Sperm motility requires the interaction of intracellular factors, including an adequate level of adenosine triphosphate (ATP), functional axonemal dynein ATPases, and an intact axoneme bathing in a proper ionic environment. These factors also represent the minimal conditions required to initiate and maintain the motility of modeled spermatozoa (i.e., spermatozoa demembranated by a detergent treatment in which motility is initiated by the addition of ATP and ions (1–4). Extracellular factors that affect these minimal requirements will cause an arrest in sperm motility. Factors such as sperm agglutinating antibodies that act at the surface of cells by forming a physical network of spermatozoa bound to each other obviously act via different mechanisms. This chapter will not cover the effects of sperm immobilizing or agglutinating antibodies on sperm motility, but it will focus on the actions of factors, such as infections, proteins of the immune system, polymorphonuclear leukocytes, and reactive oxygen species (ROS).

Infection, Bacteria, and Bacterial Products

Several criteria were suggested as indicators of an infection in the male sex glands, including: (1) history of urogenital infection and/or abnormal rectal palpation, (2) presence of leukocytes or bacteria in expressed prostate secretions and/or urinary sediments after prostatic massage, (3) growth of pathogenic (> 1000/ml) or nonpathogenic (> 10,000/ml) bacteria in twofold diluted seminal plasma, (4) presence of leukocytes (> 106/ml) in semen, and (5) disturbed secretory function of the accessory sex glands (5). Any combination of two of these criteria makes the diagnosis of an accessory gland infection...
likely, but far from definitive (5,6). Many men are asymptomatic while having elevated levels of bacteria and leukocytes in semen.

Infection, which is a major cause of infertility in women, may have a similar deleterious effect in men, but the evidence is often conflicting and controversial (6) unless pathogens completely block any segment of the male reproductive tract, therefore causing azoospermia. The negative effect of *Escherichia coli* on sperm motility in vitro that were first reported by Schirren and Zander (7) were confirmed by several authors (8–12). A sperm-to-bacteria ratio of 1 clearly decreases sperm motility parameters (percentage and progressiveness). Bacteria themselves rather than their secretory products cause these effects. Adherence of *E. coli* to sperm would be mediated via a mannose-binding site and would be involved in the triggering of membrane damage to spermatozoa (12,13)

Cytokines

The immune response is modulated by several factors, such as cytokines and cytokine inhibitors (14). Cytokines are a family of polypeptide hormones that are produced primarily by cells of the immune system involved in response to various stimuli, including foreign antigens. Both male and female genital tracts are immunologically dynamic tissues that contain products of local, as well as systemic, immune responses, both humoral and cell mediated. Thus, spermatozoa could be affected by these products before (in the male genital tract) and after ejaculation (in the female genital tract) (15).

Incubation of spermatozoa with transforming growth factor-β (TGF-β), interleukins 1 and 2 (IL-1, IL-2), granulocyte macrophage colony-stimulating factor (GM-CSF), and B-cell growth factor (BCGF) did not affect sperm motility, sperm function, and subsequent fertilization, except when used at very high concentrations (16). On the other hand, two cytokines—interferon (INF)-α and γ, and tumor necrosis factors (TNF-a)—had negative effects on sperm motility and penetration rates in zona-free hamster oocytes (17,18). Relatively high concentrations of INF-α and TNF-a, however, were required in short-term culture in order to observe such effects. Huleihel et al. (14) reported that sperm cells from fertile and oligoasthenoteratozoospermic infertile men constitutively produced IL-1. This report is surprising because motile spermatozoa, as selected from normal ejaculated semen by swim-up technique, should be devoid of cytoplasmic ribosomes, which makes it impossible for IL-1 to be constitutively synthesized by mature sperm cells. The presence of remnant leukocytes or immature germ cells in the sperm swim-up fraction may explain the result of Huleihel et al. (14).

IL-6 is probably the most specific marker for the detection of male accessory gland infection (95% sensitivity), and the correlation observed between the concentration of IL-6 and the level of reactive oxygen species (ROS) produced in semen (19) may be linked to the stimulating effect of cytokines