Meeting report

Muscular activity and energy expenditure: biochemistry and physiology of exercising muscle
A report of The Rank Prize Funds Mini-Symposium 1990

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At a meeting organized by The Rank Prize Funds, a small group of invited young research scientists discussed their work on muscular activity and energy expenditure with some senior people. An account of those aspects of the meeting which dealt with methodology, factors influencing energy expenditure and possible differences in the mechanical efficiency of muscular activity have been discussed elsewhere1. The present account concentrates on papers concerned with the mechanism of muscular contraction, particularly in relation to exercise and fatigue. Key references suggested by the participants have been incorporated in the text.

Biochemistry and biophysics of contraction
A general introduction to the biochemistry and biophysics of the contraction process was presented and an explanation given as to why less force is developed during shortening than in isometric contraction2-4. Attention was drawn to differences between current understanding and the general accounts of contraction in standard textbooks and it was pointed out, for example, that not all cycles of attachment and detachment of cross-bridges lead to the splitting of ATP. Some recent findings on the energetic cost of work production were presented by C. Yin, in collaboration with R.C. Woledge, who contrasted results from frog and mouse. It was concluded that an unknown process must occur during or after a working contraction in mouse soleus muscle and that this probably explains its higher energetic cost of work production compared with frog muscle. A, evidencing the idea of 'unexplained heat' during a contraction and its related recovery process in mammalian muscle was provided by S.K. Phillips. Use of 31P NMR showed a difference between the time course of recovery heat and the resynthesis of phosphocreatine from inorganic phosphate and such findings extend the results of earlier reports5-8.

Novel findings were presented by P. Bolger, in collaboration with A. Rowe, on the effect of divalent cation on the cross-bridges of vertebrate skeletal muscle thick filaments. The presence of non-specific low affinity divalent cation binding sites had been demonstrated in synthetic myosin filaments6 and such sites have now been demonstrated in purified native myosin filaments. It appears that the elasticity of the cross-bridges can be altered by an interaction between the low and high affinity sites in such a way as to make them more elastic as the muscle becomes activated. This may in turn alter the interaction kinetics7 and hence provide another form of regulation in addition to the actin-linked stereic-hindrance system. New approaches which should advance our understanding of the molecular mechanism of muscular contraction were discussed by K.J.V. Poole. Studies in collaboration with G. Rapp and R.S. Goody have been concerned with dynamic X-ray diffraction measurements following photolytic relaxation and activation of mammalian muscle fibres. Of particular interest is the location of strain-sensitive rates in the cross-bridge cycle since these will reflect the important energy transducing steps in the muscle ATPase mechanism. The time course of changes in the equatorial diffraction patterns from different muscle types on photolysis of caged-ATP has been examined using the DESY synchrotron source in Hamburg8.9. Some of the implications of such investigations have been discussed previously by Huxley10.

Muscle fatigue
Skeletal muscle fatigue can be defined as a failure to maintain force or power output1 and numerous investigations have been concerned with elucidating its mechanisms. A general introduction to the problem of fatigue was presented by E.A. Newsholme and this was followed by two presentations on its physiology. An interesting hypothesis based on studies of human adductor pollicis suggests that the extra potentiation and reduced fatigability at low stimulation frequencies, which are preceded by high frequency, is the result of increased myofilbrillar Ca2+ availability and/or sensitivity11. Alterations in force dynamics in fatigued muscle were discussed by C.J. Barclay who advanced a scheme to account for the observed changes in isometric force and force dynamics that occur in fatigued mouse muscle. Results were discussed in relation to earlier studies on muscle contraction and fatigue12, 13. A significant finding was reported in relation to exercise-induced hyperkalaemia and fatigue in man: regular training increases the concentration of Na+, K+-pumps in vastus lateralis muscle14. This could help to explain the reduction in exercise-induced hyperkalaemia associated with training. Beneficial effects of training could thus arise, not only because hyperkalaemia is associated with fatigue and is detrimental to physical performance but also because the less pronounced hyperkalaemia will reduce the risk of the cardiotoxic effects of exercise. Evidence for the role of specific amino acids in relation to fatigue was reviewed in relation to its aetiology and the overtraining syndrome in athletes15. This led to a consideration of plasma glutamine concentration as an important link between skeletal muscle and cells of the immune system during exercise. These cells use glutamine at very high rates and this is essential for lymphocyte proliferation16. A decrease in plasma glutamine concentration may thus result in impairment of immune function and in overtraining syndrome there is indeed an increased incidence of viral infection. The possibility is that regulation of plasma glutamine levels occurs at the point of its release from

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the muscle cell membrane and it has been found that plasma levels are lower in athletes after long-term exercise or at rest in overtrained subjects.

**Exercising muscle**

Further aspects of the biochemistry of exercising muscle were considered in relation to intracellular acidosis and nucleotide loss in the human and equine athlete. Studies on high intensity exercise indicate that there is a threshold to the start of adenine nucleotide loss which corresponds to a given fall in pH and accumulation of lactate above a given level. This loss of adenine nucleotide occurs mainly as ATP and the extent of its fall appears to be reduced by administration of sodium bicarbonate. Other investigations were concerned with the effects of training on muscle metabolism during treadmill sprinting and recovery. For example, 8 weeks of sprint training was found to result in a 12% improvement in peak power output and this was accompanied by an increase in post-exercise muscle lactate and a decrease in post-exercise blood pH. There was, however, no further change in the post-exercise muscle pH or its buffering capacity, and the possibility is that H⁺ efflux could be enhanced by sprint training. Consideration was also given to the influence of nutrition on muscle metabolism and performance during high intensity exercise. It was reported, for example, that changes in muscle pH and glucose 6-phosphate are greater during a fixed period of high intensity exercise after a low carbohydrate, high fat, high protein diet than after a high carbohydrate diet.

The use of a non-invasive method for assessing whole muscle glycogen stores was discussed by A.M. Frencithe. This method uses indirect calorimetry and obviates the need for muscle biopsies. Its value for investigating high intensity exercise remains to be determined. Glycogen availability is not at present considered to be a limiting factor for the performance of high intensity exercise, since whole muscle glycogen levels are high at the point of fatigue. However, important new evidence suggests that the use of whole muscle substrate and metabolite levels as indicators of the metabolic response to high intensity exercise could be misleading because of a marked difference in response between fibre types. Previous investigations have suggested that skeletal muscle is an important thermogenic organ in man. This hypothesis was not supported by results on adrenalin-induced oxygen consumption in forearm skeletal muscle presented by I.W. Gallen. However, these results remain to be confirmed by direct measurement of muscle oxygen consumption in various sites. The possibility also exists that there could be a differential response between fibre types and this suggestion remains to be investigated.

The symposium provided an excellent opportunity for bringing together individuals with a wide range of research interests. Not only did it provide opportunities for discussion and exchange of ideas but it also highlighted important new areas for research.

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**References**