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Human toxicity from COVID-19 rapid home test kits



The persistence of the COVID-19 pandemic has necessitated the development and widespread availability of methods to detect the COVID-19 virus in humans. COVID-19 tests, which were initially only available in healthcare facility settings, are now manufactured for home use in the form of rapid diagnostic tests and generally contain a nasal swab, reagent solution, and test device (e.g., card or strip). These kits typically involve application of reagent solution to the test device; in the presence of biological material obtained from the nasal swab, this initiates a chemical reaction that produces the test result.

Multiple COVID-19 rapid antigen home test kits, including those manufactured by Abbott (BinaxNOW™), Beckton, Dickinson and Company (BD Veritor™), Celltrion (Celltrion DiaTrust™), and ACON Laboratories (Flowflex™), contain sodium azide as a component of the reagent solution [1–3]. The reagent in some kits may contain other constituents, including Triton-X, inorganic phosphate, and Pro-Clin 300. The latter ingredients are unlikely to cause human toxicity if small amounts are ingested, but they may cause allergic reactions or local irritation after ocular or dermal exposure. However, sodium azide is well-known for its ability to cause harmful effects in humans, especially after oral exposures and potentially including the ingestion of reagent solution. Additionally, since the reagent solution packaging may include ampules that allow for application of drops of solution to the test device, inadvertent ocular sodium azide exposures can occur if the ampule is mistaken for an eyedropper.

Sodium azide is a water-soluble, tasteless, and odorless chemical that is commonly used as a preservative agent [4]. It is also found as a propellant in some automobile airbags; upon impact, sodium azide ignites and transforms into hydrocarbon gases that cause airbag expansion [5]. Although data concerning acute sodium azide toxicity in humans are limited, the chemical can cause serious adverse events after oral exposure to relatively low doses. In one study, sodium azide was administered at doses of 0.65 and 1.3 mg to healthy and hypertensive individuals (for a 70-kg adult, this corresponds to a dose of 0.01 and 0.02 mg/kg) [6]. Hypotension occurred rapidly, within 45–60 s in some subjects, and lasted for 10–15 min. Despite the fall in blood pressure, reflex tachycardia was not noted, but a detailed description of other adverse events was not provided by the authors. In the same study, one hypertensive subject who received oral doses of 0.3 mg (or 0.004 mg/kg for a 70-kg individual) experienced a change in blood pressure from 183/104 mmHg pre-treatment to 115/68 mmHg post-treatment. Ingestion of higher doses of sodium azide (>700 mg or 10 mg/kg) by adults is associated with cardiac arrhythmias, metabolic acidosis, and death [7–9].

The reagent fluid in many COVID-19 rapid antigen home test kits contains sodium azide in concentrations of 0.0125–0.0946%, and personal communication with test kit manufacturers revealed that the reagent fluid volume in these kits is small (0.3–0.625 mL) [1–3]. Thus,

reagents with sodium azide concentrations less than 0.09–0.095% generally contain extremely low amounts of sodium azide (0.04–0.08 mg), or well below the amount expected to cause transient hypotension in adults. Kits that have reagent fluid with higher sodium azide concentrations (greater than or equal to 0.09%), including the BD Veritor™ and Celltrion DiaTrust™ testing systems, contain approximately 0.3 mg of sodium azide [10,11]. Ingestions of this magnitude may result in hypotension, decreased end-organ perfusion, and syncope. Children may experience serious adverse events after exploratory oral exposures to minimal amounts of the reagent solutions due to their smaller body size and should be monitored closely for hypotension or other sequelae after ingestion of even minute quantities of reagent fluids. Since the onset of hypotension after oral exposure to sodium azide is rapid, prolonged observation is likely unnecessary for individuals who remain asymptomatic after reagent fluid ingestion. The treatment of symptomatic sodium azide intoxication is supportive in nature and includes intravenous fluids and vasoactive medications.

While home COVID-19 tests have remained in short supply throughout most of the current pandemic, the United States government began offering free tests to its residents starting in mid-January 2022. Prior to this distribution of free tests, numerous cases involving oral exposure to COVID-19 home test reagent fluid were reported to United States poison centers. From June 16, 2021 through January 19, 2022, the online webPOISONCONTROL® tool received 153 reports of human exposure to COVID-19 home test kits or reagents. Many of these cases were associated with no adverse effects, suggesting that exposures involving reagent fluid are unlikely to cause significant human toxicity. The expanded access to home tests will likely result in a further increase in human exposures to the reagent fluids. Emergency physicians, pharmacists, and poison center staff should maintain awareness of the potential toxicities associated with ingestion of the reagent fluids and should also be prepared to treat patients who present for care after exposures to the contents of COVID-19 rapid antigen home test kits.

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Prior presentation

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References

- [1] Abbott. BinaxNOW™ COVID-19 Ag card home test. Available at: <https://www.fda.gov/media/144574/download>; 2022. Accessed 1.18.22.
- [2] BD. BD Veritor™ At-Home COVID-19 test product information leaflet. Available at: <https://bdveritor.bd.com/content/dam/bdveritorathome/documents/product-information-leaflet.pdf.coredownload.pdf>; 2022. Accessed 1.18.22.
- [3] ACON Laboratories. Flowflex™ COVID-19 antigen home test package insert for healthcare providers. Available at: <https://www.aconlabs.com/wp-content/uploads/2021/10/ACON-Labs-Flowflex-US-COVID-19-Home-Test-HCP-Insert-En.pdf>; 2022. Accessed 1.18.22.

- [4] Chang S, Lamm SH. Human health effects of sodium azide exposure: a literature review and analysis. *Int J Toxicol*. 2003 May-Jun;22(3):175–86.
- [5] Barnes SS, Wong Jr W, Affeldt JC. A case of severe airbag related ocular alkali injury. *Hawaii J Med Public Health*. 2012 Aug;71(8):229–31.
- [6] Black MM, Zweifach BW, Speer FD. Comparison of hypotensive action of sodium azide in normotensive and hypertensive patients. *Proc Soc Exp Biol Med*. 1954 Jan;85(1):11–6.
- [7] Albertson TE, Reed S, Siefkin A. A case of fatal sodium azide ingestion. *J Toxicol Clin Toxicol*. 1986;24(4):339–51.
- [8] Abrams J, El-Mallakh RS, Meyer R. Suicidal sodium azide ingestion. *Ann Emerg Med*. 1987 Dec;16(12):1378–80.
- [9] Judge KW, Ward NE. Fatal azide-induced cardiomyopathy presenting as acute myocardial infarction. *Am J Cardiol*. 1989 Oct 1;64(12):830–1.
- [10] BD. Veritor™ system for rapid detection of SARS CoV-2. Available at: <https://bdveritor.bd.com/content/dam/bdveritor/pdfs/BD-Veritor-IFU.pdf>; 2022. Accessed 1.19.22.
- [11] Celltrion. Celltrion DiaTrust™ COVID-19 Ag home test healthcare provider instructions for use. Available at: <https://www.fda.gov/media/153420/download>; 2022. Accessed 1.19.22.

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