Magnitude of the Source: Part Two

How Candida Auris and other Pathogens are Center Stage in the Fight Against Infections

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Martie Moore is an executive with over thirty-five years of experience with research and focus on quality, patient safety and advancing health delivery systems.

Moore has served as a Chief Nursing Officer at a Corporate, System and Magnet facility level with focus on advancing implementation science, cultural transformation, patient safety and elevating organizational performance through quality, system thinking and putting knowledge into action.

Objectives

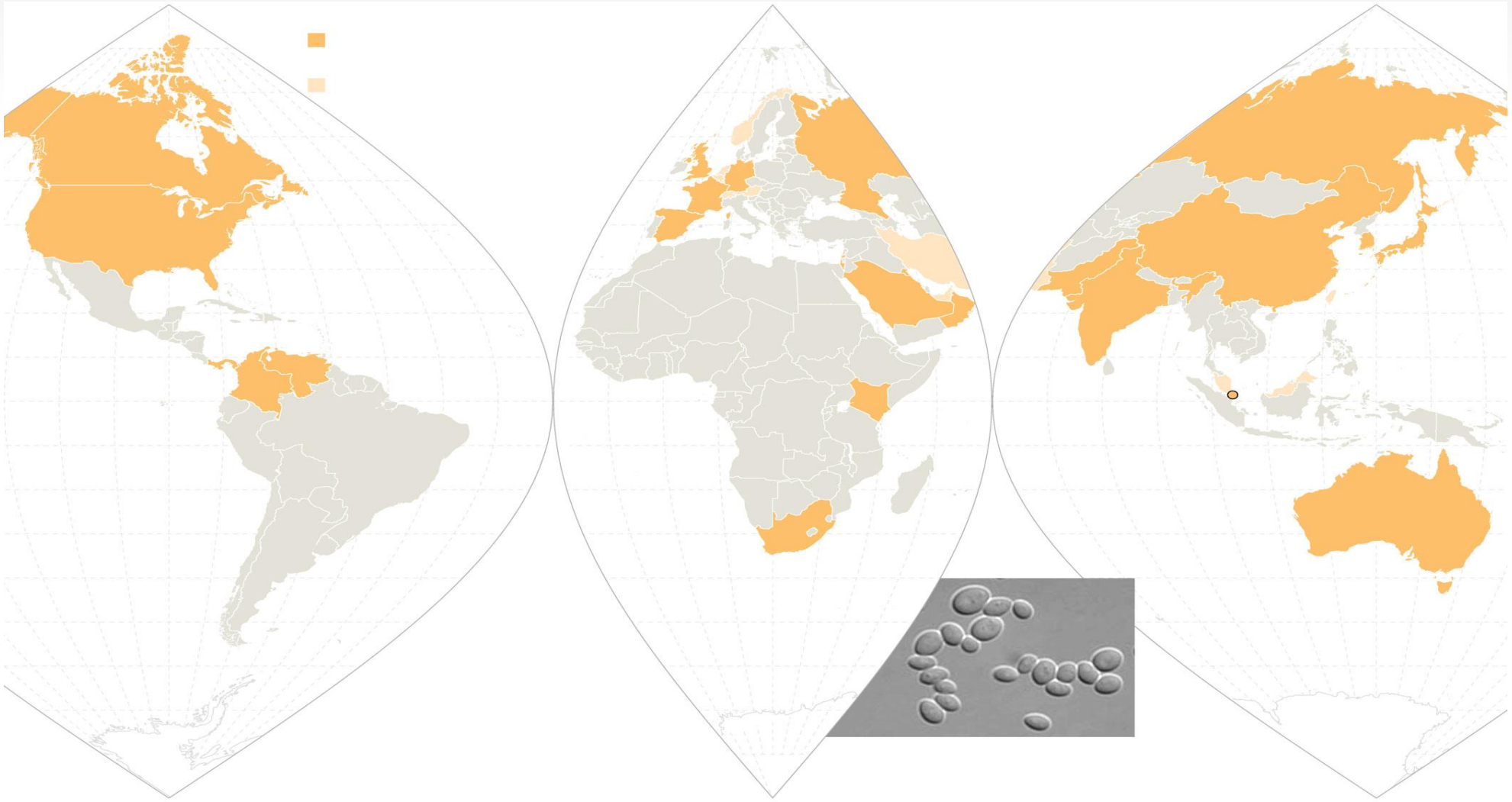
Describe the origins, clade and potential theories of the emergence of *Candida auris.*

Explain how *Candida auris* thrives and survives in healthcare and community settings.

Discuss the role that acid mantel plays in cell reproduction and defending the cells against pathogens.

Explain how low acidic pH inhibits the growth and biofilm production of *Candida auris*.

Challenges Around The Globe



Breaking News
Candida Auris Has Gone Mainstream

- *Candida Auris: The Fungus Nobody Wants to Talk About*
- *A Mysterious Infection, Spanning the Globe in a Climate of Secrecy*
- *The Last of Us: fungal infections really can kill – and they're getting more dangerous*
- *Potentially deadly fungus Candida auris is spreading at an alarming rate per CDC*

What Do We Know About Candida Auris

CANDIDA AURIS

HISTORY

First recognized in **2009** in a 70- year- old individual with external otitis in Japan

Retrospective review of strain collections found the earliest known strain back to **1996** in South Korea. This included two bloodstream isolates recovered.

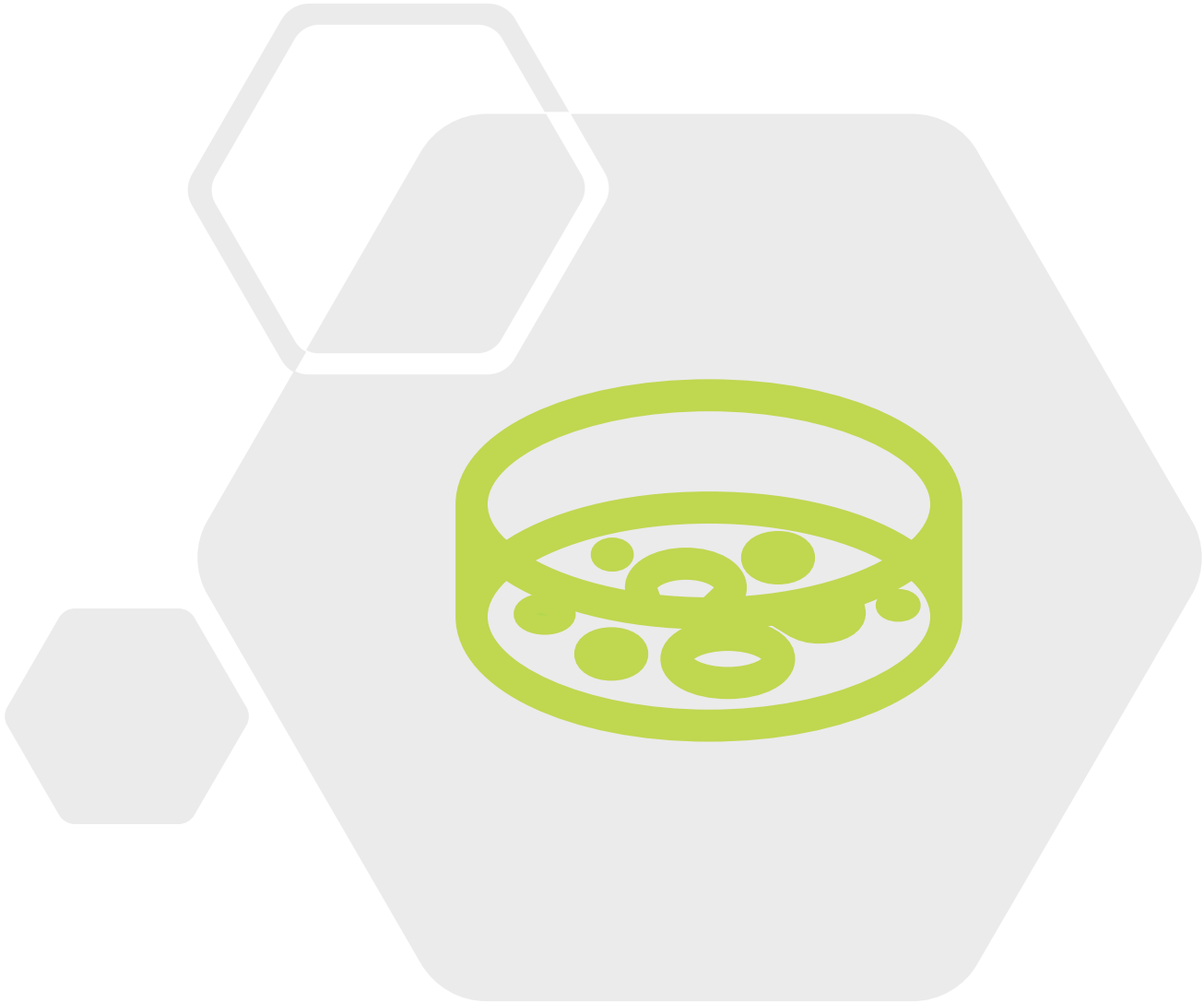
Following the first isolation in Japan, cases have been reported in several countries in **five continent**s. Although uncommon for fungi, *C. auris* has caused outbreaks, **India, United Kingdom, Spain, United States, Venezuela, Colombia, and South Africa.**

As of 2023, C. auris isolates have been identified in most countries except for Antarctic

Understanding Origin: Clade ID

- Genome sequences of *C. auris* isolates were divided into five clades that were separated by tens of thousands of single nucleotide polymorphisms (SNPs):

- **Clade I (South Asian),**
- **Clade II (East Asian),**
- **Clade III (South African),**
- **Clade IV (South American)**
- ***Clade V (Iran)***



It is not known if all had a common ancestor, but some believe yes…

Question Hypothesis

The question remains, if *C. auris* has been part of the human mycobiome for 4000 years? It has possibly had a stealth existence because of inadequacies of diagnostic techniques, lack of knowledge of the skin mycobiome, and absence of colonizing isolates.

C. auris probably existed as a minute fraction of the skin mycobiome and even dispersed to involve nares and external ear. The question remains that if *C. auris*, fully equipped with resistance and virulence genes, was already surviving on human skin for many years in extremely small quantities, why did it suddenly create such a health care havoc?

For this, we propose a possible explanation of antiseptic bias…
Written in the Journal of American Society of Microbiologist

Antiseptic Bias

Alcohol-based antiseptics perform well in the eradication of *C. auris* from skin; however, their use is largely limited to the hands of health care workers as alcohol-based hand sanitizers and rubs.

The body sites of patients are usually cleaned and decolonized using chlorhexidine, and non-alcohol-based antiseptics, which are not as effective against *C. auris* thus providing a growth opportunity for *C. auris* at these sites.

It is noteworthy that while planktonic stages of *C. auris* and *C. albicans* exhibit similar resilience to antiseptics, the biofilms of *C. auris* are much more resilient than those of *C. albicans* or *C. glabrata* to 0.5% chlorhexidine and 3% hydrogen peroxide

C. auris might form biofilms and further replenish other colonizing sites. We believe that this antiseptic bias in the selection of antiseptic and choice of body site in the past decade has caused *C. auris* to emerge in health care settings and not as a community pathogen. ?

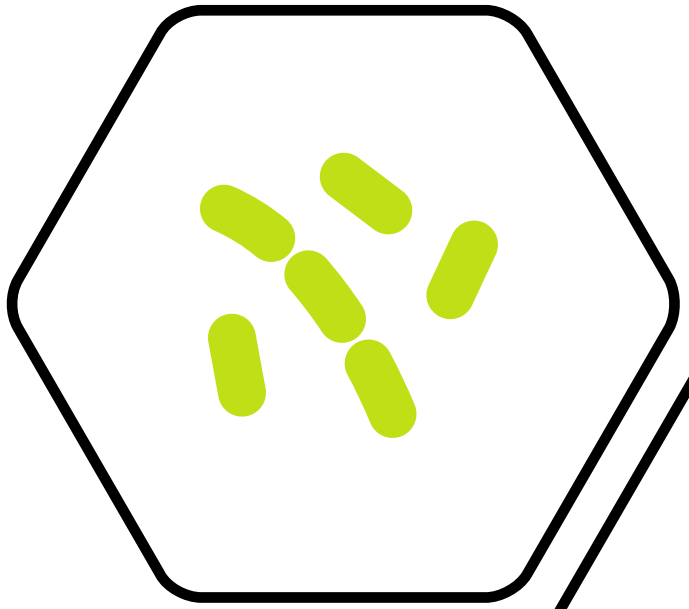
Another Theory

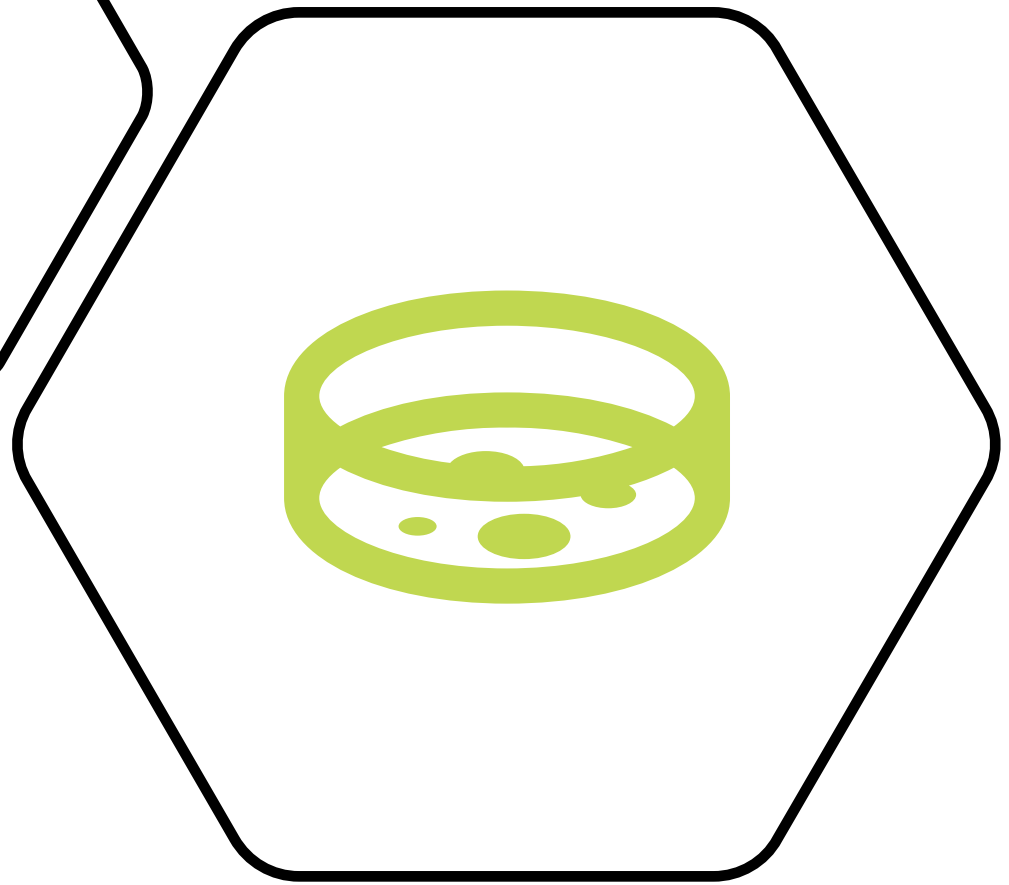
Another theory for the absence of *C. auris* isolates prior to 1996 is that it has only recently become part of the human microbiome.

It has either recently acquired sufficient virulence to cause invasive infections or been newly introduced into human populations in which invasive *Candida* infections can be identified.

For example, recent genetic recombination, hybridization, or other biological changes could potentially increase the organism's transmissibility or virulence.

What allows *C. auris* to survive longer than other *Candida* species





- It grows well at high temperatures. Other Candida species tend to be destroyed at high temperatures.
- It is able to withstand high salt concentrations. This also prolongs its survival.
- It is able to survive on human skin and surfaces , resistant to some disinfectants.
- It is resistant to common antifungal medications, which makes infections difficult to treat.
- It requires special lab methods to identify it as the source of infections.

Candida is a Chamaeleon

C. auris usually forms pink-colored colonies on CHROMagar Candida, and so it is also difficult to distinguish it not only from *C. glabrata* but also from several other *Candida* and yeast species, such as *C. haemulonii* complex members, *Candida kefyr*, *Candida guilliermondii*, *Candida famata*, *Candida conglobata*, and *Candida utilis* which also form pink- colored colonies

Furthermore, *C. auris* also undergoes morphological switching between pink, white, and dark purple colony phenotypes when grown on CHROMagar Candida medium.

A new chromogenic selective medium, CHROMagarTM Candida Plus has been developed recently; *C. auris* forms distinct cream-colored colonies with a blue halo after 48 h of incubation at 37 ◦C and is easily differentiated from other *Candida* species, including *C. haemulonii* complex members

Stress Resistance and Persistence

Welsh RM, Bentz ML, Shams A, Houston H, Lyons A, Rose LJ, Litvintseva AP. Survival, Persistence, and Isolation of the Emerging Multidrug-Resistant Pathogenic Yeast Candida auris on a Plastic Health Care Surface. J Clin Microbiol. 2017 Oct;55(10):

Survive	Thrive	Dominant
• One of the fascinating traits linked to *C. auris*' emergence as a nosocomial pathogen is its ability to persist on hospital surfaces under stringent cleaning protocols.	• Long environmental persistence of *C. auris* is particularly troubling considering the ability of *C. auris* to colonize the skin. • Since humans shed skin cells at an approximant rate of 10^6 particles per hour patients shedding *C. auris* colonized skin cells could contribute to prolonged outbreaks with high transmissibility in health care settings.	• Can *C. auris* form viable but non-culturable cells that persist in hospital environments? • **Studies Indicate: Yes**

Simply said…

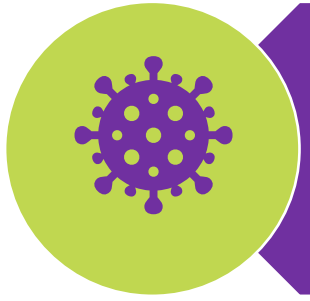
C. auris **has the ability to form 'dry' biofilms and aggregative phenotypes which are not easily eradicated.**

These characteristics promote the person-to-person transmission of infection through direct/indirect contact in healthcare settings rather easily.

A Similar Challenge

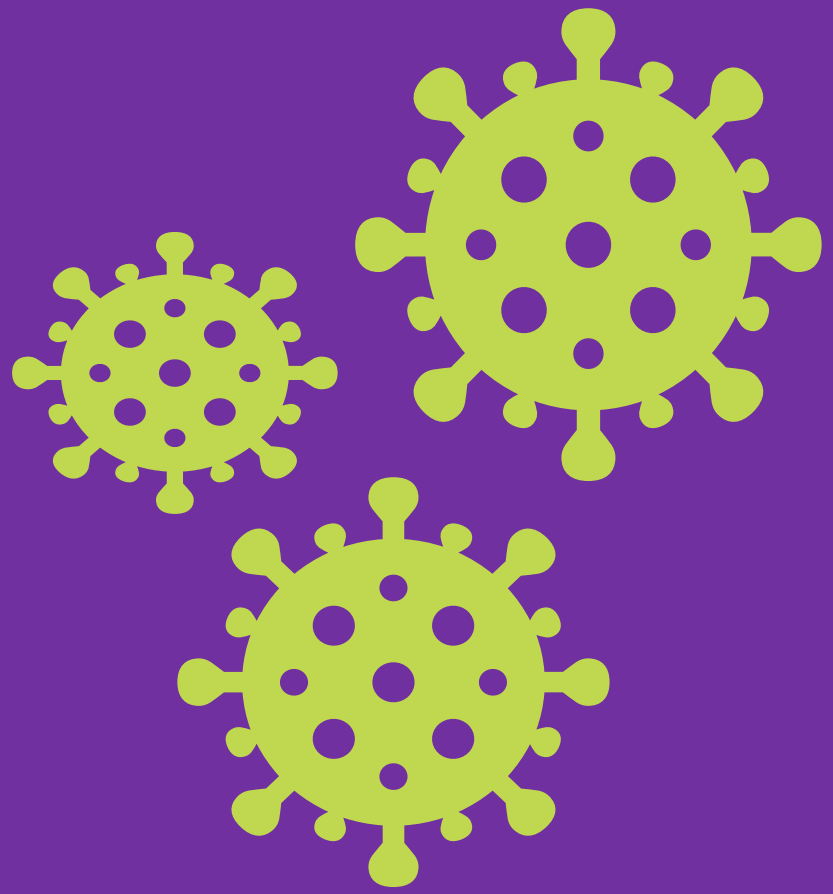
March 2020, Sars-CoV-2 was spreading, I knew we were battling a formidable foe.

I knew time was working against me



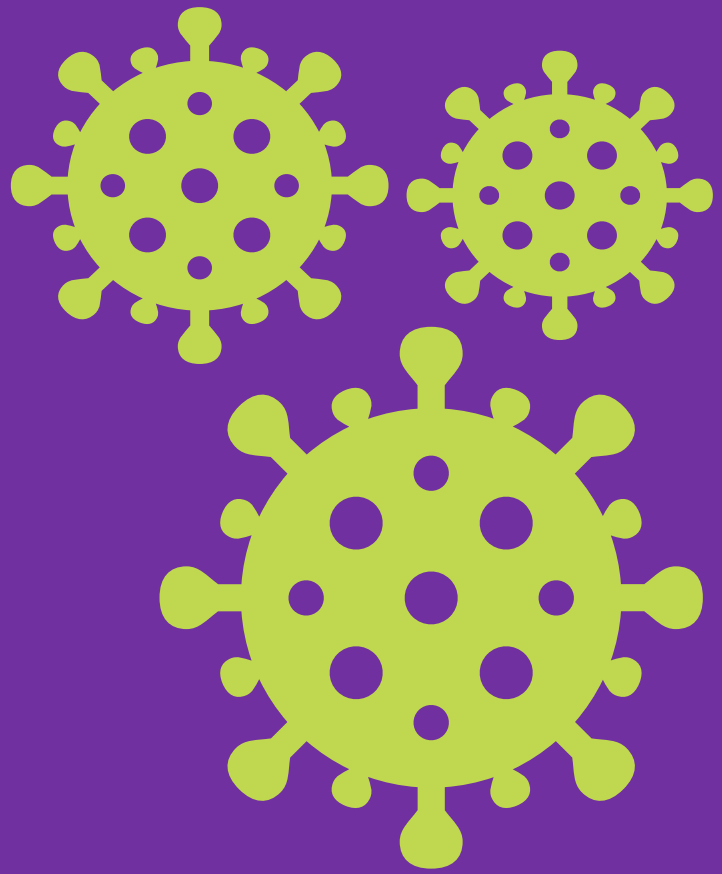
I needed new thinking and actions

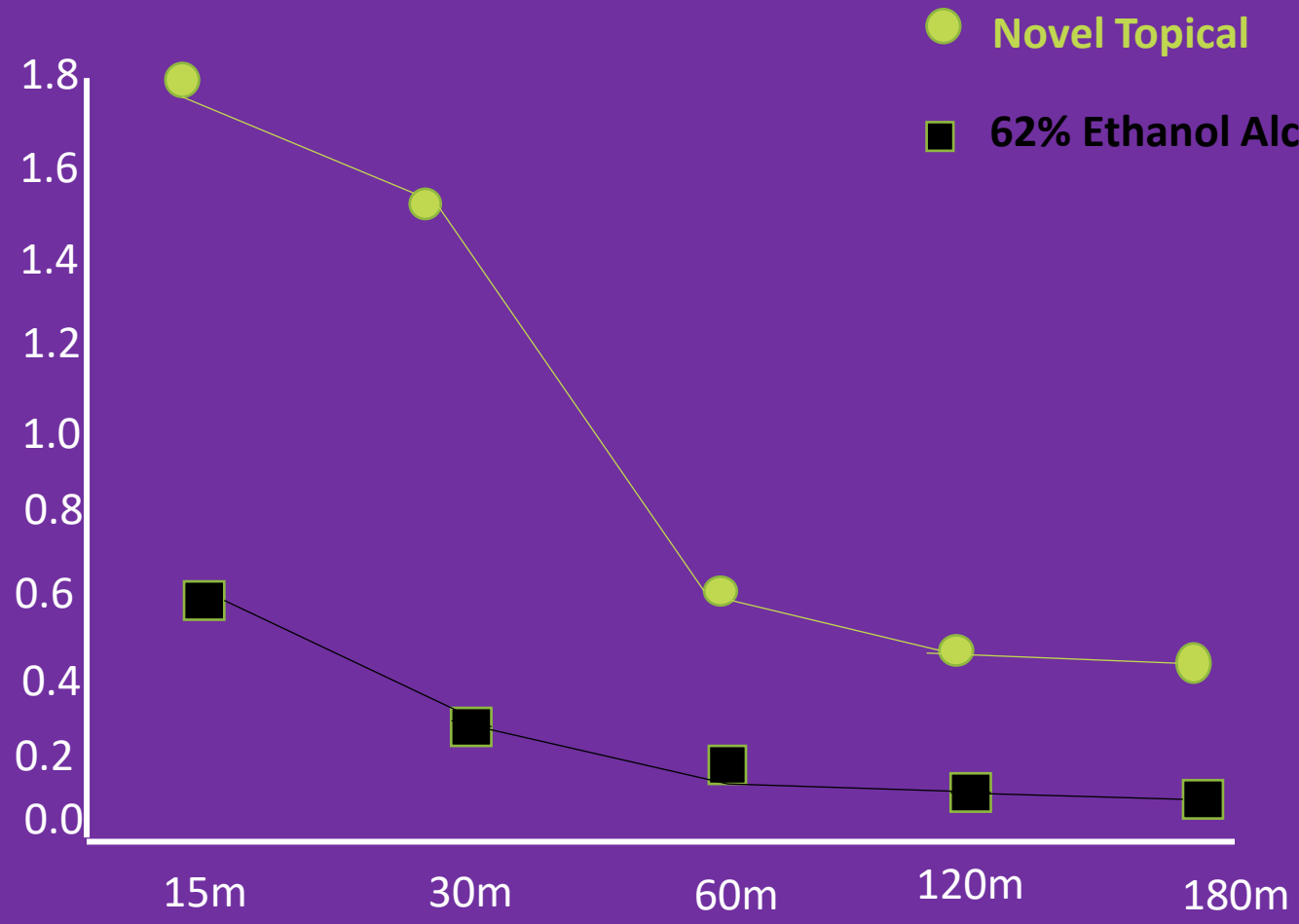
Study 1: Activity of a novel, multimodal, silver-based skin cleanser on coronaviruses, *in-vitro*



Results: At 1 and 30 minutes, there was a 1.75 log reduction (98.22%) in SARS-CoV-2 virus. At 60 minutes, there was a 2.25 log reduction (99.44%) in virus.

Study 2: Another tool in the toolbox: A novel, multimodal, silver and surfactant- based skin cleanser vs. 62% ethanol on the human coronavirus OC43 on human tissue





Antimicrobial Testing

Test Organism	ATCC No.	Initial Inoculation	Percent Reduction
C.albicans	10231	1.1×10^5	>99.9%
M.luteus	49732	1.1×10^5	>99.9%
C.ammoniagenes	6872	1.7×10^5	>99.9%
S.epidermidis	12228	1.3×10^5	>99.9%
S.aureus (MRSA)	33591	1.3×10^5	>99.99%
Acinetobacter baumannii	15308	1.4×10^6	>99.99%
E. faecalis	51575	1.4×10^6	>99.99%
E. coli	8739	1.6×10^6	>99.99%
P. aeruginosa	9027	1.2×10^6	>99.99%
C. difficile	9689	2.4×10^7	>99.99%
Carbapenem resistant E. Coli	A15667	7.8×10^8	>99.9%
Klebsiella pneumoniae	A15666	7.8×10^4	99.3%

Mechanisms of Action

Effective And Safe For Use Head-to-toe, Including The Perineum And Mucosa

pH Acidic Systems:
Inhibits the colonization of pathogens.

- **Key Ingredients:** Citrus Paradisi (Grapefruit) Seed Extract, Cocamidopropyl Betaine and Lauryl Glucoside (low-pH Surfactants).

Surfactant Systems:
Lowering the surface tension on the skin making it increasingly difficult for pathogenic adherence & disruptive to biofilm.

- **Key Ingredients:** Cocamidopropyl Betaine and Lauryl Glucoside (low-pH Surfactants).

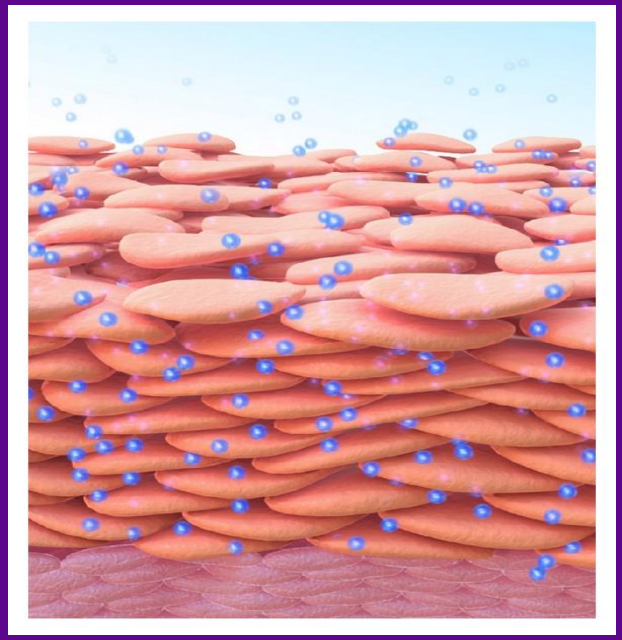
Antimicrobial Preservative Systems:
Safe for use on mucosa with effective ingredients that should not interact with mucosa.

- **Key Ingredients:** Citrus Paradisi (Grapefruit) Seed Extract, Tetrasodium EDTA, Colloidal Silver, Beta Glucan, Aloe Barbadensis Leaf Juice.

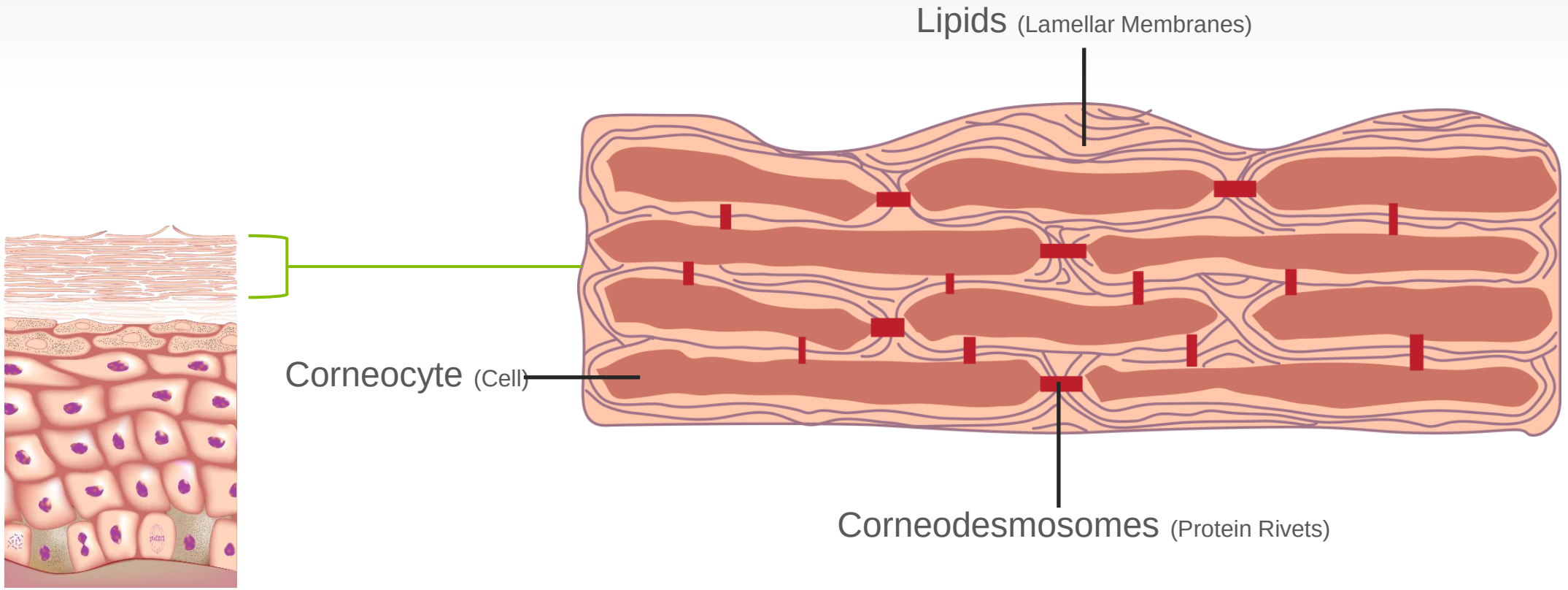
Barrier Systems:
Utilizing skin as the first line of defense, assuring that skin is intact and pliable.

- **Key Ingredients:** PEG/PPG-4/12 Dimethicone, Allantoin, Tocopheryl Acetate, Glycerin.

The First Line of Defense



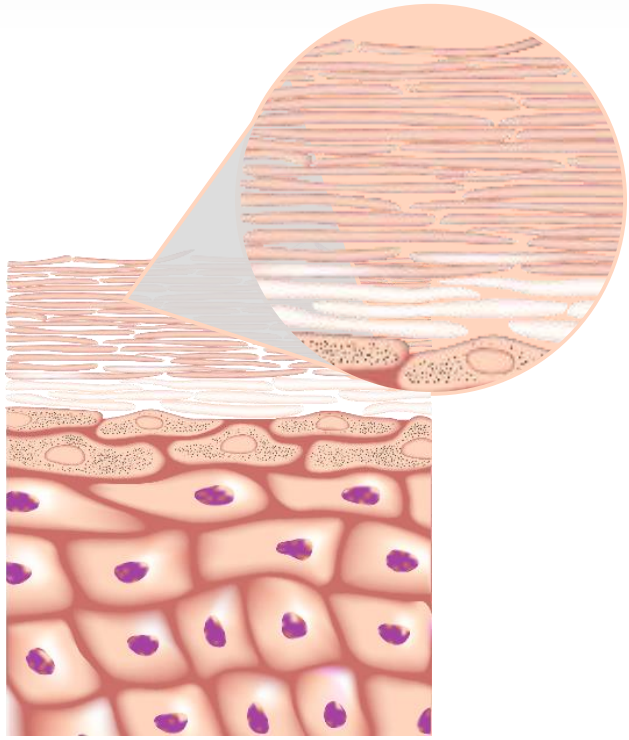
Stratum Corneum: Healthy Skin Barrier for Structural Protection



The stratum corneum, the skin's outermost layer and interface with the outside world is now well recognized as the barrier that prevents unwanted materials from entering, and excessive loss of water from exiting the body.

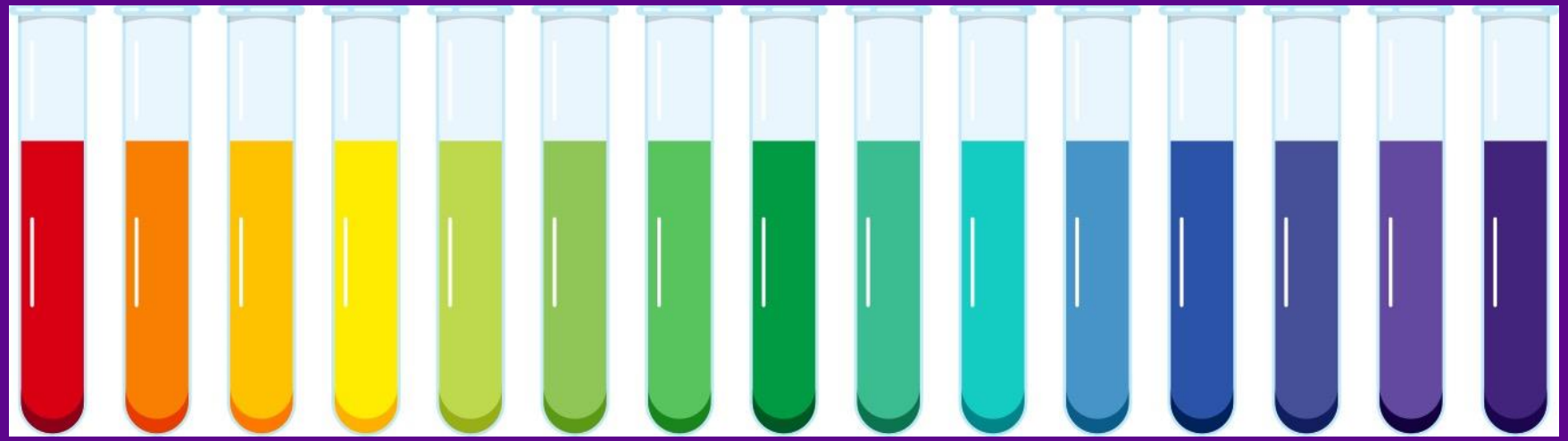
Stratum Corneum

- The nominal low pH environment in the stratum corneum also supports normal structure and development of the stratum corneum lipids, the “mortar” that provides not only additional structural protection against invasion by pathogens.
- It provides perhaps the most critical of all protections, the establishment and maintenance of the “permeability barrier” of the skin.
- It is the unrecognized weapon in the fight against infectious disease.



New Strategy:

Leaning into pH

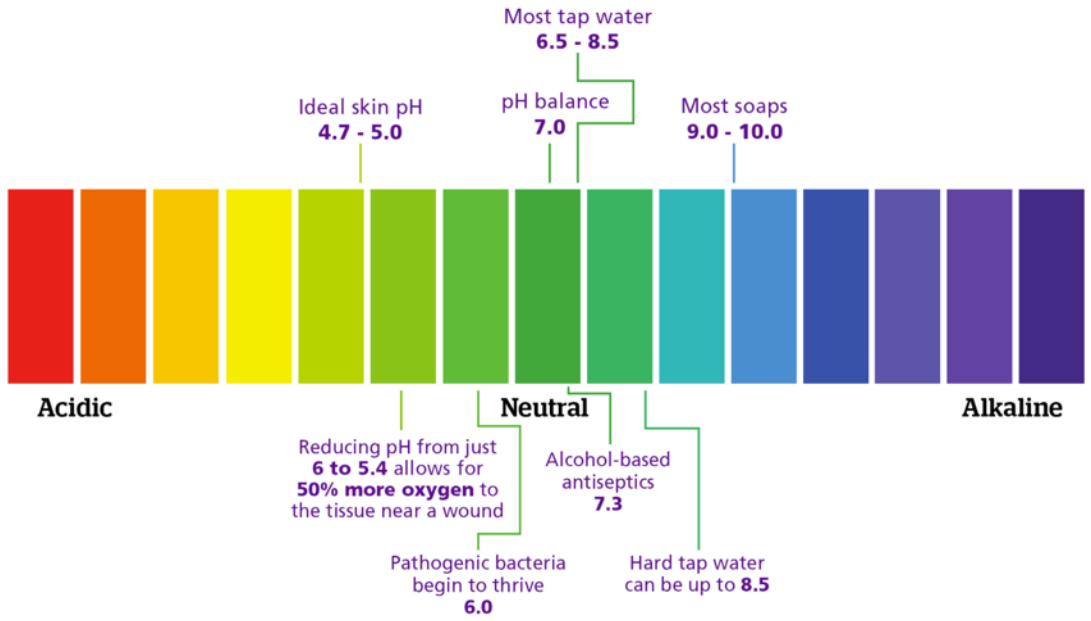


Understanding Skin pH

Healthy skin (mucosa) thrives in an optimal low pH environment. It competes successfully for nutrition and space on the skin surface, protecting against invasion by pathogens and resulting infections.

When pH rises, the normal healthy microbiome suffers, and pathogenic bacteria capitalizes on the change in pH.

pH Acidic Systems:
Inhibits the colonization of pathogens.



Candida Auris Has An Achilles Heel

- *C. auris* is the first human pathogenic fungus to be subject to international health alerts because of its propensity to colonize skin, persist in the hospital environment, cause nosocomial outbreaks, and cause severe disease.

- The ability of *C. auris* to colonize patients to extremely high levels [is certainly novel among known *Candida* spp. The preferential colonization of certain superficial body sites (axilla, groin) but not the intestinal tract fits well with the thermo- and halotolerance of the organism **and its inability to prosper in anaerobic or acidic conditions**

Efficacy: Candida Auris

TABLE 2

Test Product: Broad Spectrum Hygiene Management (4 oz Foam)
Lot Number: 16180-1

Microorganism Species (ATCC #)	Initial Population (CFU/mL)	Exposure Time	Numbers Control Population (CFU/mL)	Post-Exposure Population (CFU/mL)	Log_{10} Reduction	Percent Reduction
Candida auris (AR-Bank #0385)	5.050×10^9	4 hours	5.00×10^7	1.320×10^7	0.5784	73.6000%
		8 hours	5.150×10^7	4.250×10^6	1.0834	91.7476%
		24 hours	4.00×10^7	$< 1.00 \times 10^1$	6.6021	99.9999%
Candida auris (AR-Bank #0389)	5.10×10^9	4 hours	5.950×10^7	9.350×10^6	0.8037	84.2857%
		8 hours	6.250×10^7	3.90×10^5	2.2048	99.3760%
		24 hours	5.750×10^7	$< 1.00 \times 10^1$	6.7597	99.9999%
Candida auris (AR-Bank #0390)	5.950×10^9	4 hours	4.00×10^7	1.4550×10^6	1.4392	96.3625%
		8 hours	5.10×10^7	1.4050×10^4	3.5599	99.9725%
		24 hours	4.80×10^7	$< 1.00 \times 10^1$	6.6812	99.9999%

IN-VITRO TIME-KILL EVALUATION – RESULTS (TABLE 2)

Table 2 presents the initial populations (CFU/mL). The Numbers Control Populations (CFU/mL), and the Post Exposure Populations (CFU/mL) for the challenge microorganism, and the Log_{10} reductions produced by the test ingredients

The Ask of the CDC

Researchers and industry professionals can make a big impact in the fight against *C. auris*. Because *C. auris* emerged so recently.

We still have a lot to learn about this yeast and we need the greater medical and research community involved to figure out the best ways to stop transmission and care for patients with *C. auris*.

There is great need for the following items to combat *C. auris*:

- Rapid diagnostics
- New drugs
- *Decolonization methods*
- Registered, easy-to-use, and effective disinfectants
- *Other tools or protocols for treatment and prevention*

Small Things Start Us In New Ways Of Thinking

– V.S. Naipaul

Further research and review of clinical studies:
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