

# Key take-home messages

<u>Candida auris</u> (C. auris) is a recently discovered, opportunistic fungal pathogen that can cause serious illness, is often resistant to common antifungal medications, and is increasing in incidence globally.

#### What we know from clinical surveillance

- *C. auris* is a <u>nationally notifiable</u> <u>condition</u> according to the U.S. Centers for Disease Control and Prevention (CDC) but is still not reportable in all states. Its true prevalence is unclear.
- Most *C. auris* cases occur in hospitalized, immunocompromised individuals with serious medical conditions, but asymptomatic colonization is also possible.
- There has been a notable increase in clinical cases of *C. auris* in the U.S. with over <u>3,000 reported in 2023</u>, compared to about 1,000 in 2022 and a total of 63 between 2013 and 2016.

#### How wastewater surveillance plays a role

- Wastewater surveillance shows promise as a tool for monitoring new *C. auris* cases, with culturable *C. auris* and *C. auris* DNA having been recovered from wastewater in communities with and without known outbreaks.
- *C. auris* has been detected by positive culture in human urine and feces, as well as in skin swabs, although the relative importance of different shedding routes into wastewater is unknown.
- *C. auris* is already being tested in wastewater by the <u>WastewaterSCAN</u> program, and is in the process of being incorporated into the core pathogen panel for the <u>U.S. National Wastewater</u> <u>Surveillance System</u> (NWSS).

#### What wastewater workers need to know

- Transmission of *C. auris* can occur through direct contact with infected persons, but also through contact with surfaces contaminated with *C. auris* and potentially other routes.
- Based on the findings of environmental persistence of viable *C. auris*, and the detection of *C. auris* from wastewater using culture-based methods, it is reasonable to assume that infective *C. auris* could survive the typical range of residence times (hours to days) in collection systems.
- Understanding the effectiveness of disinfectant products, conducting job safety assessments, practicing good hygiene—including using alcoholbased hand sanitizers after hand washing—and wearing appropriate personal protective equipment are important for protecting wastewater worker health and preventing *C. auris* infection, especially for collection system workers.
- <u>Disinfectants on "List P", published by</u> <u>the U.S. Environmental Protection</u> <u>Agency</u> (EPA) are effective against *C. auris* contamination on surfaces, as is a dilute bleach solution (1 part 5.25% sodium hypochlorite with 9 parts water) with a contact time of 1 minute.
- Utilities should coordinate with local public health agencies and healthcare institutions to understand the risk of *C. auris* in their wastewater.

# Why it's a concern

<u>Candida auris</u> (C. auris) is an <u>emerging</u><sup>1</sup>, opportunistic fungal pathogen that can cause severe infections with high mortality rates, particularly in immunocompromised individuals; is often resistant to multiple antifungal drugs; can be difficult to eradicate in healthcare facilities; and is increasing in incidence globally (<u>WHO 2022</u>; <u>U.S. CDC 2023a</u>; <u>Weber et al. 2023</u>). Since first being recognized in 2009 (<u>Satoh et al. 2009</u>), *C. auris* cases have been confirmed in over 40 countries, including the U.S., and on all continents except Antarctica (<u>Rhodes and Fisher 2019</u>; <u>Nelson 2023</u>).

The first *C. auris* infection in the U.S. was reported in 2013 in New York (<u>Vallabhaneni et al.</u> 2016) and has now been identified in more than half of states. The number of clinical cases in the U.S. increased from 63 between 2013 and 2016 (<u>Barber et al. 2023</u>), to about 1,000 in 2022, and to more than 3,000 in 2023 (<u>U.S. CDC 2023d</u>)<sup>2</sup>. *C. auris* primarily infects hospitalized individuals with significant pre-existing medical conditions, but it can also result in asymptomatic colonization of otherwise healthy individuals (<u>U.S. CDC 2023a</u>).

In 2022, the World Health Organization (WHO) published its first fungal priority pathogens list in response to global increases in invasive fungal diseases (<u>WHO 2022</u>). Of the 19 fungal pathogens identified as causing "invasive ... fungal infections for which drug resistance or other treatment and management challenges exist" (<u>WHO 2022</u>, page vii), WHO classified *C. auris* as "critical" (highest priority)<sup>3</sup>. It is thought that both the incidence and geographic range of fungal infections, including *C. auris*, may increase with climate change (<u>WHO 2022</u>; <u>Lockhart et al. 2023</u>; <u>Lyman et al. 2023</u>).

# About the microorganism

*C. auris* is one of more than 150 species of fungi in the *Candida* genus (<u>Kibbler 2018</u>). Although only about 10% of *Candida* species are known to be pathogenic, they are the most common cause of fungal infections in humans (<u>Ahmad and Alfouzan 2021</u>). *C. auris* cells usually grow as single-celled budding yeast, are 2.5 to 5.0 µm in size, and are usually oval or elongated in shape (<u>Sikora et al. 2024</u>) (see **Figure 1**). Six *C. auris* clades<sup>4</sup>, or groups, have been identified (I through VI) and appear to have emerged nearly simultaneously worldwide<sup>5</sup>, with invasive infections linked primarily to Clades I, III, and IV (<u>Ahmad and Alfouzan 2021</u>; <u>Suphavilai et al. 2023</u>). Compared with its close relatives (such as *C. haemulonii*), *C. auris* is more tolerant of high temperatures (surviving in temperatures up to 42°C; Sikora et al. 2024) and high salinity (up to 10% NaCl wt/vol; <u>Welsh et al. 2017</u>), and is able to form more resilient aggregates (<u>Ashkenazi-Hoffnung</u>

<sup>&</sup>lt;sup>1</sup> WHO defines "emerging" diseases as those "that appear in a population for the first time, or that may have existed previously but are rapidly increasing in incidence or geographic range." (<u>WHO n.d.</u>)

<sup>&</sup>lt;sup>2</sup> Candida auris was made <u>nationally notifiable</u> in the U.S. by the CDC in 2018. Current and historical data on *C. auris* cases in the U.S. can be found in the <u>weekly tables for Nationally Notifiable Infectious Diseases and Conditions</u>.

<sup>&</sup>lt;sup>3</sup> Three other fungal pathogens were identified as being in the "critical" group: *Cryptococcus neoformans, Aspergillus fumigatus,* and *Candida albicans* (<u>WHO 2022</u>).

<sup>&</sup>lt;sup>4</sup> A clade is a group of organisms that includes a single ancestor and all the descendants of that ancestor (<u>Baum</u> 2008).

<sup>&</sup>lt;sup>5</sup> This article provides information on the theories related to the simultaneous emergence of multiple *C. auris* clades: <u>https://www.bbc.com/future/article/20230331-the-mystery-origins-of-candida-auris</u>

and Rosenberg Danziger 2023). C. auris often demonstrates resistance to one or more classes of common antifungal medications, with some isolates resistant to all three classes (U.S. CDC <u>2023a</u>). The ability of *C. auris* to form biofilms on human skin niches and implanted medical devices may contribute to its persistence and spread in the hospital environment and resistance to antifungals and desiccation (Horton and Nett 2020; Corzo-Leon et al. 2022). Its temperature and salinity tolerance, and ability to form resilient aggregates and biofilms, likely have implications for C. auris persistence in the aquatic environment, too. As described below, viable C. auris has been recovered from wastewater, suggesting it can persist in the aquatic environment.



**Figure 1**. A strain of *Candida auris* cultured in a petri dish at a CDC laboratory (Source: <u>CDC</u>)

# **Disease overview**

**Clinical features:** *C. auris* can cause many different types of potentially life-threatening infections, including: candidemia (bloodstream infection), myocarditis (inflammation of the heart muscle), urinary tract infection, surgical wound infection, burn infection, skin abscess, otitis (ear infection), meningitis (infection of the fluid and membranes surrounding the brain and spinal cord), and bone infection (<u>Weber et al. 2023</u>; <u>Sikora et al. 2024</u>). The symptoms of *C. auris* infection vary according to the location on the body but can be similar to those caused by bacterial infections, including fever, chills, and pain (<u>U.S. CDC 2023a</u>).

**Colonization**: Individuals can have *C. auris* on their body—usually on their skin—even if they don't have an active infection (<u>U.S. CDC 2023a</u>). An individual is said to be "colonized" if they have *C. auris* on their body but don't show signs of illness. *C. auris* colonization can be transient (such as on the hands of healthcare providers; <u>Weber et al.</u> 2023) or can persist for a long time, perhaps even indefinitely (<u>Biswal et al. 2017</u>). Colonization may not warrant antifungal treatment in the absence of an infection (<u>U.S. CDC 2023a</u>).

**Transmission**: In general, pathogen transmission can be either *direct* (such as direct contact or droplet spread) or *indirect* (such as vehicle/fomite-borne, vector-borne, or airborne). For *C. auris*, both direct and indirect modes are thought to play a role in transmission, based on information derived from investigations of outbreaks, most of which have occurred in hospitals (Weber et al. 2023). Direct patient-to-patient contact is a common form of *C. auris* transmission and can occur from either colonized or infected patients. Indirect transmission of *C. auris* is thought to occur mostly through environmental contamination (Weber et al. 2019). *C. auris* contamination has been noted on bed rails, bed pans, mattresses, linens, pillows, furniture, door handles, flooring, walls, radiators, and windowsills in hospital rooms of infected individuals, suggesting shedding into the environment (<u>Chakrabarti and Sood 2021</u>). <u>Schelenz et al. (2016)</u> described transmission of *C. auris* to an individual occupying a room that previously housed

someone infected with *C. auris*—despite the room being decontaminated between occupants. Indirect transmission through shared equipment or colonized healthcare provider's hands can also occur (<u>Weber et al. 2023</u>).

**Incubation period**: Two types of incubation periods are relevant to *C. auris*: (1) the time between exposure and colonization, and (2) the time between colonization and infection. Neither are well understood. The time to colonization is thought to be in the range of days to weeks (Sikora et al. 2024), although Alanio et al. (2022) documented a two-month lag between exposure and colonization in one patient. Invasive infections may occur days to months after colonization (Forsberg et al. 2019).

**Diagnosis:** A *C. auris* case is confirmed by a positive culture or a positive result from a validated culture-independent method, such as PCR using the method described in <u>U.S.</u> <u>CDC (2022)</u>. If the positive culture or result came from a swab taken from a site (skin, rectum, or other external body site) for the purposes of screening for *C. auris* colonization, it is considered a *colonization case*. If the positive culture or result came from a volume or result came from a clinical specimen (blood, cerebrospinal fluid, urine) or from a wound or ear drainage collected for the purposes of diagnosing or treating *C. auris*, it is considered a *clinical case* (<u>U.S. CDC 2023b</u>). Colonization and clinical cases are counted separately in the CDC's <u>National Notifiable Diseases Surveillance System</u>.

**Risk groups**: Most healthy people are not at risk of serious *C. auris* infection (<u>U.S. CDC</u> 2023a). Factors that increase an individual's risk include immunocompromised/immunosuppressed status, serious medical conditions that require hospitalization, certain procedures (such as placement of central venous and urinary catheters or ventilators), recent major surgery, exposure to broad spectrum antibiotics and antifungal agents, and admission to an intensive care unit (<u>Ahmad and Alfouzan 2021</u>).

**Mortality**: Mortality rates reported in the literature from *C. auris* infection range from 0% to 72% (<u>Ahmad and Alfouzan 2021</u>). Based on an analysis of 192 *C. auris*-associated hospitalizations between 2017 and 2022, <u>Benedict et al. (2023)</u> estimated an overall mortality rate<sup>6</sup> of 34%. Because individuals infected with *C. auris* often have other serious conditions, it can be challenging to determine the extent to which *C. auris* caused their death (<u>Jeffery-Smith et al. 2018</u>).

# Presence in wastewater

**Shedding**: *C. auris* has been detected by positive culture in human urine and feces, as well as in skin swabs (<u>U.S. CDC 2017</u>; <u>Welsh et al. 2017</u>). The relative importance of skin, urine, and feces for shedding into wastewater is unknown, however. In mice infected with *C. auris*, viable fungus was shed in both urine and feces, with concentrations in feces higher than in urine by two to three orders of magnitude (10<sup>2</sup> colony forming units [CFU]/µL of urine vs. 10<sup>4</sup> to 10<sup>5</sup> CFU/µL in feces) (<u>Torres et al. 2020</u>). It is unclear whether a similar shedding differential would apply to humans.

<sup>&</sup>lt;sup>6</sup> Note that this is a "crude" mortality rate. Also known as "overall" or "unadjusted" mortality, crude mortality is overall mortality for a population. It is distinct from adjusted mortality, which is a mortality rate calculated for a specific age, race, or other demographic group or other subset within the group (<u>Celentano et al. 2019</u>).

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**Detection and quantification**: Both culture-based and culture-independent methods have been used to detect and quantify *C. auris* in wastewater. <u>Rossi et al. (2023)</u> developed a culture-based method for isolation of *C. auris* from wastewater, as did <u>Babler et al. (2023)</u>. <u>Barber et al. (2023)</u> used qPCR based on the CDC clinical *C. auris* assay (<u>U.S. CDC 2022</u>) for detection and quantification, while <u>Babler et al. (2023)</u> also used qPCR, but with a different set of primers and probes. The largest dataset for *C. auris* concentrations in wastewater is available from <u>WastewaterSCAN (2024)</u>, which relies on a similar PCR-based approach to detect *C. auris* DNA. As of March 2024, this dataset contains >16,000 results from 194 water resource recovery facilities (WRRFs), with positive PCR detections ranging from  $4.9 \times 10^2$  to  $1.5 \times 10^6$  gene copies per gram (dry weight) of wastewater solids (influent or primary). Most (>98%) of the wastewater samples analyzed by WastewaterSCAN, however, did not contain detectable *C. auris* DNA, but samples from certain locations yielded an intermittent positive signal. Although viable *C. auris* has been cultured directly from wastewater, the detection of *C. auris* DNA with PCR-based methods doesn't necessarily mean that infective fungi are present.

**Survival and viability**: There are multiple reports of *C. auris* persistence in the environment. Viable *C. auris* was shown to survive on moist (Petri dish with non-nutrient agar) or dry (steel disk) surfaces for seven days (<u>Piedrahita et al. 2017</u>), on plastic healthcare surfaces for 14 days (<u>Welsh et al. 2017</u>), and on dry plastic surfaces for 14 days (<u>Short et al. 2019</u>). Based on the findings of environmental persistence of viable *C. auris* in these studies, and the detection of *C. auris* from wastewater using culture-based methods as described above, it is reasonable to assume that infective *C. auris* could survive the typical range of residence times (hours to days) in collection systems.

**Fate in treatment processes**: Barber et al. (2023) found that primary clarification achieved ~1-log reduction in *C. auris* DNA concentrations, presumably due to the relatively large size of the organism. However, DNA from fungal species, including *Candida* species, has been identified in bioaerosols generated during wastewater treatment (Han et al. 2020) and in wastewater effluent (Kokkinos et al. 2015; Assress et al. 2019). The relevance of this in terms of *C. auris* infectivity is unknown. In the study by Kokkinos et al. (2015), culture-based methods were used to identify *Candida* spp. in the treated effluent from three WRRFs with average daily flows ranging from 2,000 to 5,500 m<sup>3</sup>/day (0.53 to 1.5 million gallons per day). All three facilities included a chlorination step for final disinfection. *C. auris* is known to produce biofilm, which may play a role in the persistence of viable cells through treatment (Short et al. 2019). There is some evidence that ultraviolet (UV) radiation, particularly short-wave UV or UV-C, can prevent biofilm formation by, or reduce the viability of, *C. auris*. For example, Mariita et al. (2022) found that disinfection of aqueous solutions with 20 mJ per cm<sup>2</sup> of 267 and 270 nm UV achieved  $\geq$  3-log reduction in *C. auris* colony counts<sup>7</sup>.

#### Suitability for wastewater-based surveillance

As discussed above, one of the notable characteristics of *C. auris* is its persistence in the environment (<u>Weber et al. 2023</u>). Not surprisingly, then, initial research demonstrated that *C. auris* can be cultured from wastewater from a hospital with patients known to be infected or colonized with *C. auris* (<u>Babler et al. 2023</u>). Moreover, <u>Rossi et al. (2023</u>)

<sup>&</sup>lt;sup>7</sup> The typical dose for UV disinfection of treated wastewater is 50 to 100 mJ per cm<sup>2</sup> (Metcalf & Eddy | AECOM 2013).

demonstrated that viable *C. auris* can be recovered from community-scale wastewater using culture-based methods, and <u>Barber et al. (2023</u>) showed that *C. auris* DNA can be detected in those same samples with qPCR. Both studies sampled community wastewater from sewersheds containing healthcare facilities with ongoing outbreaks. However, <u>Barber et al. (2023</u>) found that wastewater collected from nearby sewersheds with no known confirmed cases also contained *C. auris* DNA, albeit at lower frequency. The results of these research efforts suggest that WBS may be valuable for tracking *C. auris*, although the background environmental occurrence of *C. auris*—which may complicate interpretation of WBS data—is unknown. Vigilant surveillance of this rapidly evolving, highly transmissible fungus is of paramount importance to predicting outbreaks, preventing global spread and emergence of newer pan-resistant strains.

Due to its public health significance and amenability to wastewater-based detection, *C. auris* is one of the core pathogen targets included in the NWSS Panel 1.0<sup>8</sup> (<u>Kirby 2023</u>). Assays for new Panel 1.0 targets, including *C. auris*, are being validated by the NWSS Centers of Excellence. Ultimately, NWSS *C. auris* wastewater data will be shared with the public <u>on the NWSS dashboard</u>. Utilities should coordinate with their public health partners to understand if and when wastewater testing in their community will be expanded to include *C. auris*.

# Preventing infection from wastewater

**Routes of exposure**: Based on the types of infections caused by *C. auris*, skin contact directly with wastewater and with objects contaminated with wastewater are probably the most likely routes of exposure to *C. auris* for wastewater professionals in systems in which *C. auris* is present. It is important to keep in mind that most surfaces near wastewater collection and treatment equipment are likely to be contaminated with wastewater, and the presence of abrasions, open wounds, and punctures may increase the risk of transmission of any pathogen, including *C. auris*. In addition to skin contact, ingestion (via wastewater splashes or pathogens on contaminated hands) and inhalation (via breathing aerosols generated during wastewater treatment or direct person-to-person contact) can be important routes of exposure for other wastewater pathogens (WEF 2020). However, because *C. auris* is not known to cause gastroenteritis or pneumonia, inhalation and ingestion are likely not as important exposure routes as skin contact.

**Infection prevention**: The worker safety recommendations of the WEF Blue-Ribbon Panel (<u>WEF 2020</u>) remain relevant for wastewater workers for *C. auris* and other infective agents in wastewater. These recommendations are consistent with the CDC's guidance for reducing health risks to workers handling human waste or sewage (<u>U.S. CDC 2023c</u>). While there are no vaccines against *C. auris*, understanding the effectiveness of disinfectant products against *C. auris*, conducting job safety assessments, practicing good hygiene, and using personal protective equipment all play a role in preventing infection. Each of these is described in more detail below.

<sup>&</sup>lt;sup>8</sup> The other NWSS Panel 1.0 core pathogens include: SARS-CoV-2, influenza A and B, respiratory syncytial virus, adenovirus 40/41, shiga toxin-producing *E. coli*, *Campylobacter*, norovirus, and mpox virus (specifically non-variola orthopoxvirus)—as well as four antibiotic resistance genes and laboratory analysis process controls such as positive and negative controls (<u>Kirby 2023</u>).

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#### Disinfectant products

- Research on the effectiveness of disinfectants used in healthcare facilities demonstrated that formulations with chlorine (with 0.63 to 0.65% sodium hypochlorite), peracetic acid (with 1,200 parts per million peracetic acid), and improved<sup>9</sup> hydrogen peroxide (with 0.5% to 4.0% hydrogen peroxide) were all effective (i.e., achieved > 5-log reduction after the contact time recommended by the manufacturer) against *C. auris* (Haq et al. 2024). However, quaternary-ammonia disinfectants were not effective against *C. auris*, and therefore should not be used for disinfection of surfaces exposed to the pathogen.
- In addition, dilute bleach (1:10 dilution of 5.25% sodium hypochlorite) and isopropyl alcohol (70%) were shown to result in a 4.1-log and 3.8-log reduction, respectively, of *C. auris* after 1 minute of contact time (<u>Rutala et al. 2019</u>).
- Disinfectants on <u>EPA's "List P"</u> are effective against *C. auris* contamination on surfaces (<u>U.S. EPA 2023</u>). This list includes various readily available products with sodium hypochlorite, hydrogen peroxide, isopropyl alcohol, and other common disinfectants as active ingredients.

#### Job safety assessments (JSAs)

- JSAs should follow the protocols outlined in <u>WEF (2020</u>). Please email <u>nwbe@wef.org</u> for JSA templates if needed.
- In addition, utilities should coordinate with local public health agencies and healthcare institutions to understand the risk of *C. auris* in their wastewater to inform their JSAs.

#### Hygiene

- After handling wastewater or touching surfaces potentially contaminated with wastewater, hands should be washed with soap and water, followed by the use of an alcohol-based hand sanitizer (ABHS). Studies have demonstrated that ABHS formulations with 70% alcohol (either isopropyl or ethyl) are effective against *C. auris* (Rutala et al. 2019). It is worth noting that, as explained in Weber et al. (2023), "[w]earing gloves is not a substitute for hand hygiene".
- While working with wastewater and near surfaces potentially contaminated with wastewater, avoid touching the face, mouth, eyes, nose, or open sores or cuts, and do not smoke or chew tobacco or gum. In addition, sores and cuts should be covered with water-resistant band aids.

#### Personal protective equipment (PPE)

- PPE should be selected to prevent contact with wastewater, either directly (through splashes, contact transfer, or whole-body contact) or indirectly (through touching contaminated surfaces).
- Appropriate PPE may include gloves, boots, coveralls (such as Tyvek suits), face shields, and safety glasses/goggles (<u>LeChevallier et al. 2020</u>).
- Care should also be taken to prevent cuts or punctures when handling wastewater through the use of durable gloves. Gloves should be changed when torn or heavily contaminated.

<sup>&</sup>lt;sup>9</sup> "Improved" hydrogen peroxide, trademarked as "Accelerated Hydrogen Peroxide", contains additives, such as organic acids and surfactants, to improve its antimicrobial effectiveness: <u>https://en.wikipedia.org/wiki/Accelerated\_hydrogen\_peroxide</u>

- Proper procedures for donning (putting on) and doffing (removing) PPE to minimize pathogen exposure should be followed. Box 1 provides an example of donning and doffing gloves, boots, disposable coveralls, and a face shield or safety glasses/goggles, while Box 2 provides steps on how to remove gloves when not wearing a disposable coverall.
- Reusable PPE, such as boots, face shields and goggles, should be cleaned after each use. Visibly soiled PPE can be cleaned with soap and water, followed by a dilute bleach solution (1 part 5.25% sodium hypochlorite with 9 parts water) or a disinfectant on <u>EPA's List P</u>. For PPE that is not visibly soiled, or not amenable to washing with soap and water, a disinfectant on <u>EPA's List P</u> can be used. In addition, PPE should also be inspected before each use.

# Box 1: Donning and doffing gloves, boots, disposable coveralls, and a face shield or safety glasses/goggles

#### Donning

- Wash hands with soap and water, followed by use of ABHS
- Remove shoes and tuck trouser legs into socks
- Step into legs of coverall, pull on boots, and place coverall legs over boots
- Pull coverall over arms and shoulders
- Put on face shield or glasses/goggles and pull up hood
- Zip up garment
- Put on gloves

#### Doffing

- Unzip coverall to waist and roll back hood without touching the inside of the garment
- Pull first arm out of garment sleeve by pulling with the other arm at your back (see <u>this</u> <u>video</u> for a demonstration), pulling your glove off as you completely remove your first arm from the sleeve (see box for glove removal without a coverall)
- Use your ungloved hand to push the garment off your second arm, only touching the inside of the garment with the ungloved hand, and pull your second arm out of garment, removing your second glove in the process
- Roll garment down body, touching only the inside or the garment with your now ungloved hands, and kick off your boots
- Dispose of the garment, again, only touching it on the inside with your ungloved hands
- Wash hands with soap and water, followed by use of ABHS
- Remove face shield or glasses/goggles from the back by lifting the head band (face shield) or earpieces (glasses/goggles), and discard or clean

#### Box 2: Removing gloves when not wearing a disposable coverall

- Remove one glove at a time
- Use one gloved hand to grasp the palm area of the other gloved hand and peel off the glove
- Hold removed glove in gloved hand
- Slide fingers of ungloved hand under remaining glove at wrist and peel off second glove over first glove
- Discard gloves
- Wash hands with soap and water, followed by the use of ABHS

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# **Other Resources**

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