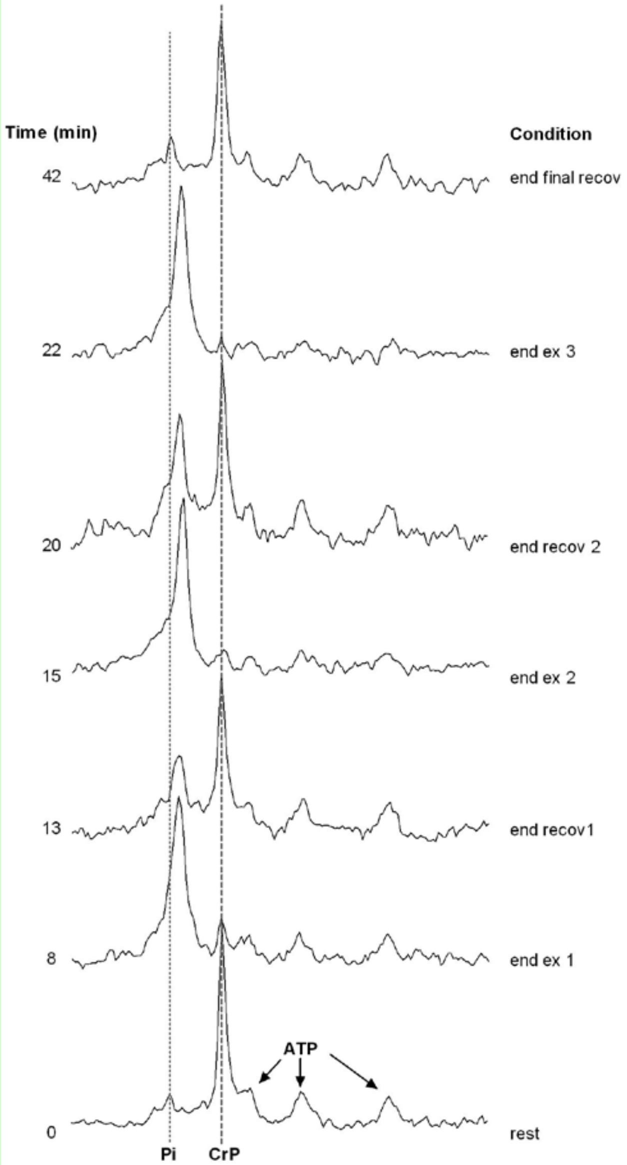
The Phosphagen System Overview



It is important to emphasize from the onset that the phosphagen system is more than an immediate energy system, which has been the historical and traditional label and explanation for the purpose of creatine phosphate and the adenylate kinase reaction. This is such an oversimplification that I want to eradicate it from your mindset and understanding of cellular energy metabolism. The phosphagen system is involved in all energy transfer within skeletal muscle. The purpose of the entire system is to support free energy flux within a cell, and for skeletal muscle, with its high rate of energy transfer during muscle contractions, this role is fundamentally important. Sure, this system has a predominantly larger role than any other energy system during repeated intense muscle contractions, such as shown in this Figure for repeated bouts of intense forearm exercise. However, the longer the duration of the repeated contractions, and for this occur, the less intense the contractions, the role of the phosphagen system does not eventually deteriorate to a non-existent state. Rather, there is compelling evidence, and there has been for more than the last 30 years, that there is involvement of the phosphagen system during even low intensity exercise. If you view the roles of the reactions of this energy system with this perspective in mind, you will gain a more thorough understanding and appreciation of the role this system has in how skeletal muscle can meet the energy needs of contraction across a broad range of intensities.

The **phosphagen energy system** consists of four separate reactions, as shown in Equations 1 to 4 and Figures 1 to 4. The reactions are as follows, based on enzyme name.

1. ***Creatine kinase***
2. ***Adenylate kinase*** *(also known as myokinase)*
3. ***AMP deaminase***
4. ***ATPase***

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$$CrP + ADP + H^+ \overset{\text{creatine kinase}}{\leftrightarrow} Cr + ATP$$ Equation 1

$$ADP + ADP \overset{\text{adenylate kinase}}{\leftrightarrow} ATP + AMP$$ Equation 2

$$AMP + H_2O + H^+ \overset{\text{AMP deaminase}}{\leftrightarrow} IMP + NH_4$$ Equation 3

$$ATP + H_2O \overset{\text{ATPase}}{\rightarrow} ADP + Pi + H^+$$ Equation 4

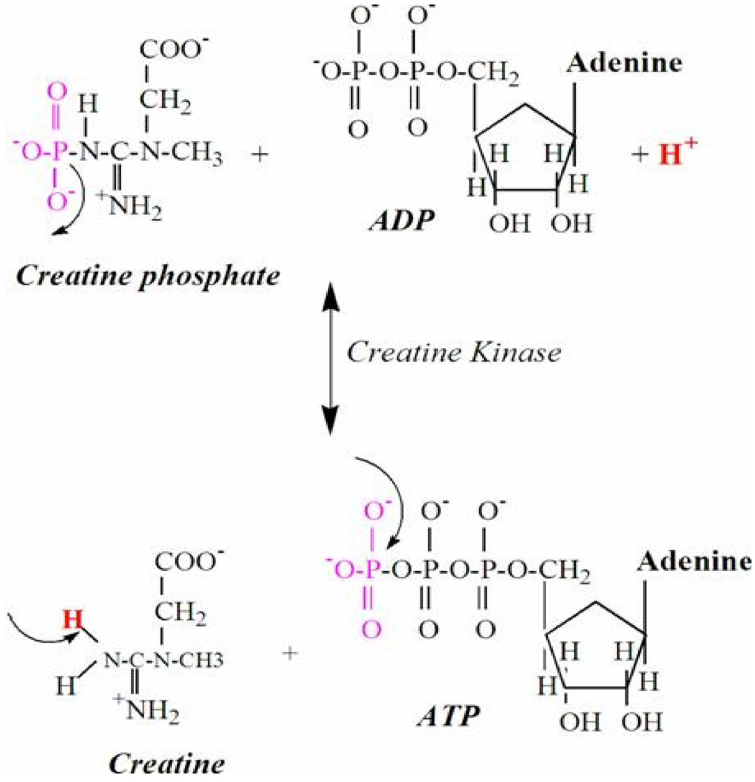

Figure 1. The creatine kinase reaction.

Remember that each of these reactions is occurring near simultaneously. For some complex reasons pertaining to substrate availability and enzyme kinetics, the creatine kinase reaction is the most sensitive of these reactions to small changes in each of ATP (small decreases) and ADP (small increases). As the muscle [ADP] changes become more apparent (though still a very small absolute change), as would occur with more prolonged intense muscle contractions, the involvement of the addenylate kinase reaction begins to increase.

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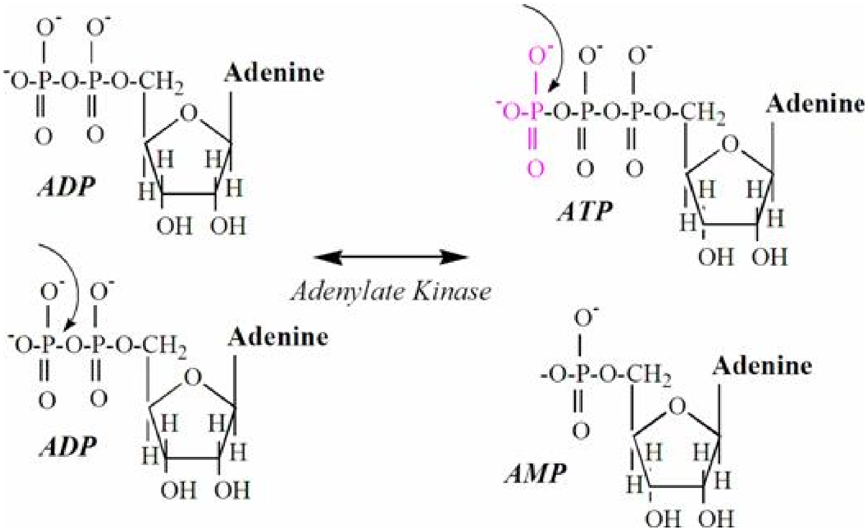

Figure 2. The adenylate kinase (myokinase) reaction.

Note that the creatine kinase and adenylate kinase reactions involve simple phosphate transfer. The ATPase reaction requires the involvement of water to cleave the terminal phosphate group (a chemical process called hydrolysis), and the AMP deaminase reaction involves the conversion of the adenosine base to inosine.

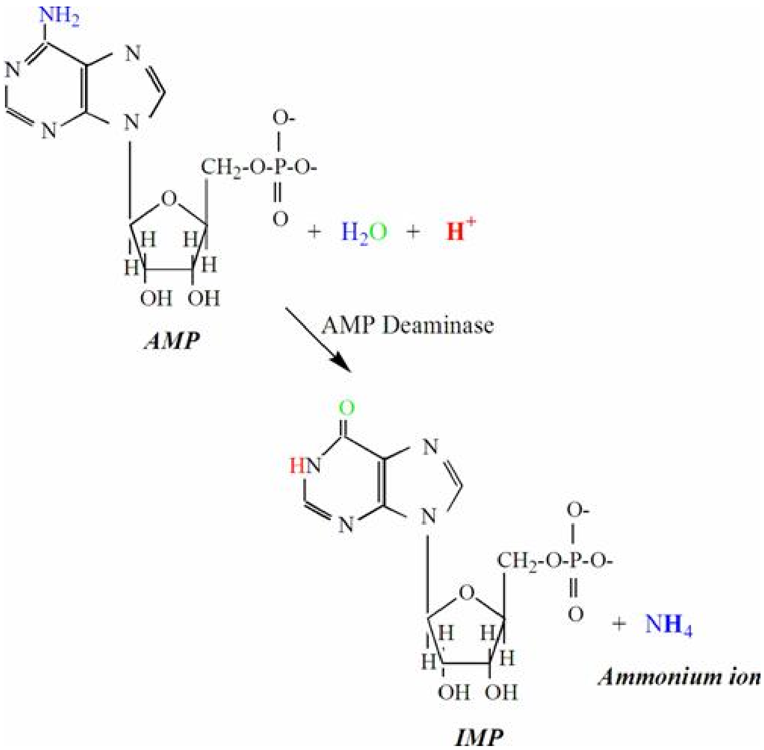

Figure 3. The AMP deaminase reaction.

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The biochemical sequence of events between these reactions is more clearly illustrated in Figure 5. Note that the metabolites colored orange, namely **creatine (Cr)**, **inosine monophosphate (IMP)**, **inorganic phosphate (Pi)** and **ammonia (NH_4)** are left to accumulate in muscle during intense exercise and/or removed into the circulation.

Although Figure 5 is a simple summary of these reactions and how they depend on each other, it is misleading when not accounting for the concentrations of the metabolites at question. Figure 1 shows that ATP is regenerated in this system, and although the ATPase reaction drives the metabolite changes for the system, the capacity of the phosphagen system is highly dependent on the muscle concentration of creatine phosphate (CrP), which approximates 30 mmol/kg wet wt. During all-out intense exercise, such a store can be depleted in < 10 s, with many biochemists viewing muscular fatigue during intense exercise to be largely (not solely) dependent on diminishing concentrations of CrP. The total capacity of the phosphagen system is the sum of the capacity of the creatine kinase, adenylate kinase and AMP deaminase reactions, with additional adjustment for any small decrease in muscle ATP (Equation 5).

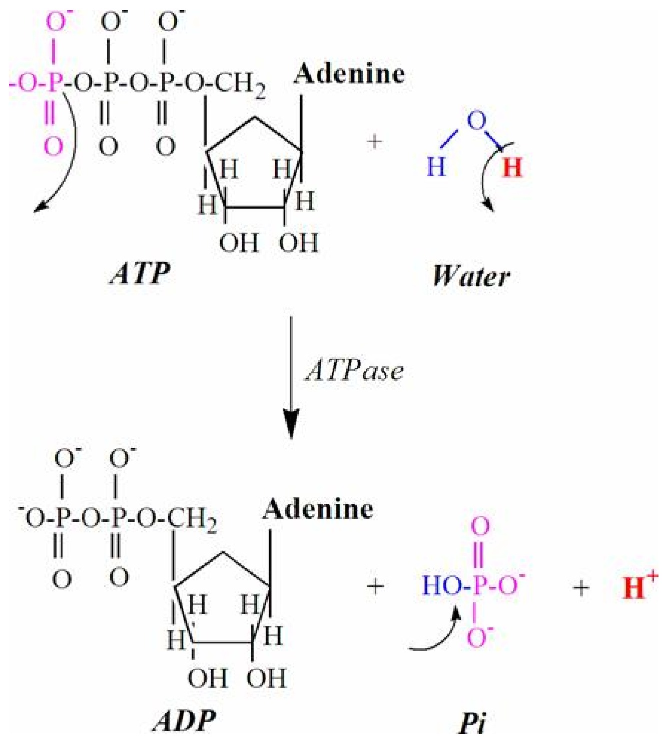

Figure 4. The ATPase reaction.

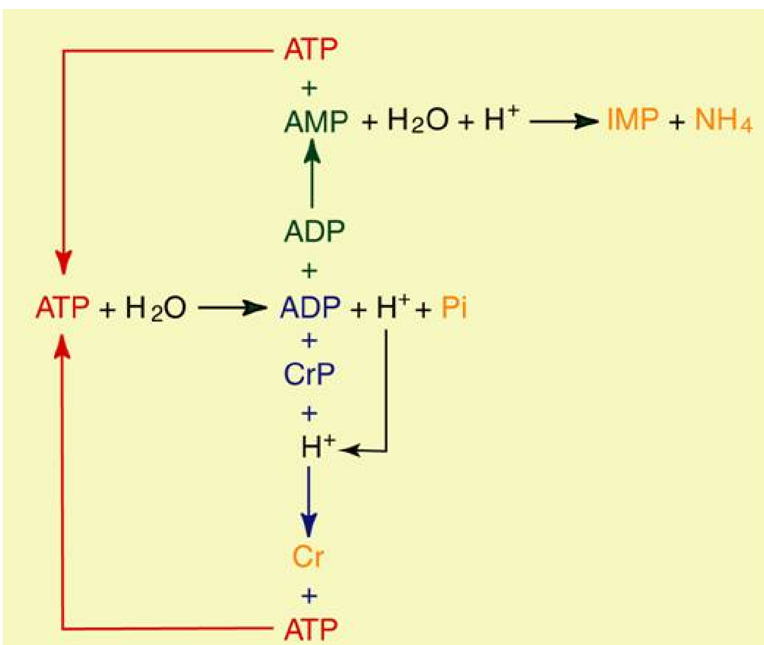

Figure 5. The biochemical sequence of events for the Phosphagen System.

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$$Phosphagen\ Capacity = \Delta CrP + \Delta AMP + \Delta IMP + \Delta ATP$$
$$= \sim 30 + 3 + 8 + 2 = 43\ mmol/kg\ wet\ wt$$

Equation 5

Figure 5 also reveals two more important facts. Firstly, that the accumulation of Pi is caused by ATP hydrolysis not the creatine kinase reaction. Secondly, that the phosphagen system is proton consuming when solely concerned with the ATP regenerated by this system. However, during exercise, when there is additional ATP regenerated from glycolysis, there is excess ATPase reaction compared to the involvement of mitochondrial respiration. This scenario causes considerably greater metabolic proton release than consumption. I will talk more about this in the section on Metabolic Acidosis.

Glossary Words

phosphagen energy system is also known as the immediate energy system, consisting of the CK, AK, and AMP deaminase reactions.

creatine kinase is the enzyme that catalyzes the phosphate transfer from creatine phoshate to ADP. This reaction also consumes a H^+ and produces free creatine.

adenylate kinase is the enzyme that catalyzes the phosphate transfer from ADP to another ADP molecule, regenerating ATP. This enzyme is also known as myokinase.

AMP deaminase is the enzyme that catalyzes the conversion of AMP to IMP, which also consumes a H^+ and produces ammonia (NH_4).

ATPase is the enzyme that catalyzes the hydrolysis of ATP to ADP + Pi.