

## Safety of $^{14}\text{C}$ -UBT for diagnosis of *Helicobacter pylori* infection in pregnancy

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### ABSTRACT

**QUESTION** A 29-year-old woman had a carbon 14 urea breath test for diagnosis of *Helicobacter pylori* infection. At time of consultation, it had been 6 weeks since her last menstrual period. Four weeks after her last menstrual period, the results of a urine pregnancy test were negative. On that day, she received an ionizing radiation dose of 74 KBq (2  $\mu\text{Ci}$ ) carbon 14 urea, followed by the breath test 30 minutes thereafter. Four days later, when the urine pregnancy test results turned positive, she was concerned about the possible effect of her exposure to ionizing radiation on the developing fetus.

**ANSWER** The amount of radiation used in these tests is extremely low—much lower than the amount a pregnant woman is absorbing through natural sources.

### RÉSUMÉ

**QUESTION** Une femme de 29 ans a subi un test respiratoire à l'urée marquée au carbone 14 pour le dépistage d'une infection par *Helicobacter pylori*. Au moment de la consultation, il s'était écoulé 6 semaines depuis ses dernières menstruations. Quatre semaines après ses dernières menstruations, les résultats d'un diagnostic urinaire de la grossesse s'étaient révélés négatifs. Le même jour, elle a reçu une dose de rayonnements ionisants de 74 kBq (2  $\mu\text{Ci}$ ) à l'urée marquée au carbone 14, suivie d'un test respiratoire 30 minutes après. Quatre jours plus tard, les résultats du test de grossesse étaient positifs. Elle s'inquiète des effets possibles de cette exposition aux rayonnements ionisants sur le fœtus en développement.

**RÉPONSE** La quantité de rayonnements utilisée dans ces tests est extrêmement faible, bien plus faible que le montant absorbé de sources naturelles par une femme enceinte.

*Helicobacter pylori* infection is the most important etiologic factor in chronic gastritis and gastroduodenal ulcer disease. Approximately 30% of patients with dyspepsia in North America are infected with *H pylori*; the annual incidence of new infections is about 0.5 per 100 persons in the susceptible population. In the developing world, prevalence among patients with dyspepsia is 80% to 90%, and the annual incidence of new infections is 3 or more per 100 susceptible persons. Presence of *H pylori* is closely related to development of gastric cancer. Eradication of the organism results in ulcer healing and reduces risk of ulcer recurrence and complications. Diagnostic methods for *H pylori* infection are direct or invasive (identifying the microorganism by gastric biopsy) and indirect or noninvasive (detecting certain characteristics of the bacteria). The latter can include the capacity of *H pylori* to hydrolyze urea (eg, urea breath test [UBT]) or quantification of specific antibodies (eg, various serologic tests).<sup>1-3</sup>

### Urea breath test

The UBT is simple, innocuous, easy to repeat, and among the most accurate methods of assessing *H pylori* status. It has been widely used to screen patients before endoscopy and to assess the success of therapies aimed at eradicating *H pylori*. The test uses the capacity of the urease

enzyme secreted by *H pylori*, when present in the stomach, to hydrolyze orally administered urea labeled with carbon 13 ( $^{13}\text{C}$ ) or carbon 14 ( $^{14}\text{C}$ ). This hydrolysis produces isotopically labeled carbon dioxide ( $\text{CO}_2$ ). The labeled  $\text{CO}_2$  diffuses into blood, is excreted by the lungs, and can be detected in breath samples. Some studies suggest using a test meal before urea administration and collecting a basal breath sample. The urea dose is less than 100 mg, usually 75 or 50 mg. Twenty to 30 minutes after urea administration, a breath sample (exhaled air) is collected; some studies suggest collecting after 10 to 15 minutes.<sup>1-4</sup>

### Dose and pharmacokinetics

Usually a 1- $\mu\text{Ci}$  (37-KBq) capsule of  $^{14}\text{C}$  urea is administered, but doses as high as 5  $\mu\text{Ci}$  (185 KBq) have been reported.<sup>5-7</sup> Carbon 14 emits  $\beta$  radiation. The biologic half-life of  $^{14}\text{C}$  is 10 to 12 days; this should not be confused with its physical half-life (5730 years).<sup>8</sup> When  $^{14}\text{C}$  urea is administered to *H pylori*-negative subjects, up to 30% of the radioactivity is excreted in the breath as [ $^{14}\text{C}$ ]CO<sub>2</sub>. The respiratory excretion of [ $^{14}\text{C}$ ]CO<sub>2</sub> increases to 60% in *H pylori*-positive patients. The biologic half-life of [ $^{14}\text{C}$ ]CO<sub>2</sub> is 15 minutes. The remaining radioactivity is excreted by the kidneys unchanged, with an elimination half-life of 12 hours<sup>4,5</sup>; about 88% is excreted via the urine within 72 hours.<sup>6</sup>

### Estimating radiation-absorbed doses

The carbon that comprises our bodies contains  $^{14}\text{C}$  at the same concentration as the atmosphere. The internal  $\beta$ -decays from this element contribute approximately 1 mrem/y (0.01 mSv/y). The radiation exposure from a 1- $\mu\text{Ci}$  dose of  $^{14}\text{C}$  is estimated to be equivalent to the amount of radiation received by the patient from the natural environment over a period of 11 hours.<sup>4</sup>

Stubbs and Marshall estimated the radiation-absorbed doses in men and women who had been tested with  $^{14}\text{C}$ -UBT: In *H pylori*-positive patients, the radiation-absorbed doses of the uterus, ovaries, and urinary bladder wall were 0.31 rad/mCi, 0.31 rad/mCi, and 0.5 rad/mCi, respectively.<sup>9</sup> (Similar results were reported by other researchers.<sup>6</sup>) In *H pylori*-negative subjects, the radiation-absorbed doses of the uterus and ovaries were about 50% lower; the radiation-absorbed dose of the urinary bladder wall was 138% higher compared with *H pylori*-positive patients.<sup>9</sup> The calculated effective dose equivalent (ie, global or total body mean radiation dose) for the  $^{14}\text{C}$ -UBT in this study (*H pylori*-positive female patients) was 0.3 rem/mCi or 0.08 mSv/MBq (0.18 rem/mCi or 0.049 mSv/MBq in *H pylori*-negative female patients).<sup>9</sup> Assuming relative biologic effectiveness of 1 for soft tissues (1 rem=1 rad/relative biologic effectiveness),<sup>8</sup> this translates to 0.3 rad/mCi. The effective dose equivalent (global mean) for an average person from natural sources was reported to be 2.4 mSv/y by the United Nations Scientific Committee on the Effects of Atomic Radiation. This means that approximately 800  $^{14}\text{C}$ -UBTs using 1  $\mu\text{Ci}$  (37 KBq) should generate the same effective dose equivalent as that of natural sources (background radiation).<sup>9</sup>

### Risk assessment

Radiation exposure from the dose of  $^{14}\text{C}$  given in the UBT is similar to or even lower than that from background radiation.<sup>4,9</sup> The fetal radiation-absorbed dose from maternal exposure to 1  $\mu\text{Ci}$  (37 KBq) of  $^{14}\text{C}$  in the UBT is estimated to be 0.31 mrad, assuming fetal exposure is equivalent to uterine dose. This estimate is 3 orders of magnitude less than the fetal radiation dose reported to be safe in pregnancy (ie, 5 rad or 5000 mrad).<sup>8</sup> Even when assuming that the fetal radiation dose is equivalent to the combined uterine, ovarian, and urinary bladder wall dose (ie, 1.12 mrad), this estimate does not change. Higher radiation doses of  $^{14}\text{C}$  reported to be used in the UBT (ie, 74 to 185 KBq or 2 to 5  $\mu\text{Ci}$ ) should still be within the safe fetal radiation exposure range (ie, 0.62 to 5.6 mrad).

### Protective measures

The ionizing radiation dose associated with the  $^{14}\text{C}$ -UBT is very small and requires no restrictions in adults and young children (3 to 6 years old) or upon repeated testing.<sup>6,10</sup> In the case of known pregnancy, the test should only be performed if the benefits outweigh the risks, even though the fetal radiation dose is much lower than the dose

considered teratogenic. Frequent voiding can substantially reduce the radiation-absorbed dose to the urinary bladder wall—42% to 53% reduction for a 2-hour bladder voiding interval compared with a 4.8-hour voiding interval.<sup>9</sup>

### Conclusion

The  $^{14}\text{C}$ -UBT is widely used for diagnosis of gastric *H pylori* infection. The ionizing radiation dose involved in this test is extremely low, much lower than the radiation dose absorbed from natural sources. It is at least a thousand times lower than the amount of fetal radiation considered to be teratogenic (0.31 to 5.6 mrad vs 5000 mrad).

In the event of inadvertent exposure during pregnancy, the pregnant woman should be reassured, given the low fetal radiation dose. Frequent voiding (eg, every 2 hours) can reduce the internal radiation-absorbed dose by 40% to 50%. Further, in this patient exposure occurred at 4 weeks' gestation. This is before the most vulnerable period for the teratogenic effects of ionizing radiation, which is 8 to 25 weeks' gestation.<sup>8</sup>

### Competing interests

None declared

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## MOTHERISK

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