What Are the Chemical Forms of Arsenic in Urine, and What Can They Tell Us About Exposure?

Both in the general environment and occupationally, people may be exposed to a number of different arsenic compounds with physical, chemical, and toxicological properties that vary considerably. Our knowledge about the metabolism and toxicity of many of the arsenic compounds is far from complete. Some of the important questions that remain are: What different forms of arsenic may occur in human urine? What forms of arsenic are measured by the different analytical techniques? What can we conclude about exposure and health risks on the basis of concentrations of various forms of arsenic in urine?

Le et al. (1) recently presented data on the metabolism of arsenosugars, which are common arsenic compounds in edible seaweed. The findings are important not only because they contribute to the understanding of arsenosugar metabolism, but also because they show that the ingestion of seaweed may increase the urinary concentration of a metabolite of inorganic arsenic and, thereby, affect the use of urinary arsenic as an indicator of exposure to inorganic arsenic.

Inorganic arsenic is generally considered the most toxic form of arsenic. It may give rise to a variety of toxic effects, including various forms of cancer. Therefore, it is important to have sensitive and accurate methods for assessing the absorbed dose, and, ideally, for assessing the target-organ dose. Exposure to inorganic arsenic is often determined on the basis of the concentration of its metabolites in urine. Inorganic arsenic is methylated to methylarsonic acid (MMA) and dimethylarsinic acid (DMAA) in the body. The methylated metabolites are less reactive with tissue constituents than is inorganic arsenic, and they are rapidly excreted in the urine (2). Thus, the methylation of inorganic arsenic is a form of detoxification. Typically, arsenic in human urine is 10–15% inorganic arsenic, 10–15% MMA, and 60–80% DMAA (1, 3–5).

Early in this century it was reported that ingestion of seafood could cause a considerable increase in the urinary concentration of arsenic (6, 7). The concentration of arsenic in urine of subjects without known exposure to arsenic is generally in the order of 10–20 µg/L, but intake of a single meal of fish or shellfish may increase the concentration to >1000 µg/L (8). Thus, it is difficult to use total urinary arsenic as an indicator of exposure to inorganic arsenic unless the subjects under study refrain completely from eating seafood before their urine is sampled. This is often difficult, given that fish products are widely used, e.g., in feed for animals subsequently consumed by humans. A more suitable method for measuring exposure to inorganic arsenic is to determine the metabolites specifically, either separately or together, e.g., by using a hydride generation system in combination with atomic absorption spectrophotometry (5, 8). This method is not influenced by the presence in urine of arsobetaine, which, in 1977, was identified by John Edmonds and his colleagues in Western Australia as the main form of arsenic in western rock lobster (9). Since then, numerous studies have demonstrated that arsobetaine is the main form of arsenic in most fish and shellfish (for a review, see ref. 10). Arsobetaine is very stable; after ingestion, it is rapidly excreted unchanged in the urine (11). It is not degraded in the body to inorganic arsenic and it does not form an arsenic with sodium borohydride (8). Similarly, arsobetaine, another organoarsenic compound found in seafood (although in lower concentration than arsobetaine), is not degraded in vivo to inorganic arsenic and does not form arsenic with sodium borohydride (8).

The report of Le et al. (1) showed that ingestion of the seaweed product nori, which contains a single arsensugar as the main arsenic compound, may give rise to several different arsenic metabolites in the urine, one of which is DMAA. The concentration of DMAA increased two- to threefold in some, but not all, subjects. From a toxicological point of view it is important to note that the concentration of As(V) in urine did not increase, indicating that the arsensugar was not metabolized to inorganic arsenic. It was shown previously that ingestion of seafood other than seaweed may sometimes increase the urinary concentration of arsenic species that do react with sodium borohydride (3, 12). One report indicated that DMAA is the main hydride-forming arsenic compound in the urine after ingestion of several fish species (13). However, there may be other hydride-forming compounds in the urine after seafood consumption. Other arsenic compounds in fish and crustaceans, often present at much lower concentrations than arsobetaine, include trimethylarsine oxide (TMAO), trimethylarsine (TMA), and tetramethylarsion salts (10). TMAO and TMA may also be formed in fish during storage. Possibly, arsobetaine may be biotransformed to TMAO (14). TMAO, which is the main form of arsenic in urine after intake of both TMA and TMAO, reacts with sodium borohydride to form TMA. Data are needed on the urinary concentrations of TMAO after consumption of various types of seafood. The possible influence of TMAO on the separation of arsenic metabolites in urine by various methods also needs to be studied.

In conclusion, it seems clear that consumption of sea-
food, including seaweed, may increase the concentration of DMAA, and possibly TMAO, in the urine, potentially invalidating assessments of exposure to inorganic arsenic. Therefore, subjects under study for exposure to inorganic arsenic should avoid eating any kind of seafood, or any food products containing seafood, for 2–3 days before their urine is sampled. More research is needed to identify all arsenic compounds in the diet, especially seafood, and to determine their toxicokinetics—an endeavor that will require investigation of the total excretion of the various urinary arsenic metabolites. Thus, it will be important to collect all urine produced during a certain period after ingestion of food potentially containing arsenic, not just random urine samples, as is done in most studies. As shown by many examples in the literature, this is not an easy task. Controlling for the sampling efficiency can be achieved to some extent by determining the recovery of ingested p-aminobenzoic acid in the urine.

References

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