JOURNAL-BASED LEARNING EXERCISES

IBMS Institute of Biomedical Science Continuing Professional Development

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DEADLINE WEDNESDAY 5 AUGUST 2020

Primaquine-induced haemolysis in females heterozygous for G6PD deficiency. Chu CS, Bancone G, Nosten F, White NJ, Luzzatto L. *Malar J* 2018; **17** (1): 101. doi: 10.1186/s12936-018-2248-y. Assessment No: 050420

01	G6PD deficiency is an autosomal rather than X-linked condition.	11	Females with an intermediate phenotype will definitely be heterozygotes.
02	Erythrocytic G6PD activity decreases physiologically as erythrocytes age in the circulation.	12	Doxiadis *et al.* observed that newborns with low levels of G6PD in their red blood cells had an increased frequency of neonatal jaundice, which was often severe.
03	In most malaria-endemic areas, testing for G6PD deficiency is available.	13	Over the past 90 years, 8-aminoquinolines have been prescribed mostly with testing for G6PD deficiency.
04	Primaquine was the first 8-aminoquinoline used for the radical curative treatment of *Plasmodium vivax* malaria.	14	In females, if the G6PD activity is ≤25% of normal, females receive the same treatment as G6PD-deficient males.
05	Nitrofurantoin, ciprofloxacin and rasburicase are known to cause haemolysis in G6PD-deficient individuals.	15	Tafenoquine has a long terminal elimination half-life which allows a single dose to be given. Thus, unlike primaquine, which can be stopped at the first sign of toxicity, tafenoquine cannot be stopped.
06	The extent of haemolysis in patients receiving tafenoquine was greatest following the administration of 200-mg doses of this drug.	16	In somatic cell mosaicism, the ratio of the two cell types that make up the mosaic is the same for all females.
07	Anecdotal evidence of G6PD deficiency has been recorded since antiquity.	17	Lyonization refers to the random inactivation of one X-chromosome in the somatic cells of a female.
08	The average proportion of G6PD-deficient red cells in heterozygotes is 50% and will always be less severe than a hemizygous male.	18	In a male population there are two evident phenotypes; G6PD normal and deficient.
09	In normal subjects, G6PD activity is often around 7–10 IU/gHb.	19	The WHO malaria treatment guidelines have long recommended the addition of primaquine to chloroquine (or now to artemisinin-based combination therapy) for the treatment of *P. vivax* and *P. ovale*, and this recommendation is often followed.
10	Males with a G6PD-deficient phenotype are hemizygous for a mutant allele.	20	As malaria programmes progress towards the elimination of *P. falciparum* malaria, the proportion of malaria infections attributable to *P. vivax* outside sub-Saharan Africa declines.

REFLECTIVE LEARNING

01	Critically discuss the challenges a laboratory would face when introducing testing for red cell enzymopathies.	02	Red cell polymorphisms provide a selective advantage in areas of high malaria prevalence. Critically discuss this statement.

DEADLINE WEDNESDAY 5 AUGUST 2020

An audit of liquid-based cytology samples reported as high-risk human papillomavirus and borderline nuclear change in endocervical cells. Manley KM, Luker R, Park C. *Cytopathology* 2020; **31** (2): 130–5. https://doi.org/10.1111/cyt.12803. Assessment No: 050820

01	This audit was a prospective study carried out between 2016 and 2018.	11	The sensitivity, specificity, PPV and NPV were calculated on the colposcopic assessments of high-grade dysplasia for the women in the audit.
02	68.2% of the patients identified for this study had high-grade dysplasia at diagnostic biopsy.	12	The age range of women identified in the audit was 25–49 and the majority of these were smokers (81.8%).
03	The positive predictive value (PPV) of colposcopic impression was 100% and the negative predicative value (NPV) was 43.8%.	13	Eight of the 22 women in the audit were found to have CIN2 or CIN3, and seven were found to have CGIN.
04	The incidence of borderline change in endocervical cells in this study was 1.2%, which falls into the range identified in the referenced literature of 0.5–1.8%.	14	The time from referral to attendance at colposcopy for the 15 women with high-grade dysplasia varied from two to 12 weeks with a median of four weeks.
05	NHSCSP guidance released in 2016 recommended all women with BNC in endocervical cells and high-risk HPV (HR-HPV)-positive on triage should be seen in colposcopy within two weeks of referral.	15	There was a difference in patient characteristics between the women identified with low-grade versus high-grade dysplasia.
06	NHSCSP guidance issued in 2016 for the management of women with BNC in endocervical cells and HR-HPV-positive was based on evidence prior to the introduction of HPV triage.	16	One patient in the audit had a type 3 TZ on colposcopic impression, with the remaining 21 patients having either a type 1 or type 2 TZ.
07	Evidence used in the NHSCSP guidance from 2016 indicated rates of 10–33%, 10% and 1.8–22% for CIN, CGIN and invasive lesions, respectively, in women with BNC in endocervical cells.	17	Colposcopic assessment was found to have a specificity of 100% and sensitivity of 37.7% for high-grade dysplasia in women with a TZ type 1–2.
08	Evidence from outcomes following HPV triage suggest 50–62% of women with BNC in endocervical cells and HR-HPV-positive will have high-grade changes requiring treatment.	18	The authors suggest the audit findings support the USA recommendations of endocervical sampling for all women with any grade of glandular changes reported on cytology, irrespective of colposcopic impression.
09	Guidance issued by the British Association for Cytopathology (BAC) in 2014 suggested MDT discussion for women with a cytological glandular abnormality, either BNC or ?neoplasia, confirmed on histopathology or colposcopy should be reviewed at MDT.	19	23% of the women did not attend colposcopy within the NHSCSP-recommended timescale of six weeks from referral date, and, of these, three had CIN3 and two had high-grade CGIN at LLETZ.
10	The data collected and recorded were identifiable to each individual patient.	20	If all cases of BNC in endocervical cells are treated as high-grade referrals (seen in two weeks) as the authors recommend, this will likely have a significant impact on the workload of colposcopy departments.

REFLECTIVE LEARNING

01	Carry out an audit of the cases between 2016 and 2018 reported within your laboratory as BNC in endocervical cells, and the outcomes. Do your findings correlate with the findings identified in this study?	02	Did the management in these cases adhere to NHSCSP guidance at the time? Could the authors' suggested algorithm here have resulted in a more favourable outcome for the patients identified in your audit?