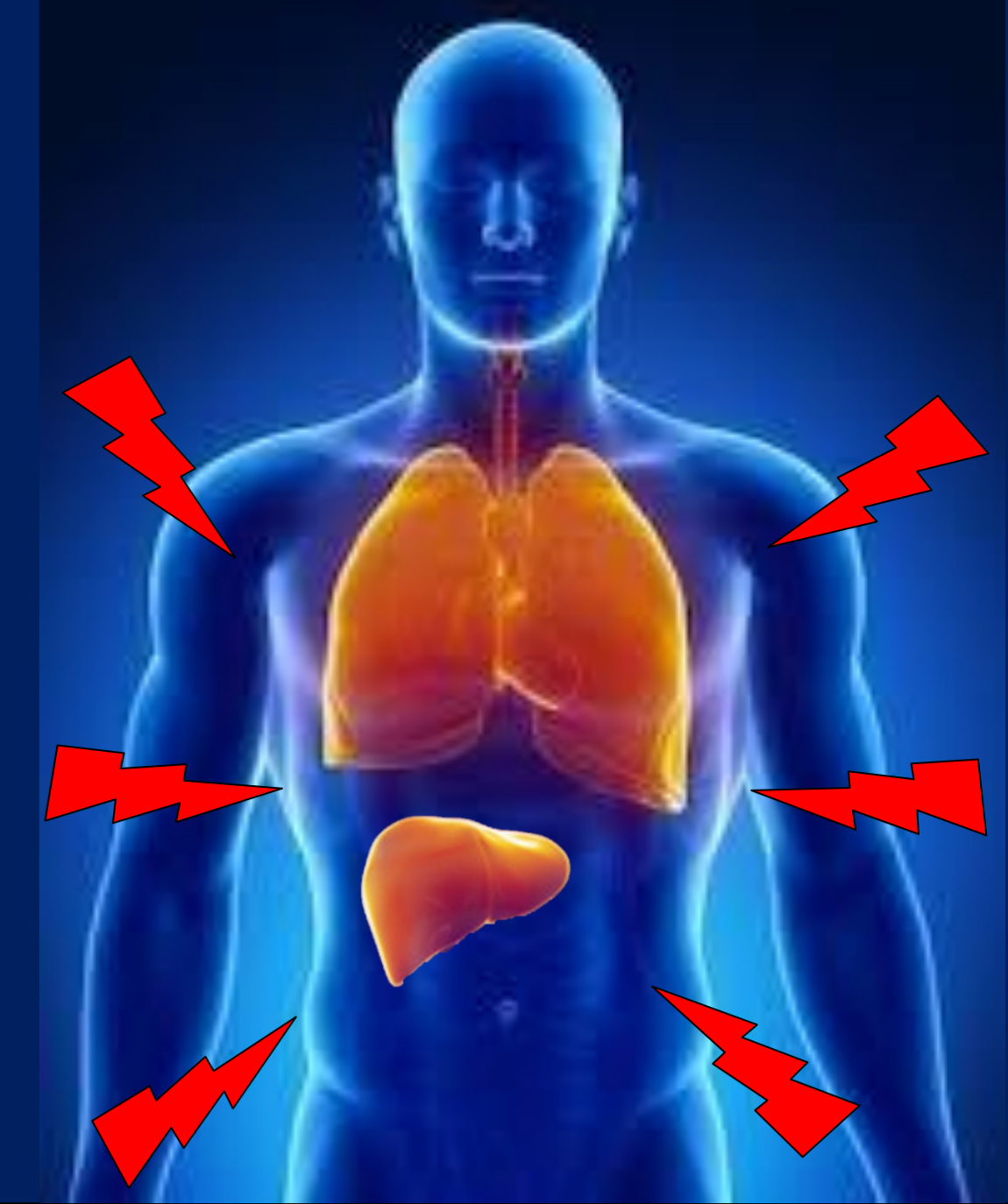


A RIPE PAIN

Two cases of paracetamol-induced hepatic transaminitis in tuberculosis patients

AUTHORED BY: Kate Woods, Pharmacist, Gosford Hospital, Central Coast Local Health District NSW



Background

The standard first-line, four-drug treatment for tuberculosis (TB) is: rifampicin, isoniazid, pyrazinamide and ethambutol (known as RIPE-therapy).

RIPE-therapy has a high success rate but the pharmacokinetic drug interactions are well documented to **cause hepatic toxicity**.

However, what is more often overlooked, are drug interactions between patient's TB regime and **other medications that may exacerbate this adverse reaction**, such as paracetamol.

Rifampicin
Isoniazid
Pyrazinamide
Ethambutol

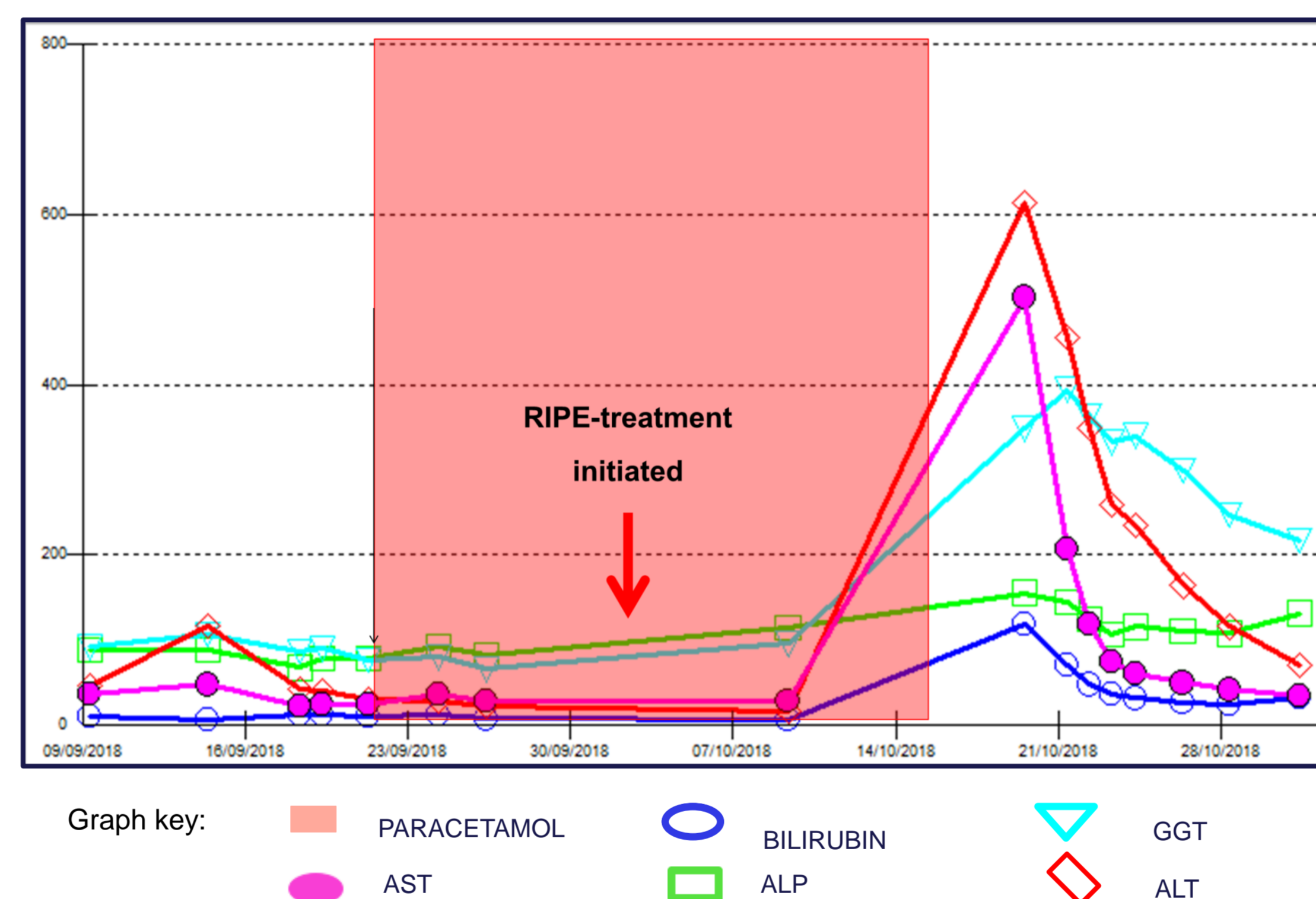
Clinical features

This report **outlines two cases of severe hepatic transaminitis in patients taking RIPE-therapy**, attributed to concurrent administration of standard-dose paracetamol whilst admitted to a tertiary referral hospital.

PATIENT – 1

- 78-year-old Caucasian male admitted with acute cystitis.
- RIPE-therapy commenced** after TB was coincidentally detected on chest x-ray.
- Patient **concurrently prescribed paracetamol 1g QID** for 5 days until discharge.
- Readmitted 10 days later with **severely deranged LFTs** - ALT 614U/L, AST 502U/L, GGT 348U/L, ALP 156U/L, bilirubin 118umol/L (See Graph 1).
- Medication reconciliation at readmission identified **continued paracetamol use**.
- Hepatic transaminitis** diagnosed.

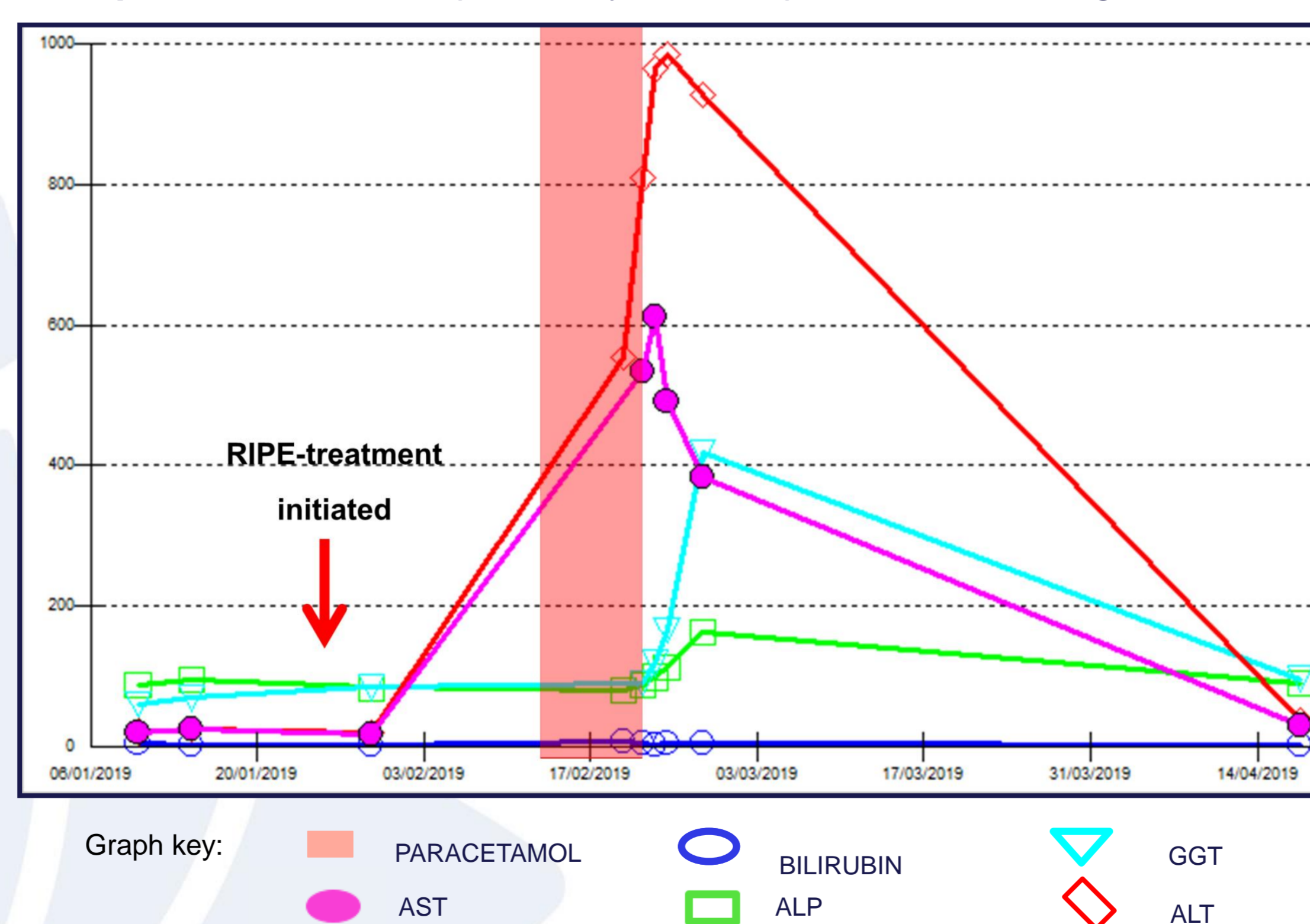
Graph 1 – Patient-1 Hepatic enzymes and paracetamol dosing over time



PATIENT – 2

- 36-year-old Filipino female presented to ED with gastric illness.
- RIPE-therapy** was initiated six weeks prior.
- Paracetamol 1g BD self-administered for 2-3 days** before presentation.
- Further five doses of 1g paracetamol given** every six hours in ED.
- Pathology on day 2 of admission revealed **markedly raised LFTs** - ALT 985U/L, AST 611U/L, GGT 120U/L, ALP100U/L, normal bilirubin (See Graph 2).
- Hepatic transaminitis** diagnosed.

Graph 2 – Patient-2 Hepatic enzymes and paracetamol dosing over time



Literature Review

Several case reports have been published describing patients undergoing RIPE-treatment who experienced hepatotoxic reactions whilst taking paracetamol.^{1,2,4} The clinical features of these cases were described as marked elevations in hepatocellular enzymes with moderate rises in bilirubin.⁴

Review of the literature and these cases suggest **paracetamol at normal doses may potentiate hepatotoxicity of standard TB treatment through isoniazid and rifampicin inducing P450-enzymes, specifically CYP2E1, responsible for the oxidation of paracetamol to its toxic metabolites**⁴.

Outcome

In both cases, **paracetamol and RIPE-therapy were withheld until transaminases returned to normal** (Patient-1 = 30 days, Patient-2 = 40 days) and RIPE-therapy recommenced. Patient-1 successfully completed the full RIPE-course and Patient-2 is still undergoing active treatment.

Conclusion

Pharmacists who identify patients on RIPE-therapy should be alert to drug interactions that can potentiate hepatotoxicity. Specifically, paracetamol is often routinely prescribed to inpatients; pharmacists should recommend avoiding its use or use sparingly to avoid severe liver injury in this group.

References

- Murphy R, Swartz R, Watkins PB. Severe acetaminophen toxicity in a patient receiving isoniazid. *Ann Intern Med* 1990; 113: 799-800
- Moulding TS, Redeker AG, Kanel GC. Acetaminophen, isoniazid and hepatic toxicity. *Ann Intern Med* 1991; 114: 431
- Crippin JS. Acetaminophen hepatotoxicity: potentiation by isoniazid. *Am J Gastroenterol* 1993; 88: 590-2
- Nolan CM, Sandblom R, Thummel KE, et al. Hepatotoxicity associated with acetaminophen usage in patients receiving multiple drug therapy for tuberculosis. *Chest* 1994; 105: 408-11

Acknowledgements:

Dr Paul Roach, Senior Staff Specialist Gosford Hospital
Claire McCormack, Senior Pharmacist Gosford Hospital
Angela Tagaroulas, Team Leader Gosford Hospital



Health
Central Coast
Local Health District