuses and creams. Products containing glycerol, sugars, amino acids or proteins would clearly represent such ideal media for microbial growth that their preservation is sometimes difficult to achieve even with added preservatives. Even in the absence of these nutritionally rich materials, many bacteria and fungi are still able to utilize other components of the formulation as food sources. Several of these have already been mentioned, but in addition to surfactants and various viscosity-raising agents, the volatile and fixed oils used as flavourings or emulsion components are particularly suitable as nutrients for microorganisms.

The rate of spoilage progression will vary with temperature, although the period of time for which a manufactured medicine is usually stored before use is normally so long that the difference in bacterial growth rate between, say, 15 °C and 20 °C may become insignificant in the context of a 2-year shelf-life. However, there is the possibility of organisms growing during the course of manufacture, and so it is important for production scientists to be aware just how rapidly the population of contaminants may rise. Figure 14.1 shows that the concentration of *Pseudomonas aeruginosa* rose 10,000-fold in 44 hours at ambient room temperature in a multidose veterinary injection that was supposedly preserved with benzethonium chloride. Clearly, the potential for a rapid increase in numbers is even greater where there is no antimicrobial agent present at all.

Most bacteria have an optimum pH for growth that is near neutrality, whilst most fungi favour slightly acidic conditions and grow best at pH values of 5–6. Although product pH may markedly influence growth rate itself, it also has a bearing on the activity and stability of any antimicrobial chemicals present, so the magnitudes of these various effects may have to be considered at the product formulation stage, and a compromise value selected for the product pH. This is considered further in the next section of this chapter.