Plenary 5: Nutrition and Ageing

**Calorie restriction and life extension**
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**Background** – Long-term calorie restriction (CR) extends the life of many lower animals, including rats, mice, fish, flies and worms. However, in humans there are no life-long studies, only short term trials over 2 to 6 years which indicate that CR reduces the risk factors for cardiovascular disease and diabetes.

**Review** – In 1935 McCay (1) clearly showed that prolonged CR extended the life of rats. This has been repeatedly confirmed by later investigators, who also showed that CR delays the onset of various age-related diseases and thereby extends life. No life-long CR studies have been performed in humans. However the inhabitants of Okinawa (islands south of Tokyo) who are the longest lived people on earth eat 40% fewer calories than the Americans and live 4 years longer (2). The Okinawans have a lower mortality from stroke and cancer. In developed countries human life expectancy has increased in the 20th century by an average of nearly 30 years, mainly due to reduced deaths from infectious diseases, accidents and cardiovascular disease (3). During the latter part of the 20th century diets in developed countries were improved by increasing the intake of fruit, vegetables and fish and decreasing saturated fat consumption. However, calorie intake has increased since 1970 by about 30% in USA and in many countries is leading to overweight, which is life-shortening. Overweight in middle age shortens life by 3 years and obesity by 7 years (4). Obesity in young adults takes 13 years off life. Thus CR to prevent overweight and obesity could add 3 to 13 years to life expectancy. The semi-starvation (20% CR) of wartime in the 1940s in Scandinavian countries reduced the incidence of cardiovascular disease. In the 1990s, 20% CR studies on healthy adult humans over a 6 year period produced significant falls in the risk factors for cardiovascular disease and diabetes (5). A recent 25% CR study on overweight adult humans over 6 months reduced their body weight and decreased body temperature and plasma insulin, which are biomarkers of longevity (6) indicating increased life expectancy.

**Conclusions** – Thus CR over 6 months to 6 years has been able to reduce the risk factors (body weight, blood pressure, cholesterol, glucose) for the major diseases that kill humans and improve metabolic functions (body temperature, plasma insulin) that determine life expectancy. While these studies indicate that CR should extend human life, the only proof will come from very long-term CR studies over 50 or more years.

**References**
5. Fontana L, Meyer TE, Klein S. et al. Long-term calorie restriction is highly effective in reducing the risk for atherosclerosis. PNAS 2004; 101:6659-6663