Neonatal Screening Profile:

G6PD and Neonatal Thyroid Stimulating Hormone (TSH)

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Neonatal Screening

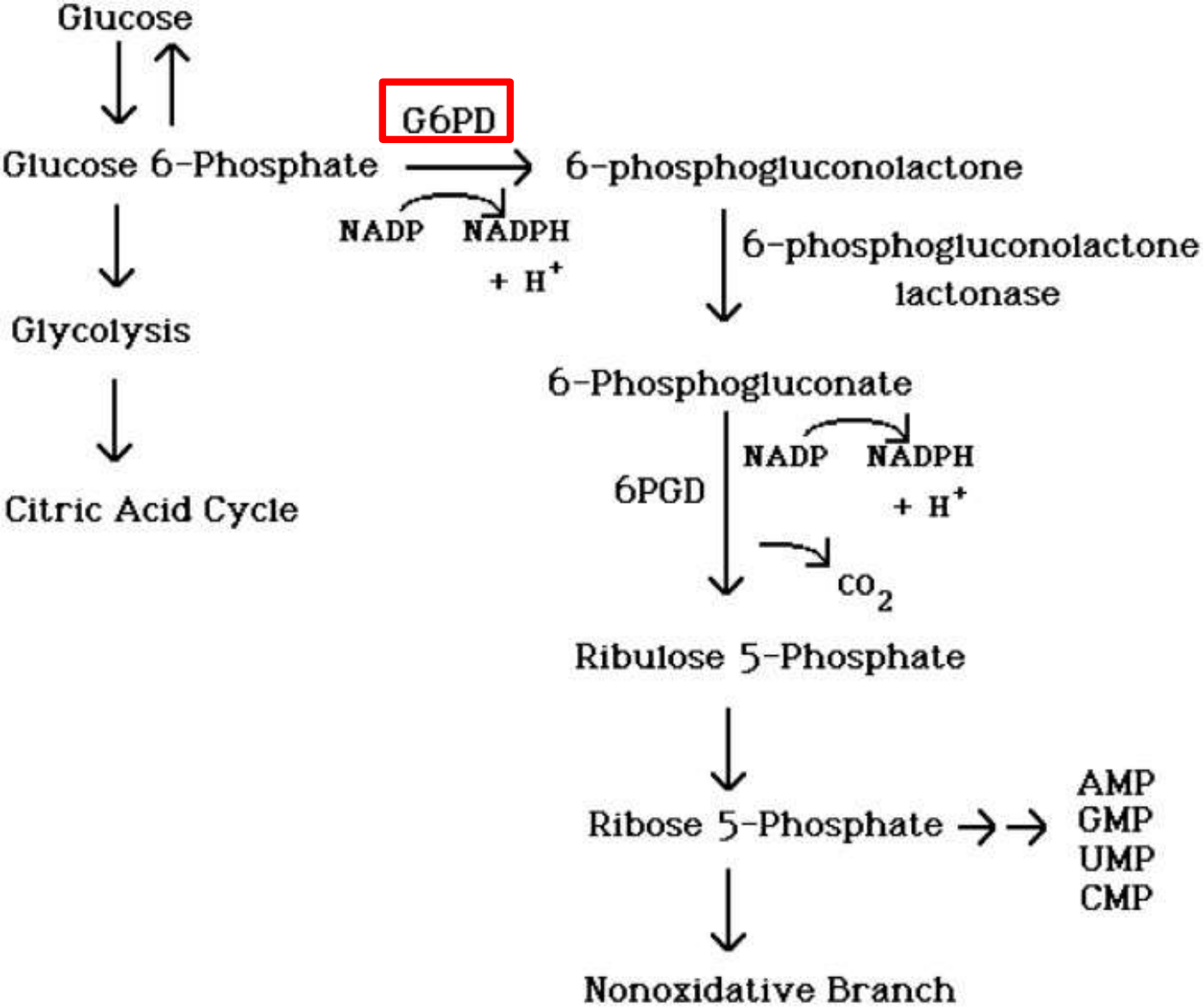
Neonatal screening is a public health program of screening in infants shortly after birth for conditions that are treatable, but not clinically evident in the newborn period. The goal is to identify infants at risk for these conditions early enough to confirm the diagnosis and provide intervention that will alter the clinical course of the disease and prevent or ameliorate the clinical manifestations.


Glucose-6-phosphate
dehydrogenase (G6PD)

Introduction to G6PD

- Glucose-6-phosphate dehydrogenase (G6PD) is an enzyme active in virtually all types of cells that involved in the normal processing of carbohydrates.
- G6PD catalyzes a reaction in the pentose phosphate pathway that supplies reducing energy to cells by maintaining the level of reduced form of Nicotinamide Adenine Dinucleotide Phosphate (NADPH).

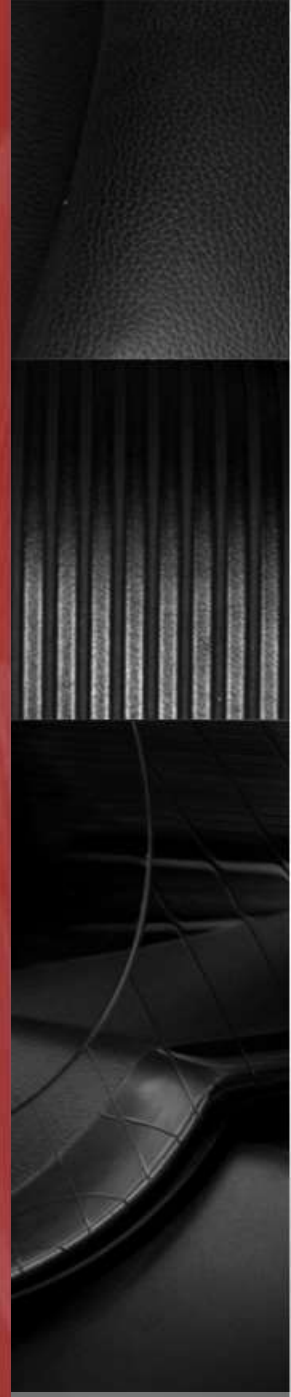
Pentose phosphate pathway



Importance of G6PD

- The intracellular redox potential (which is determined by the level of oxidants and reductants) has been shown to play an vital role in the regulation of cell growth. The principal intracellular reductant is NADPH, which is mainly produced by the pentose phosphate pathway through the actions G6PD, the rate-limiting enzyme of the pentose phosphate pathway, and by 6-phosphogluconate dehydrogenase.

- G6PD plays a vital role in erythrocytes by protecting them from damage and premature destruction.



G6PD Deficiency

- Glucose-6-phosphate dehydrogenase deficiency is a genetic disorder whereby affected individuals comes with a defect in glucose-6-phosphate dehydrogenase due to the mutations in the G6PD gene.

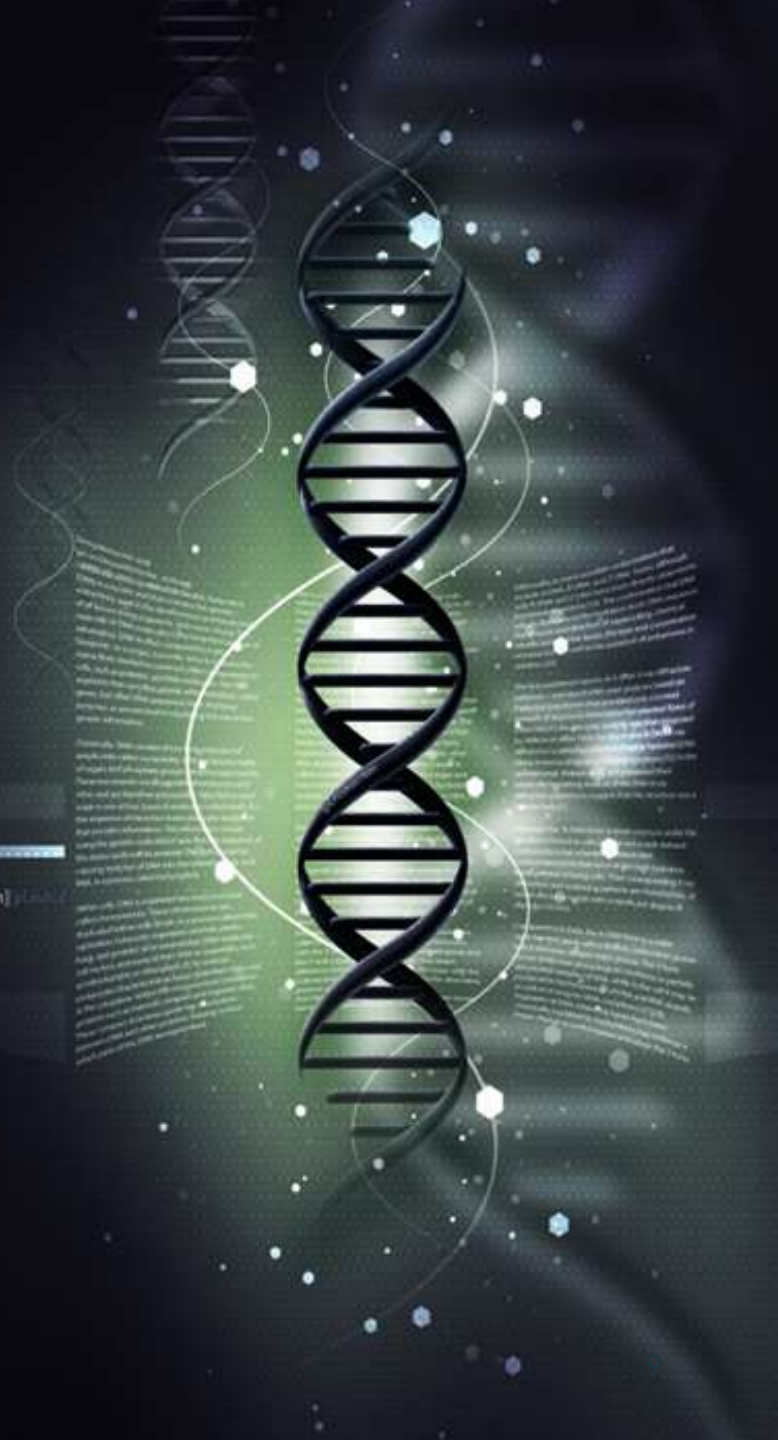
- G6PD deficiency is also a significant cause of mild to severe jaundice in newborns.

G6PD Deficiency

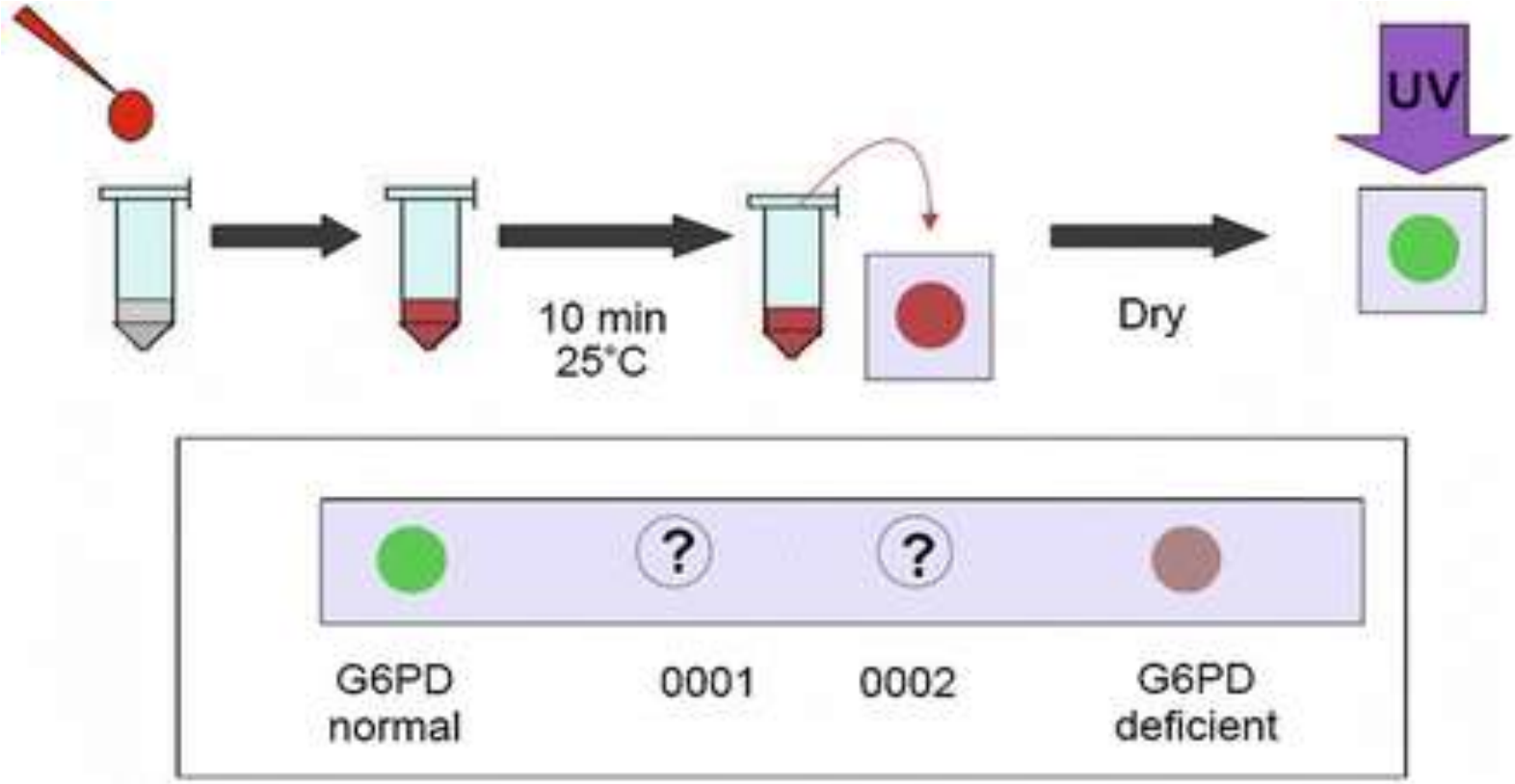
- The most common medical problem associated with glucose-6-phosphate dehydrogenase deficiency is haemolytic anemia, which occurs when erythrocytes are broken down prematurely before the body can replace them.

G6PD Screening Test

The diagnosis of G6PD deficiency is made by a quantitative spectrophotometric analysis or, more commonly, by a rapid fluorescent spot test detecting the generation of NADPH from NADP. The fluorescent spot test is positive if the blood spot fails to fluoresce under ultraviolet light.

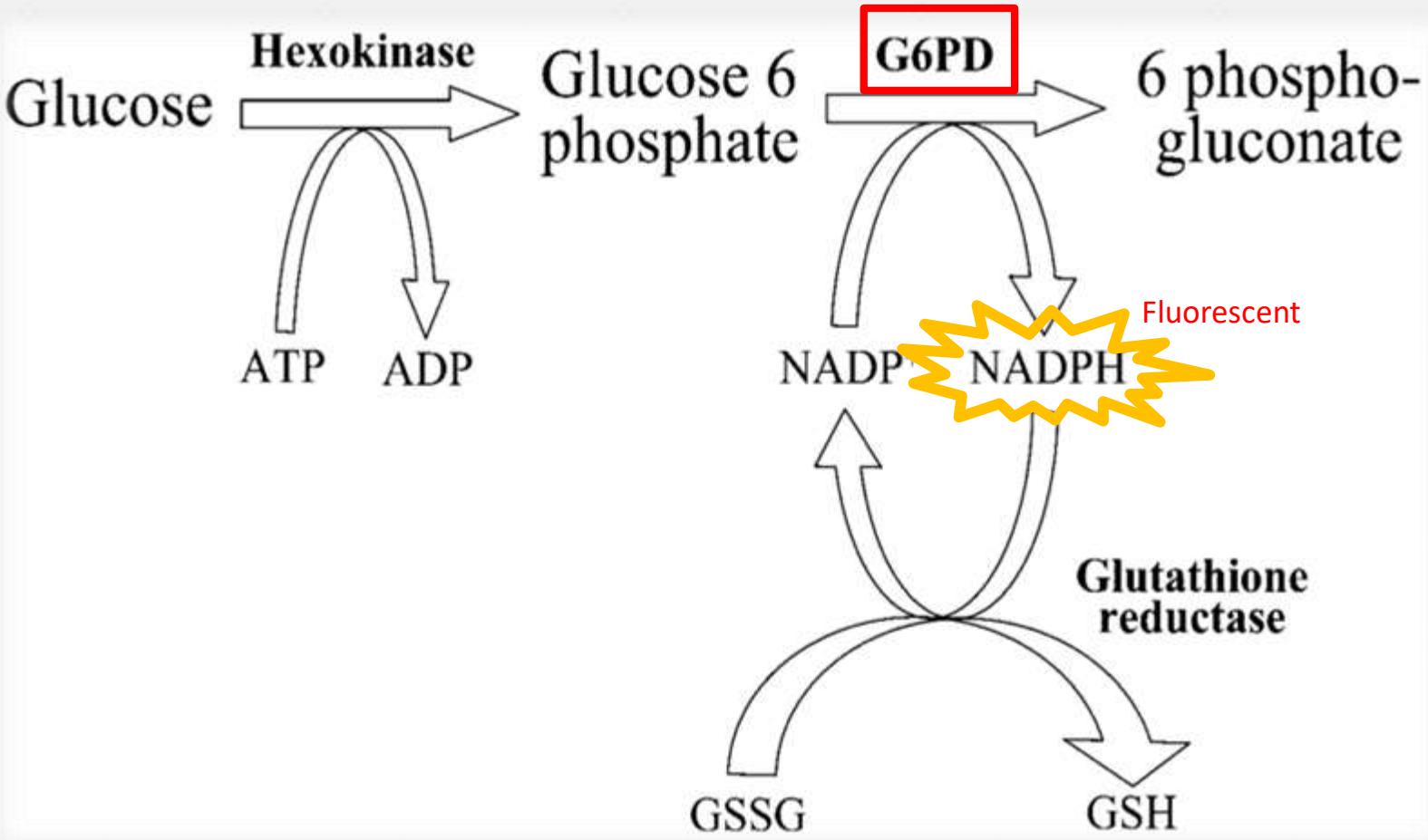


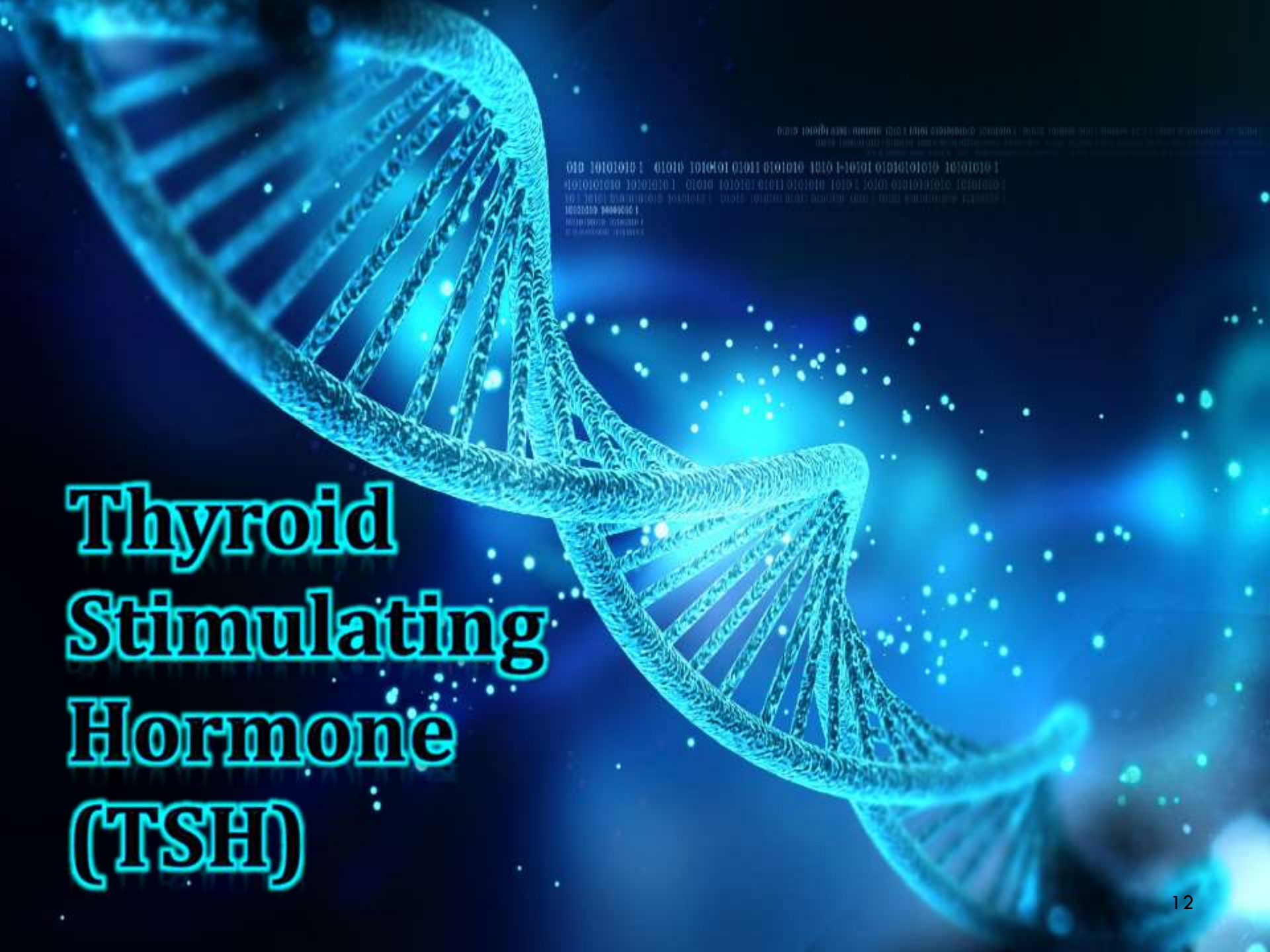
Fluorescent Spot Test



A small amount of blood is incubated with glucose-6-phosphate and NADP in the substrate reagent, and then is spotted on filter paper. Once dried, the spots are viewed under long-wave ultraviolet (UV) light—the by-product of the reaction (NADPH) is fluorescent.

Fluorescent Spot Test




Thyroid
Stimulating
Hormone
(TSH)

Introduction to neonatal TSH

- ✓ Thyroid stimulating hormone (TSH) is a hormone produced by the pituitary gland to regulate thyroid hormones made in thyroid gland which function to maintain body's metabolic rate, heart and digestive functions, muscle control, brain development and maintenance of bones.
- ✓ When TSH binds to the receptor on the thyroid cells, it stimulates them to produce thyroxine (T4) and triiodothyronine (T3) and release them into the bloodstream. T3 and T4 have a negative effect on the pituitary gland and stop the production of TSH if the levels of T3 and T4 are too high. They also stop the production of thyrotropin-releasing hormone (hormone produced by hypothalamus that also stimulates pituitary gland to release TSH.

Introduction to neonatal TSH

- ✓ During pregnancy, the fetus is dependent on maternal thyroxine (T4) crossing the placenta. The fetus de-iodinates the T4 to produce triiothyronine (T3), which is important for neurological development. Maternal T3 does not cross the placenta.
- ✓ The normal term newborn has a rapid TSH surge within 30 minutes of birth that stimulates thyroidal T4 secretion, with peak fT4 and fT3 (free triiodothyronine) levels at 24 to 36 hours of life. Newborn bloodspot screening is performed after 48 hours of age so as to avoid measuring the early rise in TSH.

Neonatal congenital hypothyroidism

- Congenital hypothyroidism in neonates is characterised by decreased, or in rare cases, no thyroid hormone production. Early diagnosis is critical to prevent neurodevelopmental disability and to optimise developmental outcomes.
- All newborns have screening for congenital hypothyroidism at 48-72 hours age with the newborn bloodspot screening test, which measures elevations in TSH. Infants at risk of a late TSH rise may have second and subsequent bloodspot tests requested by The Victorian Clinical Genetics Services (VCGS).
- Newborn bloodspot screening is the only test required to detect congenital hypothyroidism in well, term, singleton infants regardless of the aetiology of maternal hypothyroid status (including Hashimoto's thyroiditis and subclinical hypothyroidism of pregnancy).

Neonatal congenital hypothyroidism (cont.)

- The newborn bloodspot screening test will not detect low levels of TSH. Therefore, infants with clinical signs suggestive of central hypothyroidism or suspicion of hypothalamic-pituitary axis dysfunction (i.e. hypopituitarism) should have thyroid function tests taken via a capillary or venous sample no earlier than day five of life.

Neonatal hyperthyroidism

- Neonatal thyrotoxicosis is a rare condition that can be life threatening if untreated. It is caused by trans-placental transfer passage of TSH receptor antibodies (TRAb), usually in the presence of maternal Graves' thyrotoxicosis (and rarely from Hashimoto's thyroiditis) in the third trimester causing stimulation of the fetal thyroid gland.
- If a person has too little thyroid stimulating hormone, it is most likely that their thyroid gland is making too much thyroid hormone, that is, they have an overactive thyroid or hyperthyroidism, which is suppressing the thyroid stimulating hormone. People with an overactive thyroid have the opposite symptoms to those with hypothyroidism, i.e. they lose weight (despite increasing the amount they eat), feel too hot and can experience palpitations or anxiety. They may also have a slightly enlarged thyroid gland.

Neonatal hyperthyroidism (cont.)

- Treatment is medication in the form of tablets, which reduce the activity of the thyroid gland and return all thyroid hormone levels to normal. Rarely, problems in the pituitary gland can also result in a low thyroid stimulating hormone, and low free thyroid hormone levels.
- Neonatal hyperthyroidism will not be detected through newborn bloodspot screening.