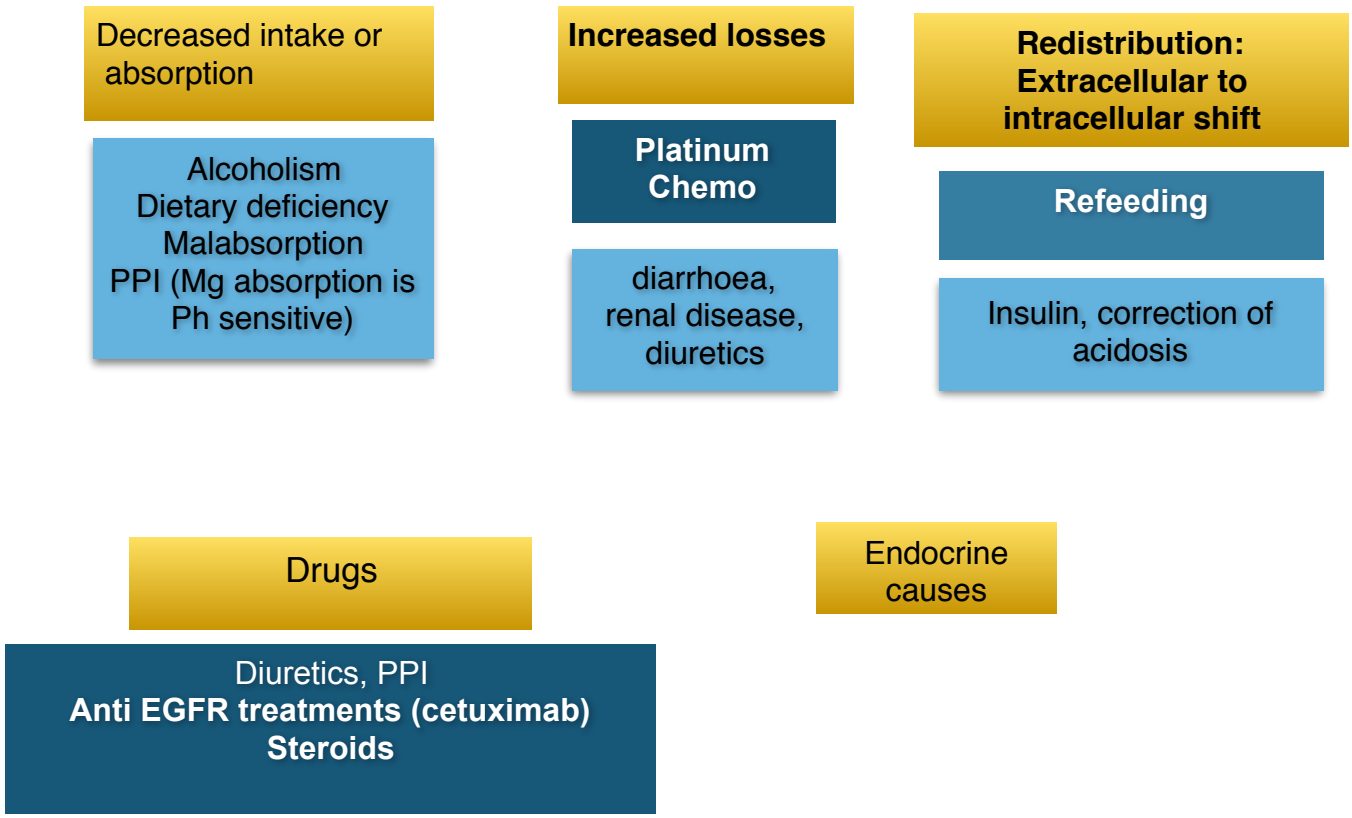
Magnesium and Phosphate in Cancer

Platinum chemotherapy, Refeeding and Tumour Lysis Syndrome

Hypomagnesemia

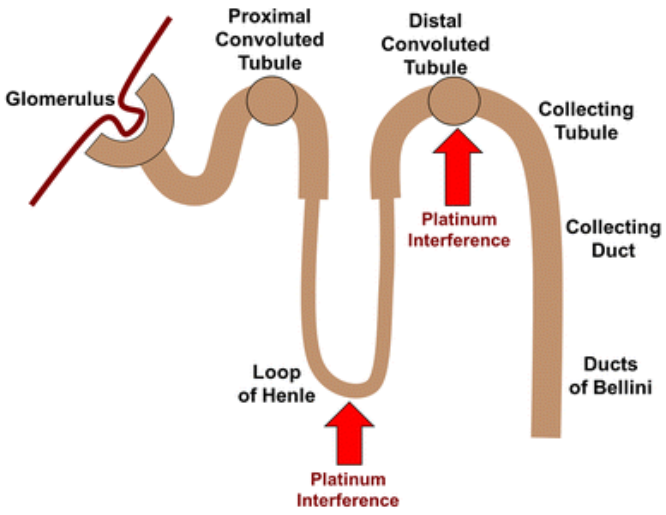


Platinum-based chemotherapy with cisplatin (the prototype of platinum agents) and its derivatives, carboplatin and oxaliplatin, is traditionally the first-line cytotoxic treatment of lung, colorectal, ovarian, breast, head/neck, bladder and testicular cancers.
An expected side effect of these widely administered platinum-containing regimens is electrolyte disturbances, **in particular low magnesium with cisplatin.**

Magnesium is predominantly located intracellularly or deposited in bone; thus, serum levels are poor indicators of total body stores and the presence of hypomagnesemia defined as a concentration <1.5 mEq/L usually indicates a more severe underlying cellular deficit

Gastrointestinal and renal losses are the two major mechanisms responsible for the induction of magnesium deficiency and hypomagnesemia

In one review, **a low magnesium state is particularly associated with cisplatin affecting 40–90% of patients,** as opposed to 10% of patients treated with carboplatin. This is due to direct toxicity of filtered platinum agents by the kidneys. Cisplatin accumulates in



kidney tubules and causes direct damage at Loop of Henle and DCT - resulting in Mg loss. It is also highly emetogenic - causing vomiting and diarrhoea which increases GI losses.

Platinum-induced hypomagnesemia, has been reported to persist for up to 6 years after cessation of treatment.

Electrolyte abnormalities that are associated with hypomagnesemia are:

1. Concomitant Hypokalemia (Low Mg results in an impaired Na–K–ATPase, thus less cellular uptake of K+ and increased urinary potassium wasting). Hypokalemia is often refractory to treatment unless Low Mg is corrected.

2. Hypocalcemia. Due both to lower parathyroid hormone secretion. (Low Mg inhibits PTH) and end-organ resistance to its effect. (Low Mg results in resistance to PTH)

Therefore, K+ and Ca++ levels should be checked.

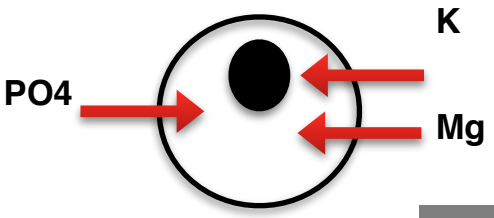
Refeeding Syndrome

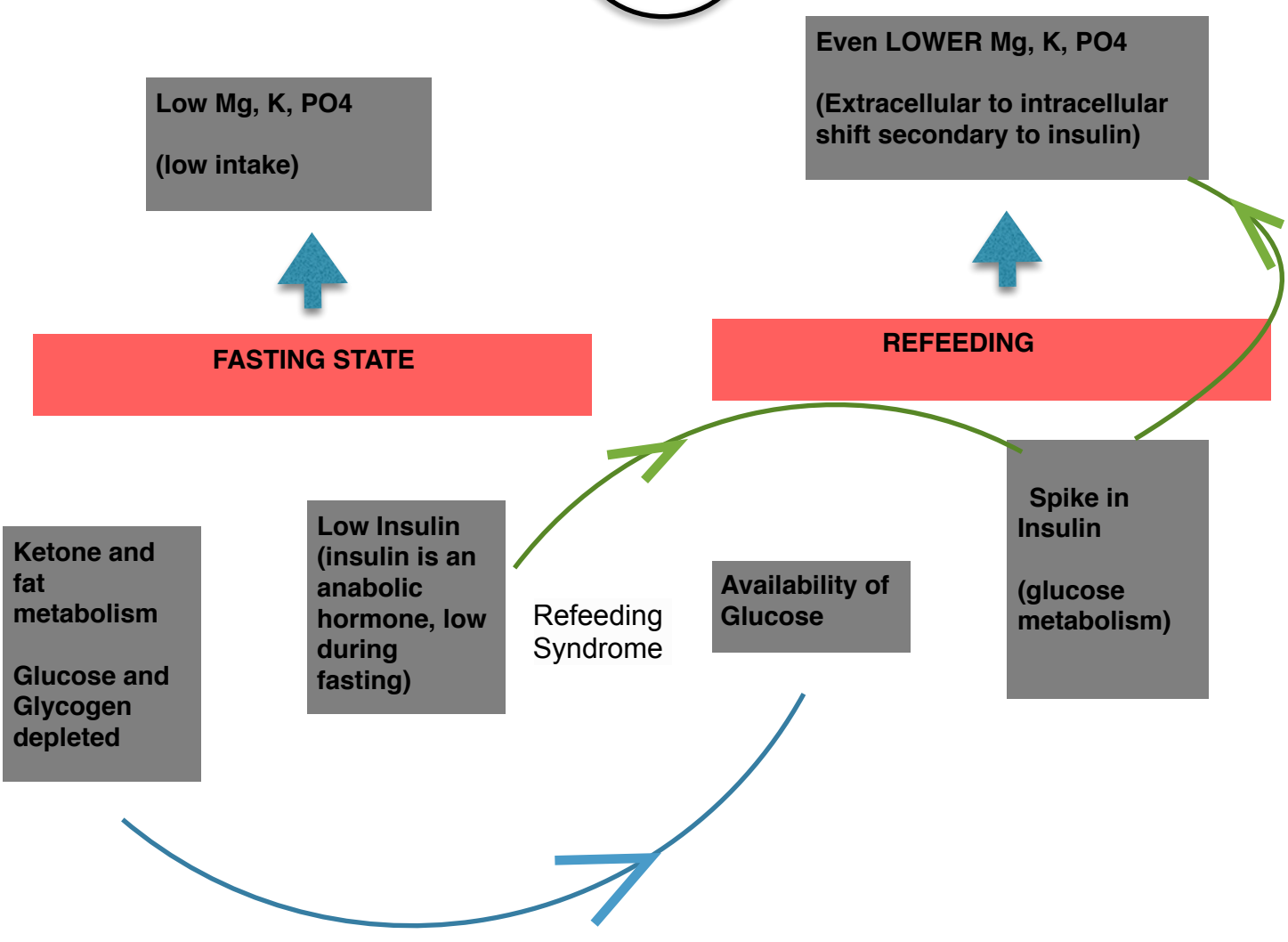
Who is at Risk: Greater than 10% weight loss over a couple of months. Patients are at risk if they have not been fed for 7 to 10 d. The total incidence of the refeeding syndrome has been put at as high as about 25% in cancer patients who are nutritionally supported.

Clinical Manifestations:

1-4 DAYS	First Week	Few Weeks
Low Phosphorus, low K, Low Mg	Cardiac complications, heart failure	Delirium, encephalopathy, paraesthesia, seizures

Pathophsyiology:





occurs in a fasting state where the body stores of Magnesium, Phosphorus and Potassium are depleted. Body Insulin levels are low (insulin is an anabolic hormone) The body has utilised glycogen stores and is now metabolising ketones and proteins for energy. When 'refeeding' starts - the body shifts back from protein to carbohydrate metabolism. This causes a spike in insulin release.

Insulin causes Mg, K and PO4 levels to shift from extracellular to intracellular space. This further deplete the levels of these electrolytes resulting in the "REFEEDING SYNDROME"

Electrolyte levels should be measured once daily for one week, and at least three times in the following week.

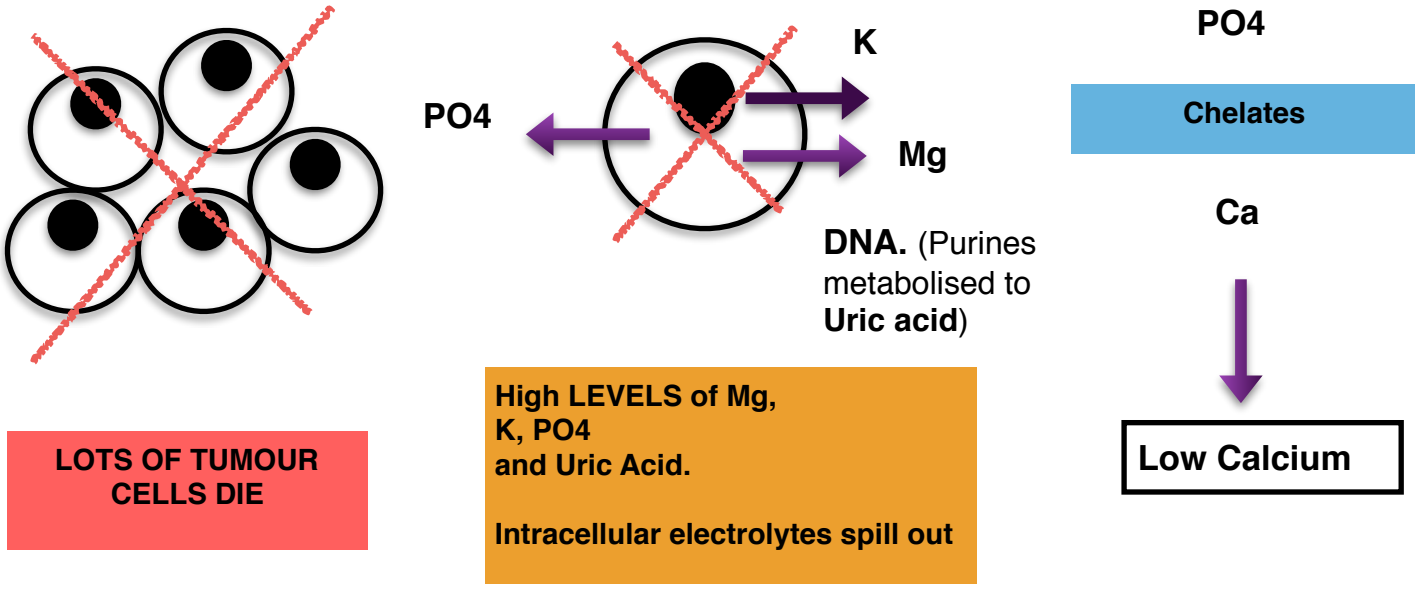
Vitamin replacement for 10 days. (Thiamine and B complex vitamins needed for glucose metabolism)

Electrolyte replacement to be guided by Trust Guidelines.

Tumour Lysis Syndrome

A 54 year old lady was admitted at 10 pm with a new diagnosis of Burkitt lymphoma. She received her first cycle of chemotherapy and bloods earlier that day showed high Mg, high potassium, high phosphate and low levels of calcium.

What diagnosis is this picture compatible with? Why?



Should she be started on IV fluids + allopurinol OR IV fluids + rasburicase ?

Allopurinol decreases uric acid production (PREVENTS URIC ACID FORMATION)
Rasburicase converts uric acid into soluble and excretable allantoin (TREATMENT FOR HIGH URIC ACID)

References:

Bryan Oronsky, Scott Caroen, Arnold Oronsky, Vaughn E. Dobalian, Neil Oronsky, Michelle Lybeck, Tony R. Reid Corey A. Carter. Electrolyte disorders with platinum-based chemotherapy: mechanisms, manifestations and management. Cancer Chemotherapy and Pharmacology
November 2017, Volume 80, Issue 5, pp 895–907