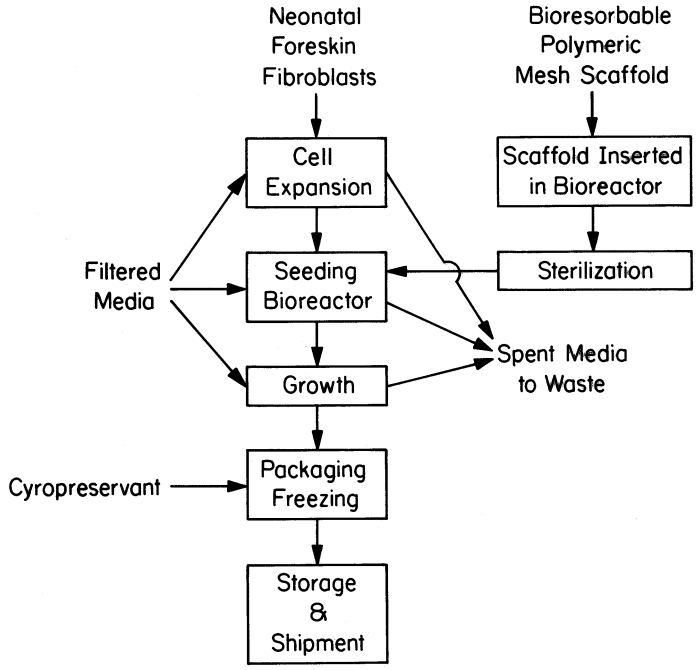

Figure 15.1. Conceptual process diagram for production of a human skin substitute.

components: collagen fibrils, proteoglycans, and cells known as chondrocytes. These cells are present in low numbers (1% by volume) but are responsible for synthesis and release of these other compounds, forming cartilage. When chondrocytes are cultured as two-dimensional (monolayer) cultures, the cells are no longer differentiated and do not make normal hyaline matrix proteins. However, if cultured in three dimensions, such as a suspension in agarose, or *in vivo,* the cells redifferentiate and begin to manufacture hyaline-like matrix.

Because of immunological responses it is advantageous for patients to supply their own cells for expansion in number before being reinjected into the knee. A manufacturing process for individual cell growth is needed. The supply and reuse of cells from an individual is termed *autologous implantation*.

The basic procedure entails biopsy of a patient to obtain a small number of chondrocytes, monolayer culture of primary chondrocytes and expansion of cell numbers, release of cells from monolayer and into suspension, assembly of cells in three dimensions, and injection into the patient's own knee. This product is known as Carticel™. The implanted cells produce hyalinelike cartilage and fill in defects in the patient's knee. Patients can often reenter vigorous physical activity in twelve months.

The primary manufacturing challenge here is the need for separate culture for each individual. To accomplish this for mass production is a challenge to any manufacturing process. There is expected to be a demand for other therapies (e.g., cancer treatment), where cells from an individual will need to be efficiently cultured and returned to the individual.