Hereditary Tyrosinaemia type 1 (HT1) Clinical Management Guidelines

Presumptive positive – HT1

Lab notifies HT1 Clinical Liaison Service (CLS) on the day of the result

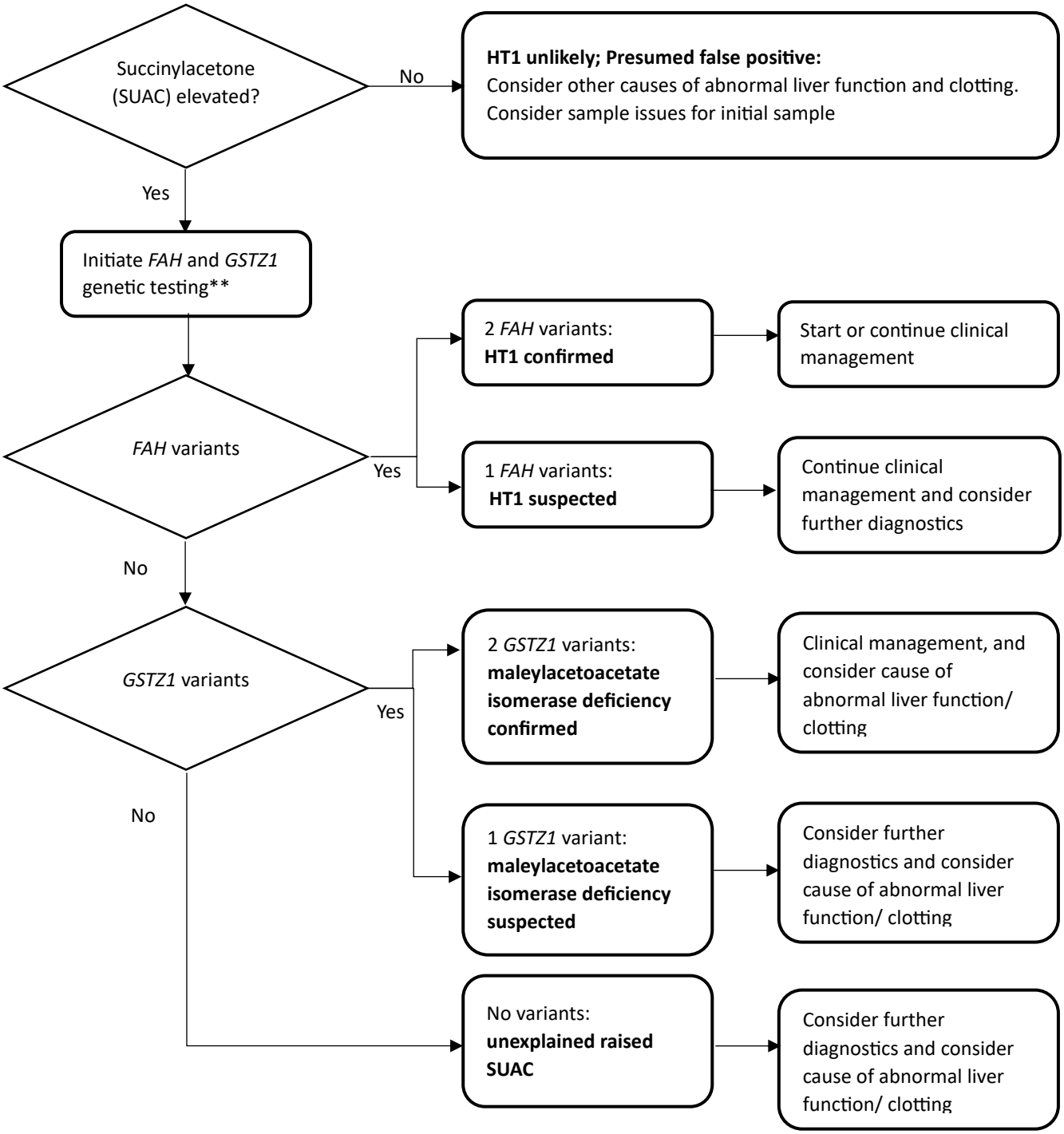
ON THE SAME DAY

1. CLS contact specialist team as per local protocol
2. Specialist team to CONTACT FAMILY and arrange **same day review**
    a. Initial review in local hospital with paediatric cover or metabolic centre with acute facilities.
    b. If initial review is in local hospital, specialist team to liaise with the local hospital (Paediatric Consultant, or registrar/equivalent grade if unable to contact). Email information to hospital for clinicians and parents, BIMDG HT1 guidelines, "HT1 is suspected" leaflet, contact numbers for the HT1 specialist team.
    c. If initial results show baby is likely affected, they will require urgent transfer to metabolic unit
3. Initial assessment
    a. Clinical assessment, history, examination
    b. Obtain investigations:
        i. **Specific diagnostics**
            1. Succinylacetone (SUAC) (Dried bloodspot sample)
            2. Urine organic acids including succinylacetone (SUAC)
            3. Plasma amino acids
            4. DNA sample for *FAH*/*GSTZ1* testing
        ii. **Initial tests**
            1. Liver function tests including aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyltransferase (GGT), albumin
            2. Clotting profile
            3. Glucose
            4. Urea and electrolytes
            5. Alfa fetoprotein (AFP)
    c. If clotting and/ or liver function tests abnormal → Presumed affected
        i. Commence initial management*
    d. If clotting and liver function tests are normal → Presumed unaffected:
        i. monitor daily liver function and clotting
        ii. Continue normal feeds
        iii. Admit for observation or allow home for review next day
        iv. If liver function or clotting become abnormal, switch to Presumed Affected management pathway
        v. Review Specific diagnostic test results.
            1. If succinylacetone significantly elevated (blood >2μmol/L), switch to presumed affected pathway
4. Specialist team to inform GP (as soon as practicable), send HT1 GP letter via email
5. Specialist team to inform maternity services and health visiting services.
6. Review Specific diagnostic test results

***Initial Management (Presumed Affected)**

1. Arrange transfer to metabolic specialist unit
2. Stop feeds (encourage breastmilk expression and storage if appropriate) and commence IV 10% dextrose/electrolytes; if clinically appropriate can give 10% glucose polymer feed instead of IV fluids
3. Discuss case management with hepatology team and follow guidance of management of acute liver failure; give Vitamin K 1mg IV or SC daily
4. Commence Nitisinone (NTBC) 1mg/kg/day in 2 divided doses by mouth or nasogastric tube (PO/NG).
    a. If using 2mg capsule, round up dose to nearest whole capsule
    b. If international normalised ratio (INR) is greater than 4 after vitamin K, increase NTBC to 2mg/kg/day for 1 week
5. Consider transfer to a liver unit if:
    a. INR not improved after 1 week high dose NTBC
    b. Encephalopathy is present
    c. Conjugated bilirubin is greater than 50 μmol/L
6. Initiate dietary management in accordance **HT1 Dietetic Management Pathway** (on BIMDG website)
7. Treat infection in accordance with clinical requirement and guidance from hepatology team
8. Continue to monitor liver function and clotting

Review Specific Diagnostic Tests



Other diagnostic test results: indicative interpretation

	Tyrosinaemia type 1 (HT1)	**Maleylacetoacetate isomerase (MAAI) deficiency**
Succinylacetone	Significantly elevated	Mildly elevated (usually <2μmol/L in blood)
Alfa fetoprotein	Elevated	Normal
Clotting	Abnormal	Normal
Plasma amino acids	Elevated tyrosine	Normal
Urine organic acids	Elevated succinylacetone, hydroxyketoheptanoate, dihydrocyheptanoate, liver-related metabolites	Elevated maleic acid

**Genetic testing via NHS Genomic Medicine Service (R98) or equivalent service.