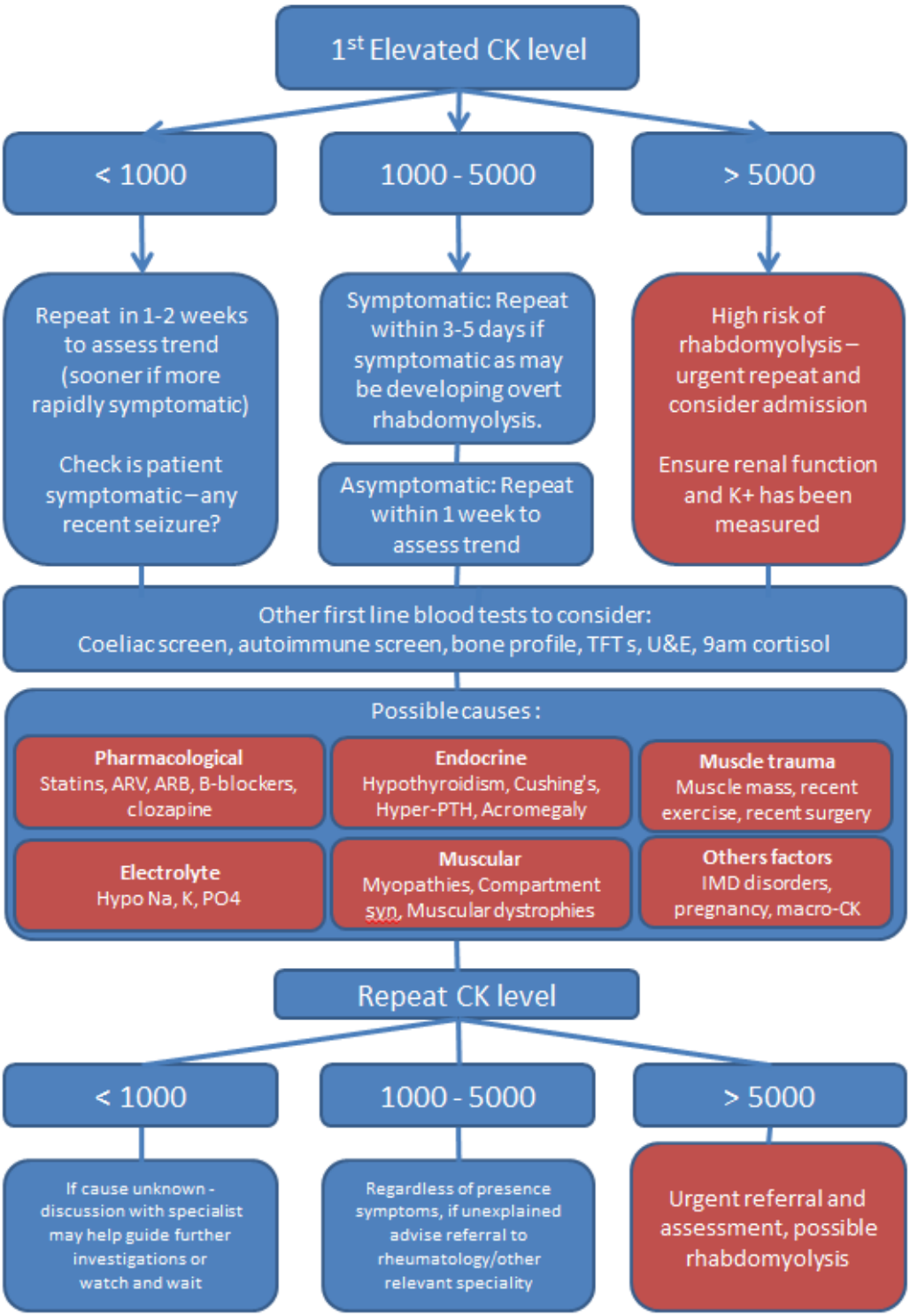
Investigation of elevated Creatine Kinase



1. Introduction

The purpose of this protocol is to provide the duty Clinical Biochemist with background information and recommended tests to perform when Creatine Kinase is elevated up to and including to levels suspicious of Rhabdomyolysis (>5000mIU/L). Mild elevations of CK encompass a wide differential diagnosis and require careful consideration of the need for further investigation.

Myoglobinuria- Myoglobin gives a positive reaction with conventional urine dipstick testing for haem containing components. Myoglobin imparts its characteristic red-brown colour to urine at concentrations above 300 mg/L. Myoglobin quantitation is **not** offered as a routine biochemical test

2. Mild to moderate CK elevations

Mild to moderate elevations of CK upto levels of 5000mIU/L have a wide variety of causes. Patients may or may not be symptomatic at this level. Common causes of mild to moderate elevations of CK include:

Ethnicity	CK values are typically slightly higher in non-caucasian individuals
Muscle trauma/overuse	Recent surgery Intensive exercise (upto roughly 30x upper limit of normal) Recent surgery Seizures** Long lie of immobility** Burns** Crush syndrome**
Electrolyte imbalance	Hyponatraemia, Hypokalaemia**, Hypophosphataemia
Medications/drugs	Statins**, Fibrates**, anti-gout medications (colchicine, allopurinol), antihypertensives (beta blockers, ARBs), anti-retrovirals,
Toxins	Snake/Insect venom**, Hemlock ingestion, illict drugs** (cocaine, ecstasy, opiate abuse), neuroleptics
Endocrine disorders	Hypo and hyperthyroidism, Cushing's syndrome, Acromegaly, Hyper-PTH
Metabolic disorders	Glycogen Storage disorders Lipid metabolism disorders DKA/HHS
Macro-CK	Macromolecule of CK – if suspected CK isoenzymes are possible to be requested and sent to: Royal Free London Biochemistry as MISC test.
Muscular disorders	Inflammatory myopathies** Motor Neurone Diseases and Muscular Dystrophies** Compartment syndrome

	Connective Tissue Disease
Miscellaneous causes	Malignancy, pregnancy, Coeliac disease, renal disease**, cardiac disease (acute myocardial infarction** or chronic cardiomyopathes), vascular ischaemia, infection**

Management of CK's at this level depends on:

- How close the value is to the critical cut-off of 5000mIU/L
- The persistence of any CK elevation >1000mIU/L
- The likely underlying cause requiring further investigation or treatment or onward referral

3. Investigation and diagnosis of possible Rhabdomyolysis

Rhabdomyolysis is the consequence of injury to skeletal muscle sufficient to allow leakage of cellular components into the blood and urine. The main measurable components of importance in clinical practice are myoglobin and creatine kinase (CK).

Rhabdomyolysis may be occult in a significant number of patients. There should be a high index of suspicion in the following groups:

- All patients who have lain immobile for indeterminate periods of more than one hour, particularly when drug ingestion, including alcohol, is possible.
- All patients who present after possible drug ingestion especially heroin, cocaine or ecstasy.
- Patients presenting after intensive exercise especially if accompanied by heat exhaustion.
- Patients with sepsis.

The possible causes of significantly elevated CK overlap with those described in Table 1. Those with ** indicate possible causes of significantly elevated CK.

4. Laboratory notes

In practice the common questions asked of the laboratory are:

1) Does a patient have a significant degree of rhabdomyolysis?

The presence of a raised CK of non cardiac origin indicates rhabdomyolysis.

- The finding of a raised CK and normal TnT indicates rhabdomyolysis.
- The finding of a raised CK and a raised TnT indicates either a cardiac or a mixed pattern.
- The relative elevations of CK and TnT may suggest which is predominant.

Note that measuring myoglobin will not be informative, as it will be increased from either cause.

2) In a patient with pigmented urine is the pigment myoglobin?

Myoglobin gives a positive reaction with conventional urine dipstick testing for haem-containing compounds therefore a positive test could indicate myoglobinuria, haemoglobinuria or haematuria. In the presence of a positive test a normal serum CK will exclude myoglobinuria, and causes of haematuria/haemoglobinuria must be investigated. A raised CK will indicate that myoglobin could be present and possibly be contributing to the pigmentation.

3) Does a patient with Rhabdomyolysis have a significant risk of developing acute renal failure?

There is no agreed simple answer to this question but patients with CK elevations greater than 30 X the top of normal (i.e. greater than about 5000 IU/L) probably have an increased risk as do those with a significant metabolic acidosis (bicarbonate <17 mmol/L), there is no evidence that measuring myoglobin is informative.

4 DCB Actions

1. If a raised CK, but less than 5000 IU/L, is found in a patient with suspected Rhabdomyolysis suggest repeat CK in 12 hrs. If both are less than 5000 IU/L, no measures in addition to normal clinical management are required, providing the specimens are taken within the first 3 days after the suspected insult.
2. If initial or subsequent CK is greater than 5000 IU/L suggested comment on report is “In view of degree of elevation of CK patient is at risk for complications of rhabdomyolysis.” Regular monitoring of potassium and creatinine are indicated. Any clinically obvious fluid deficit should be corrected and thereafter fluid should be administered to maintain a good urine output, providing this is appropriate to the overall clinical picture.
3. There is no sound reason to measure myoglobin in either serum or urine to answer the above clinical questions.
4. In patients presenting with unexplained acute renal failure, the retrospective analysis of specimens taken early during their admission may be of value in helping to substantiate or exclude rhabdomyolysis as a cause.

5 References

a. Beetham R, Biochemical Investigation of suspected rhabdomyolysis. Ann Clin Biochem 2000; 37-581-7
b. Investigation of elevated CK - https://www.yorkhospitals.nhs.uk/seecmsfile/?id=3319