GRAND ROUNDS

MYOGLOBINURIA

Parkland Memorial Hospital
March 7, 1963

Case History: [redacted]

A 14 year old [redacted] boy was admitted to [redacted] for the first time on [redacted], 1963 with the chief complaints of muscle pain and dark urine of four days duration. Approximately two weeks prior to admission the patient developed a cold and slight sore throat which lasted about one week and which cleared spontaneously without treatment. Four days prior to admission the patient played outside as was his custom and rode a tractor-tricycle vigorously for several hours. At the end of the play period he felt tired and took a nap for 1-2 hours. On awaking from sleep he noted a severe frontal headache and stiffness and pain of the muscles of the anterior thighs, the arms, and the lower back. That evening, several hours after the onset of the headache and muscle pain he noted that his urine was dark brown in color. During the next three days the muscles remained stiff, tender, and painful on movement. The urine remained dark and subjective fever was present. Two frank chills were noted. He was anorexic, but had no nausea, vomiting, or diarrhea. Muscle tenderness became so severe that the patient refused to move his limbs, and for this reason he was brought to the hospital.

Past history was negative except for one possible episode of dark urine following a sand lot football game about 4 months prior to admission. The patient has seven siblings, none of whom have had similar illnesses. The parents are living and well and there is no history of hematologic or muscle disease.

Physical examination revealed a slender Negro male who was in obvious pain. He was somnolent and irritable, and refused to move the extremities. The vital signs were: T - 102°, P - 114, R - 18, and B P 110/60. Examination of the head, eyes, ears, nose, and throat was normal except for slight periorbital fullness. The thyroid was not palpable. The lungs were clear and the heart was normal in size. There were no murmurs. The abdominal wall was tender to palpation. The liver and spleen could not be felt. The muscles of the anterior thighs were swollen, tender, and hot to the touch. All motion was resisted and attempts were accompanied by great pain. The muscle findings were less marked in the back and upper extremities. Neurological examination was normal.

Admission laboratory work revealed a hemoglobin of 15.1 Gm% with a hematocrit of 44. The white blood cell count was 8,850 with 44% neutrophils, 16% lymphocytes, 5% monocytes and 35% eosinophils. Sickle cell preparation was normal. The urine was dark brown in color. The specific gravity was 1.040, pH 6.0, and albumin 1+. Rare white and red blood cells were seen but no casts were present in the sediment. The urine was strongly positive to hematest and guiac tests. Blood was drawn to obtain serum which was noted to be normal yellow in color at a time when the urine was deeply pigmented. Test for porphobilinogen was negative. Blood chemistries revealed a BUN of 14 mgs %. CO_2 content was 25 m.e./liter, sodium 124 m.e./liter, potassium 4.9 m.e./liter and chloride 86.1 m.e./liter. Selected laboratory work done subsequent to admission is detailed below to illustrate the patient's course. Admission diagnosis by the house staff was idiopathic myoglobinuria.

Laboratory studies:

	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Hematology						
Hemoglobin	15.1	11.0	10	9.5	10.9	11.8
Hematocrit	44	33	32	30	33.5	33
Sed rate	16	11				
WBC	8,850	8,900	9,000		5,400	4,600
Poly	34%	41%	80%		50%	50%
Lymph	16%	25%	9%		36%	35%
Monocyte	5%	3%	5%		6%	8%
Eosinophil	35%	30%	1%		8%	6%
Sickle prep	neg	neg	neg			
Platelets	-	125,000	135,000			
Reticulocyte	-	1.0%	0.5%		1.2%	

	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Urine						
pH	6.0	6.5	7.5			
Specific gravity	1.040	1.029	1.019			
Albumin	1+	1+	N			
Sugar	neg	neg	N			
Acetone	neg	neg	N			
RBC	0-4	0-4	0			
WBC	1-3	0-3	rare			
Casts	-	granular	granular			
24 hour creatinine		3.6 G	3.6 G			
24 hour creatine			4.0 G			
Blood Chemistry						
BUN	14		20		11	
Creatinine		0.8			0.5	
Glucose	123					
CO_2	25	27				
Chloride	86.1	99				
Na	124	128				
K	4.9	4.6				
Total protein		6.8	5.5			
Albumin		4.1	3.1			
Globulin		2.7	2.4			
Phosphorous		4.9	3.5			
SGOT		800	766	422	85	28
LDH		574				
Bilirubin		0.5	0.4			

Additional studies

PSP - 86.7 % hours
Liver function - all normal
Leptospiral agglutinins - negative
Latex fixation - negative X3
LE cell prep - negative
Psittacosis complement fixation negative
Anti nuclear test - negative
Cold agglutinins - negative
ASO - 166
Coombs test - negative X3
Osmotic fragility - normal X2
Cold hemolysins - negative
Methemalbumin - negative
Hemoglobin electrophoretic pattern - AA
EKG - normal
Chest X-ray - normal
Blood cultures - normal
Electromyography - normal
Bone marrow - Probable granulocytic hyperplasia, eosinophilia, and erythrocytic hypoplasia

Special laboratory studies

80% $(NH_4)_2SO_4$ - Pigment precipitated twice [redacted] and on [redacted] Pigment in supernatant twice on [redacted].

Spectrophotometry of urine - interpreted as hemoglobin, inconclusive
Sephadex column chromatography - benzidine positive protein compatible with myoglobin.

Lactic acid response to exercise

Prior to exercise	10 mgs %
1 minute after exercise	37 mgs %
2 " " "	41 mgs %
3 " " "	50 mgs %
4 " " "	41 mgs %
5 " " "	22 mgs %
10 " " "	10 mgs %
Non occluded arm	10 mgs %

Muscle biopsy	Patient	Control	
Glycogen	1.27%	0.73	(normal 0.5-1.5)
Total phosphorylase activity (µG P/G/10 minutes)	7.8	10.7	(normal 7.9-12.8)
Glucose oxidation*	64	48	
	49	51	
Pyruvate oxidation*	10291	9629	
	9996	9010	
Citrate oxidation*	190	116	
	153	160	
Palmitate oxidation*	109	132	
	127	90	

*$C^{14}O_2$ cpm/10 mg, duplicate

Glycogen synthesis (from glucose-6-C^{14})	2240	2030

Histochemical studies: Normal glycogen
Normal phosphorylase (amylophosphorylase)
Normal branching enzyme (amylo 1-4, 1-6 transglucosidase)

Light and electron microscopy of muscle: Minimal focal degenerative changes.

Course in the hospital: On the day following admission the patient continued to have pain and dark urine. Temperature was 103°. Because of a definite drop in the hemoglobin and hematocrit and the results of the $(NH_4)SO_4$ and spectrophotometric tests it was elected to treat the patient for a hemolytic process. Fifteen mgs of prednisolone was started three times daily. At the same time an alkalinizing solution was started by mouth (Shoal's solution - 15 mls q. 6 h). On the fourth hospital day the patient was much improved. Steroids were decreased prior to discontinuation. By the fifth hospital day the patient was asymptomatic and has remained so. He was discharged [redacted] 1963.

DIFFERENTIAL DIAGNOSIS OF ACUTE MUSCLE PAIN AND PIGMENTED URINE

Condition	Attacks Precipitated	Site of Pain	Plasma Color	Urine Pigment	Urine Sediment	Specific Test
Idiopathic Myoglobinuria	Usually exercise; Also infection, Alcohol Fasting	Lower extremities, particularly thighs, later may be generalized	Normal	Benzidine Positive	RBC may or may not be present	Precipitin reaction Electrophoresis Sephadex chromatography.
Cold Hemoglobinuria	Cold	Primarily flank, back and abdomen	Pink to Red	Benzidine Positive	No or few RBC	Donath Landsteiner test (cold hemolysins)
Paroxysmal Nocturnal Hemoglobinuria	Sleep	Primarily flank, back and abdomen	Pink to Red	Benzidine Positive	No or few RBC	Ham and Crosby tests (acid hemolysis)
Acute Intermittent Porphyria	Unknown except for brbituates	Abdomen and extremities	Normal	Benzidine Negative	No RBC	Erlich reaction for Porphobilinogen
Acute Glomerulcnephritis	Group A Streptococcal Infection	Pain not frequent. May have vague aching in back and flanks.	Normal	Benzidine Positive	RBC RBC casts	ASO Precipitin reaction Electrophoresis Sephadex chromatography

CLASSIFICATION OF MYOGLOBINURIAS

I. Primary Myoglobinuria

1. Exertion induced
   a. McArdle's Syndrome
2. Non-exertion induced

II. Secondary Myoglobinuria

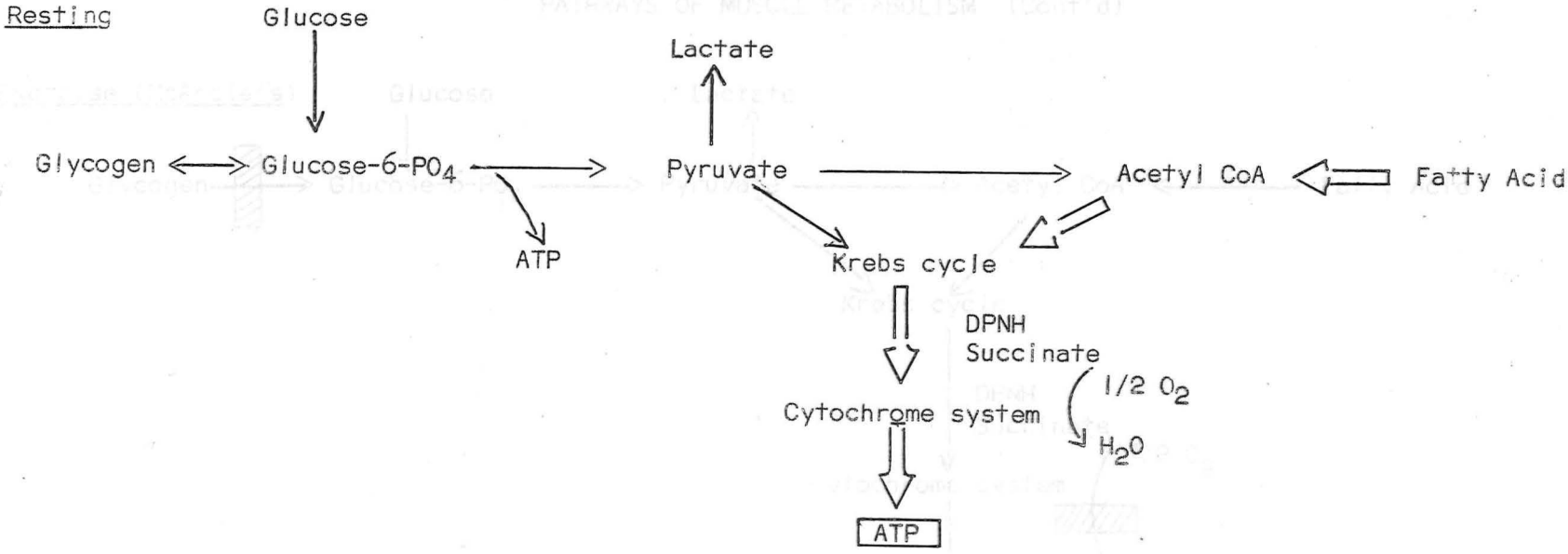
1. Ischemia
   a. Crush syndrome
   b. Postural pressure
   c. Intravascular occlusion
2. Toxic or infectious
   a. Haff disease
   b. Sea snake poisoning
   c. Alcohol
   d. Carbon monoxide
   e. Barbituate
3. High Voltage Shock
4. Convulsions
5. Polymyositis
6. Exercise myositis (squat-jump syndrome)

CHARACTERIZATION OF PRIMARY MYOGLOBINURIAS

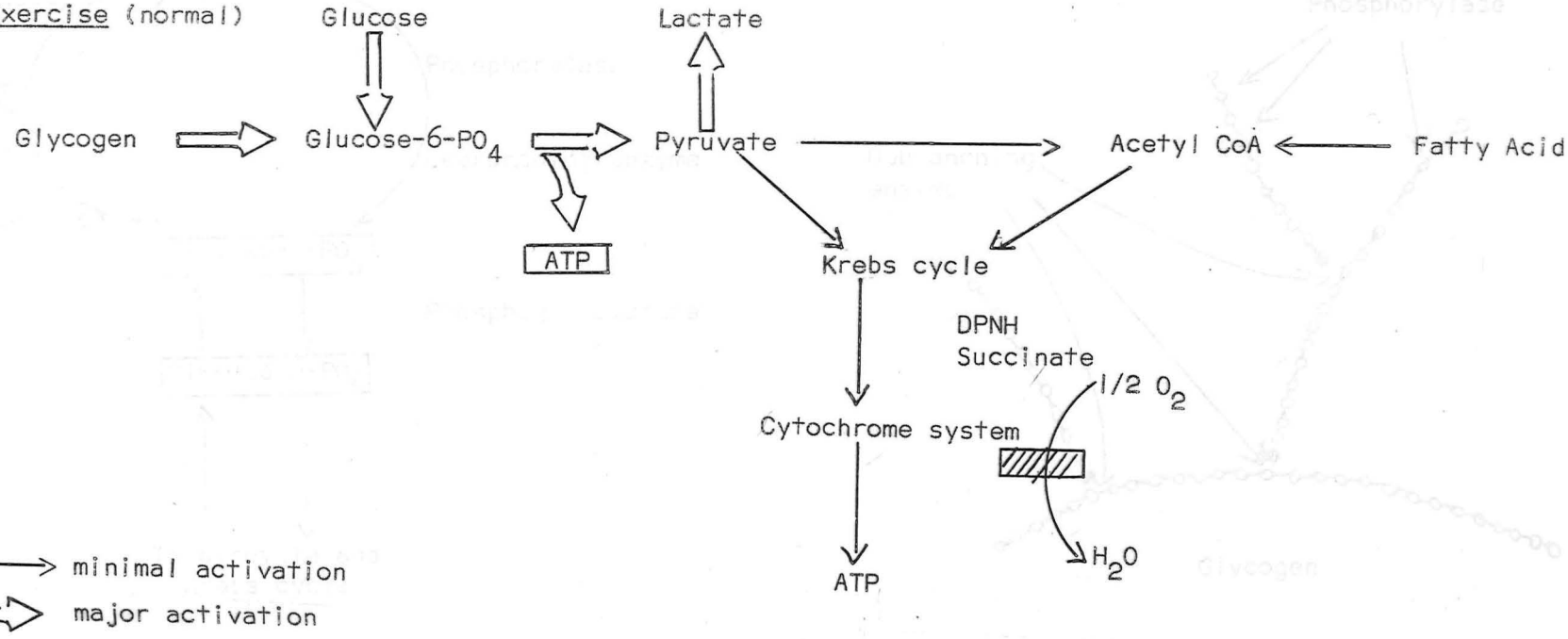
	Exertional (21 cases)	Non-exertional (19 cases)
Age of onset	80% adolescence	70% childhood
Sex distribution	95% male	68% male
Family history	33%	20%
Precipitated by	100% exertion	58% infection
Number of attacks	90% multiple	63% single or one recurrence
Fever, leukocytosis	33%	82%
Muscle atrophy	33%	11%
Mortality	10%	42%

PATHWAYS OF MUSCLE METABOLISM

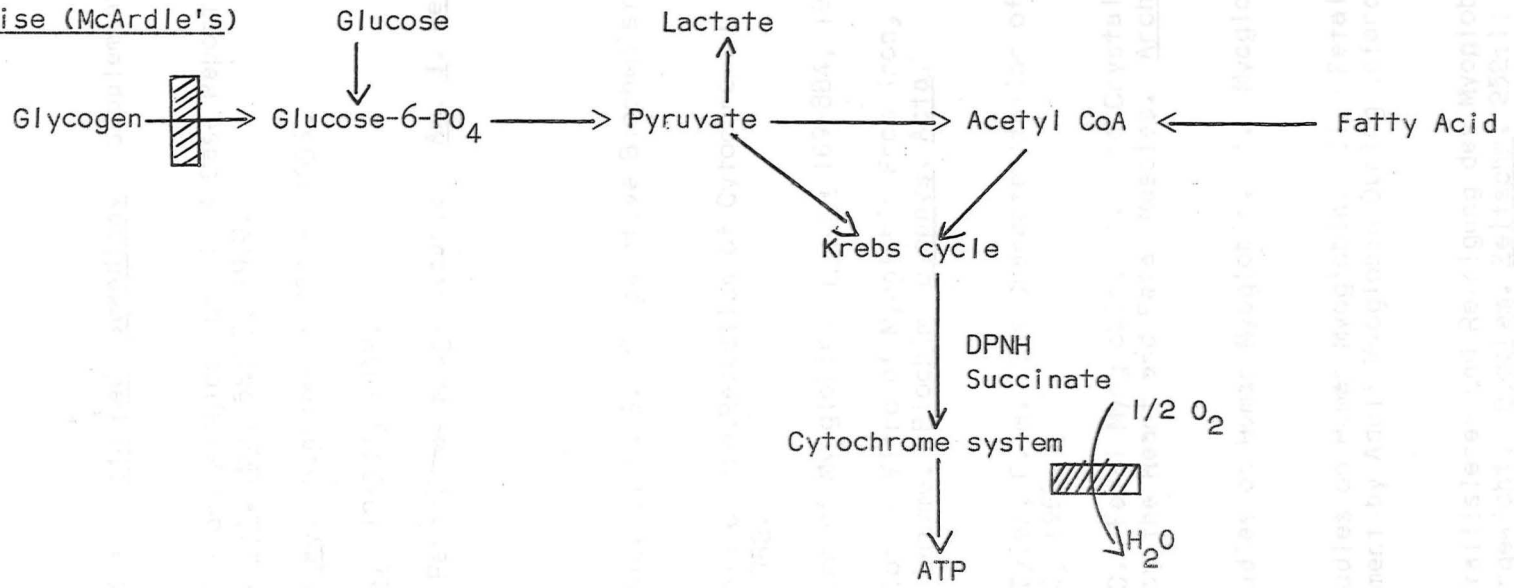
I. Resting

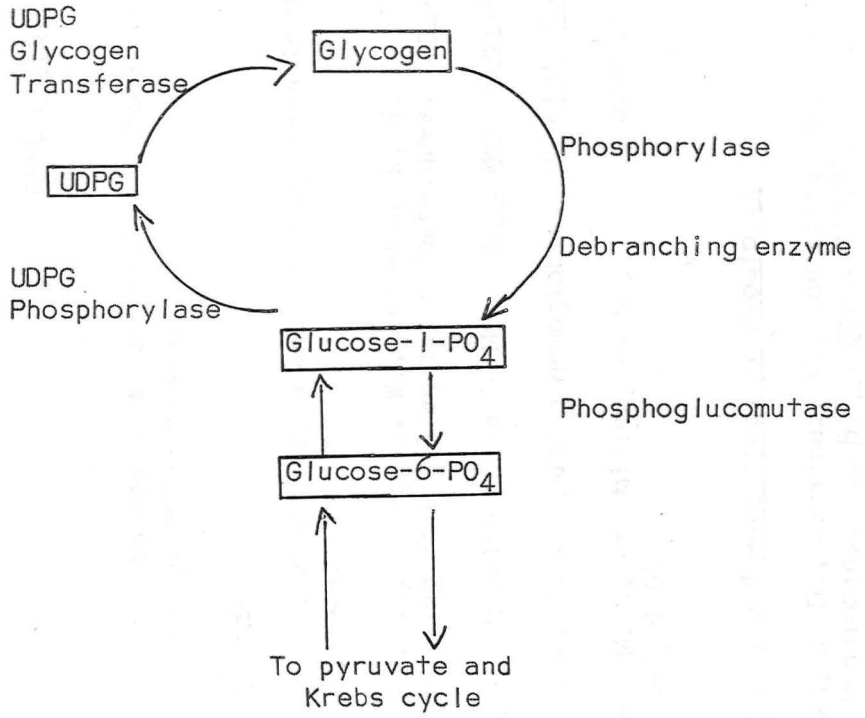


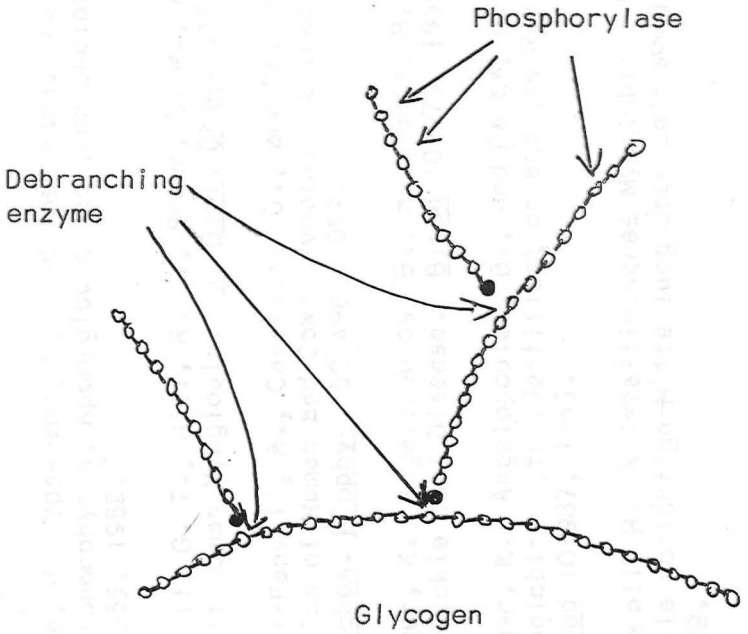
II. Exercise (normal)



III. Exercise (McArdle's)







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