To a large measure, wrinkles were ignored as a serious subject by most scientists until about 35 years ago when scientific articles began to appear on the nature and origin of wrinkles.\textsuperscript{1,2} Since that time there has been some controversy about what exactly constitutes a wrinkle. One dictionary definition is: “Wrinkles are configuration changes in the skin as a result of mechanical stresses acting on lax and excessive skin ...”\textsuperscript{3} While this definition is correct, it does not shed insight into the cause or prevention of wrinkles.

Some believe that wrinkles are due to a clone of abnormal cells that have been reproduced. Others believe that wrinkles are due to the loss of subcutaneous fat and bone. The loss of the supporting structures over which the skin drapes will result in wrinkles as the same amount of skin is covering less underneath. This leads to redundancy in the skin, commonly known as a wrinkle. Thinning of the skin due to loss of collagen and decreased elasticity due to loss of elastin also make the skin drape poorly. Probably all of these beliefs are correct and it is the combination of causes that is closer to the truth. This chapter will cover the structure of wrinkles, how they form, what can be done to help prevent them, and finally, explore some current treatment methods for wrinkles.

**Skin aging pattern**

To form a wrinkle you need loose skin. The process called “aging” can contribute to laxity of the skin, and in time certain physical changes are manifested. (See Figure 15-1.) At 25, the eyebrows move down over the
superorbital ridge of the eye, resulting in a sagging, droopy appearance. There is some intraorbital fat that herniates, or falls down, into the eyelids causing the baggy look of the aged face. The culprit in this process is lax, or loose skin.

Figure 15-1. Wrinkling of the face can be characterized by these folds that contribute to the appearance of an aged face.

At about 30, the nasolabial folds become more prominent as they deepen. At 40, forehead wrinkles appear and crow’s-feet are etched at the outer canthus of the eyes. By 50, the outer canthus starts to slope downward and the nose starts to droop. This is accompanied by the appearance of wrinkles about the mouth and neck. Around this time, the cheeks start to sink in due to loss of fat.

At 60, the eyes seem smaller because of the folded skin around them; there is more fat absorbed in the cheeks and in the chin area. During this period the bones of the skull begin to shrink and more loose skin is produced. From here on, it is a continuing process of fat absorption and elastic reduction that produce the sagging skin associated with many people 70 and older.

The most obvious place to look for wrinkles is on the face. Here they begin and here they stay, and oh, how you wish they would go away. Consider the
anatomy of the facial muscles. Here a clue to the behavior and nature of the wrinkle becomes apparent. **Figure 15-2** shows a complex group of muscles, all of which relate in some manner to facial expressions. Now if the wrinkle pattern is superimposed over these muscles, it is easy to see that the **wrinkles form perpendicular to the long axis of the muscle.** In the case of the circular muscles about the eyes and the mouth, the wrinkle line is perpendicular to a tangent drawn to the curved area. (See **Figure 15-3.**) It is this observation that has led to the popularity of chemodenervation produced by botulinum toxin. The relaxation of the muscles over which the skin is pulled can improve wrinkles that appear when the face moves, known as wrinkles in motion.

**Figure 15-2.** Note the direction of muscle. All these muscles are used in facial expressions. The black shows the direction of wrinkles across the muscles. Normal folds run parallel to muscles.

At this point it is important to distinguish between a wrinkle and a crease. **Creases are normal folds in the skin that occur at joints and other areas of the body associated with movement and lax skin.** Normal folds occur at all ages and are necessary for normal functions. Wrinkles occur only on sun-damaged skin or aged skin. These types of folds or creases are called wrinkles at rest. They are treated with fillers, which are substances injected beneath the skin to take of the loss of tissue, usually subcutaneous fat and bone. Only by replacing the volume in the face can these folds be treated.
Figure 15-3. Side view of facial muscles used in expression. The black shows the direction of wrinkles. Crinkles may occur anywhere on the skin.

**Histopathology of wrinkles**

Histology is a department of anatomy that deals with the minute structure, composition and function of tissues. It is also called microscopic anatomy. Frequently certain stains or dyes are used to visualize the tissues. Histopathology is the study of abnormal tissues using the techniques of histology. When a small piece of skin with a wrinkle is examined under the microscope very little is seen.

In 1969, Wright and Shellow published their results of the histological examination of wrinkled skin and could not distinguish wrinkled skin from normal skin.\(^2\) This finding was confirmed by Montagna and Carlisle in 1979.\(^4\) Kligman and co-workers, in an extensive study of wrinkled skin, were able to find only fine changes in the structure of elastin in wrinkled skin. This finding was so small that it required an electron microscope to detect it. However, the finding was consistent and implicates the elastin fiber was one of the major culprits in wrinkle formation.

In 1999, a study by French scientists\(^5\) involving 157 biopsies of 46 subjects between 57–98 confirmed the previous results and shed light on the pathogenesis of wrinkles in that biochemical studies as well as histological studies were performed. Their findings indicated that significant biochemical changes
contributed to the formation of wrinkles. In particular, markers of cellular differentiation were significantly decreased. Filagrin, keratohyalin granules, and the enzyme transglutamase I were decreased. These components are essential for the maturation of corneocytes and deficiencies produce water loss and desquamation defects.

At the dermoepidermal junction there was a decrease in collagens IV and VII and a loss of oxytalin fibers, all of which contributed to weakening the interface between these two structures. In the dermis, glycosoaminoglycans were noted to vary in distribution around the wrinkled area, while a marked decrease in chondroitin sulfate was noted in the papillary dermis. These substances are like sponges that maintain the water content of the skin. Without hydration, the skin is full of wrinkles. Increased water in the skin is the easiest way to eliminate wrinkles. Hydrated skin is smooth and soft while dehydrated skin is rough and wrinkled. It is this principle that is used by most moisturizers to reverse wrinkles and aging. Injectable fillers also use this same principle as they contain hyaluronic acid, which is one of the glycosaminoglycans in the skin. This topic is discussed in more detail in the Chapter 29.

Classification of wrinkles

For a body of knowledge to be called a science, it must be arranged in a systematic form called classification. So the types of wrinkles seen in skin must be classified. The classification in this chapter is slightly modified from Kligman and co-workers. There are three major groups of wrinkles.

1. **Crinkling-type wrinkle.** These are fine wrinkles formed from folded skin. They usually are seen in persons around 75, and in sun-damaged individuals with post-inflammatory changes in the skin called elastosis.

2. **The glyphic wrinkle.** From the Greek word *glyphein*, which means “to carve,” this wrinkle has a crisscross pattern and frequently is seen on the cheeks and the neck.

3. **The deep wrinkle.** This wrinkle forms a major line or deep groove that is long and straight. This is the most troublesome wrinkle because it is so visible and so difficult to eliminate.

Development of a wrinkle

The structure of wrinkles has been discussed and they have been classified. Now let’s look at the why and how of wrinkles, and then explore what can be done to help eliminate them. In Figure 15-4, a half face of a young woman and