

**CHAPTER TWO:  
REVIEW OF LITERATURE**

## **INTRODUCTION**

This review of literature will discuss changes that occur as an individual advances in age, and to review documented changes in muscle function found in aging animals and human subjects.

Advancing age is accompanied by sarcopenia in both animal and human subjects (Rodgers & Evans, 1993). Sarcopenia is associated with a number of aging properties such as, changes in muscle mass and force/strength. These changes are directly related to fiber loss and injury to skeletal muscle (Zebra et al., 1990; Lexell & Downham, 1992; Booth et al.,1994).

While some researchers have focused on describing changes in muscle function and histology, others are concentrating on theories of why “aging” occurs. Over the years, several theories have merged including programmed cell death (Lockshin & Zakeri, 1990), DNA-RNA replication & cross-linkage (Curtis & Miller, 1971), immunologic (Smith & Walford, 1977), and the free radical theory (Emerit & Chance, 1992).

However, accumulation of ROS, which are a subgroup of free radicals, and their impact on muscle function, is gaining much attention. For this reason, the ROS association with age will be discussed.

## **MUSCLE MASS AND FORCE/STRENGTH**

Muscle mass and strength decreases with age, and these declines are accelerated with physical inactivity. Muscle atrophy and weakness are believed to be the leading

cause of falling accidents among the elderly. This problem is well documented in several articles (Marwicks, 1997; Kramer et al., 1997; Myers et al., 1996). In these articles, the investigators found that among the individuals who had fallen, each had significantly decreased values for power and strength in muscles associated with balance. These included the knee flexors and extensors and the ankle plantar and doriflexors (Lipsitz et al., 1991). Likewise, others have shown that the loss of muscle strength is greater in the legs than in the arms and hands (Shephard, 1981; Rice et al., 1989; Faulkner et al., 1990). Of course, the rate of decline in a mature adult population will vary from person to person, irregardless of whether or not an individual has lived an active or sedentary lifestyle. Researchers have shown that active older adults fair far better than their sedentary counterparts. For example, Alexander et al. (1991) compared old able adults (rise without the use of armrests) to old unable adults (rise with the use of armrests) on time rising from a chair. Their results showed that old unable adults took more time to rise from a chair than it took old able adults. The old unable adults also experienced difficulty with hand positioning when rising. This suggests that the old unable adults may be experiencing the loss of grip strength as well as motor control.

Studies have not only focused on old age, they have also concentrated on the role of gender in muscle mass and strength changes. Fleg and Lakatta (1988) determined that muscle mass between the ages of 30 and 70 years was reduced by 23% and 22% in men and women, respectively. Another study found a ~30% reduction in total muscle mass over a lifetime of 50 years (Tzankoff & Norris, 1978) following maturation.

In a cross-sectional study of muscle strength and mass in 45 to 78 year old men and women, Frontera et al., (1991) found that muscle mass and strength were lower in the older group (65 to 78) than in the adult group (45 to 54). The results also demonstrated that absolute muscle strength difference among the sexes are minimized when values are normalized for fat-free mass.

Once muscle mass and strength decrease, the likelihood of fatiguability is increased. The notion of increased fatigue (failure to maintain force or power output) with age was investigated by Lindstrom and colleagues (1997) for both sex and age. The fatigue rate was measured in 22 healthy young subjects (average age of 28 years, 8 women and 14 men) and 16 healthy old subjects (average age of 73 years, 8 men and 8 women). The data showed no significant difference among the four groups with respect to their relative strength. However, age appears to have an impact on fatigue rate (difference between young and old men was 29% and between young and old women was 7%). Unfortunately, the present research is contradictory and future research may clarify this topic.

In animal studies, muscle mass and force decrease with aging, but the extent of loss will vary from muscle to muscle (Klitgaard et al., 1989; Eddinger et al., 1995; Lynch et al., 1993; Brown & Hassler, 1996). Klitgaard and coworkers showed a 29% decrease in force production in the soleus (a slow muscle) between 9 and 24 months, with no further changes at 29 months. Larsson and Edström (1986) found no difference in force production between young Fischer 344 (6 mo.) and aged Fischer 344 (20-24 mo.) in the soleus or tibialis anterior when the cross-sectional area (CSA) was asserted in the results. The force production of skinned fibers from the extensor digitorum longus (EDL) in rats aged 9 and 30 months showed no difference (Eddinger et al., 1985). However, they also found an increase in the force production of the soleus from old rats. Lynch et al. (1993), also found no significant differences in force production of the EDL between adult and old

rats using skinned fibers. The soleus force production of these rats was unchanged between adult and aged rats. In a study by Brown and Hasser (1996), a significant age-related decrease in muscle mass after 28 months in male Fischer 344/Brown Norway rat hybrids was observed. The study showed a muscle mass reduction in the soleus (18%), extensor digitorum longus (EDL) (16%), plantaris (37%), and gastrocnemius (38%). Those reductions would suggest that weight-bearing muscles atrophy before nonweight-bearing muscles with age progression.

### **FIBER LOSS AND INJURY**

A reduction in muscular strength is also associated with the decline of skeletal muscle function (Booth et al., 1994; Ermini, 1976). This decline involves weakness due to decreased muscle mass, the loss of type II fibers (Brooks & Faulkner, 1994). This weakness lead to increased fatigue and decreased force.

Progressive loss of muscle strength is related to a loss of muscle mass with age. In older adults, individual muscle fibers may be atrophied or the number of fibers may be reduced. Conflicting data have brought about the necessity for further investigation involving atrophy and the number of fibers with age. Discrepancies in reported results may be primarily based upon extraction technique. Using a midsection technique (counting fibers from the middle of the muscle), Maxwell et al., (1974) and Gollnick et al., (1981) showed a significant decrease in fiber number. Prior studies have also shown a decrease in fiber number but not muscle size (Grimby & Saltin, 1983; Tanchi et al., 1982; Hooper, 1981; Inokuchi et al., 1975; Lexell et al., 1983). However, when Brown (1987)

used nitric acid to extract fibers, she found no change in fiber numbers of the soleus and extensor digitorum longus in 6-28 month old rats.

Even though there is some agreement that fiber type composition changes with advancing age, controversy surrounds the degree and shift change between type I and II fibers (Aniansson et al., 1980; Klitgaard et al., 1990). Type I fibers are characterized as slow, oxidative fibers with high resistance to fatigue, and slow shortening velocity and absolute force output. Type II fibers can be further categorized as type IIa and IIb. Type IIa and IIb fibers are fast glycolytic fibers with a white appearance due to low myoglobin content. Physiologically, type II fibers consist of fast shortening velocity and high absolute force output. Type II fibers have a low resistance to fatigue.

Previous reports have shown a decrease in the mean numbers of type II fibers (Lexell & Downham, 1992). While others have documented a great increase of type I fibers in older individuals (Larsson, 1978; Örlander et al., 1978). Reduction in type II fibers was correlated with large weight-bearing muscles which may alter gait and balance in both animals (Holloszy et al., 1991) and humans (Hortobagyi et al., 1995).

## **FREE RADICALS EFFECT**

The free radical theory states that cellular aging occurs due to “molecules which have either an extra or missing electron making them highly reactive and likely to combine with and destroy essential cell components” (Harman, 1968). Damage from free radicals accumulate over time because cells become less able to protect themselves. Fleming et al., (1982) hypothesized that free radicals cause the greatest damage to nerve and muscle cells because older cells become less effective against free radical attack..

The production of reactive oxygen species (ROS) which are part of the free radical family, is thought to contribute to the progression of sarcopenia. Burton et al. (1985) suggested that effective scavenging of ROS damage can happen if the following criteria is met : (1) the scavenger must penetrate to the intracellular site where the free radical is produced, (2) the scavenger must be present at the time in which the cell is injured, (3) the scavenger-free radical interaction must be high to compete with biomolecules (the major reaction takes place with the scavenger), and (4) the scavenger must attain a suitable concentration in order to compete effectively with neighbouring biomolecules. If these criterias are met then suggestively, the progression of sarcopenia may be retarded.