Similar to many other diseases, the aetiology of male infertility is commonly multifactorial. Aside from the typical andrological diseases, as listed in the following chapters and summarized in the diagnostic flow chart, there are three complementary groups of factors that may exert an unfavourable influence on men’s reproductive potential (Fig. I.3.3).

Genetic factors include the well-known abnormalities in the number of chromosomes and structural defects such as translocations. These and the alterations found in patients with congenital bilateral agenesis of the vasa deferentia and seminal vesicles associated with mutant cystic fibrosis transmembrane conductance regulator (CFTR), and the microdeletions of the DAZ region of the Y-chromosome, are to be classified as congenital abnormalities.

However, other minor genetic defects may play a role in the pathogenesis of sperm deficiency, and may possibly come to expression if the DNA repair mechanisms (McMurray and Kortun 2003; Karagiannis and El Osta 2004; Rockett et al. 2004) of spermatogenic cells are unable to correct the defect(s). The latter could well result from oxidative overload, which itself may be due to a number of factors at the testicular level (e.g. varicocele), the genital tract (e.g. infection or inflammation) (Depuydt et al. 1996), or from external origin (Aitken 2003; Schrader and Cooke 2003).

Lifestyle factors include nutritional state and intake of certain subgroups of essential fatty acids, obesity and overweight, abuse of alcohol (more than 6 units per day) or tobacco (more than ten cigarettes per day) (Mahmoud et al. 1998), the regular use of hot baths, tight clothing, and severe stress. These may directly suppress spermatogenesis and/or are associated with the generation of excessive amounts of reactive oxygen species.

Another group of factors with adverse effects are the exposure to toxic substances such as heavy metals (Bonde et al. 2002), carbon disulphide (Vanhoorne et al. 1994), or benzenes at the workplace. Also, exposure to high ambient temperature may suppress spermatogenesis. In addition, internal exposure to environmental agents that disrupt the hormonal balance, including xeno-oestrogens or antiandrogens, seem to play an important role.

Finally, several causal diagnoses may be given in the same patient, reinforcing each other’s impact because of (negative) synergy.

Evaluating the population of men consulting because of infertility by means of the sperm production

Fig. I.3.3. Subfertility/infertility: a multifactorial disease. CAVD congenital agenesis of the vasa deferentia, CAVE ICSI beware of transmission by intracytoplasmic sperm injection, MAGI Male accessory gland infection
index demonstrates a cumulative distribution (Fig. I.3.4). The sperm production index is calculated by dividing the sperm output per ejaculate (sperm concentration multiplied by ejaculate volume) by the total testicular volume. In normal men, the sperm production index is estimated at 4.9 or more million spermatozoa per millilitre of testicular volume per ejaculate. The distribution observed in Fig. I.3.4 suggests a multifactorial causality in a large proportion of infertile men (Everaert et al. 2003). For instance, smoking and varicocele have an additive effect in decreasing the sperm production index (Fig. I.3.5). This index is decreased in men with more than 2 million peroxidase-positive white blood cells who present no other abnormalities of the genital organs. In contrast, a decrease in the index is already observed when 0.3 million white blood cells are found in the ejaculate of men with varicocele, again suggesting a synergy between these two factors.

**Fig. I.3.4.** Cumulative effect of different factors on sperm production (non-azoospermic subfertile men). VAR varicocele, AbnEPID abnormal epididymis, CRYPT cryptorchidism

The body mass index of men consulting for infertility was higher than that of the average male population of the same region (Fig. I.3.6), with more patients being classified as overweight or obese. Furthermore, the intake of essential fatty acids belonging to the omega-3 group was lower in infertile men than in fertile controls, and there was a positive correlation between the nutritional intake of alpha-linolenic acid (18:3 ω3) and both sperm concentration and progressive motility (Christophe et al. 1998).

In view of these and many other findings, it is mandatory to take into account that fertility in a particular man may result from the synergistic interaction between several factors, namely the genetic constitution, the patient’s lifestyle, the amount of toxic agents he is exposed to in his workplace and local environment,