Microbe of the month

Breaking The Chain of Infection

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APRIL 2023 NEWSLETTER

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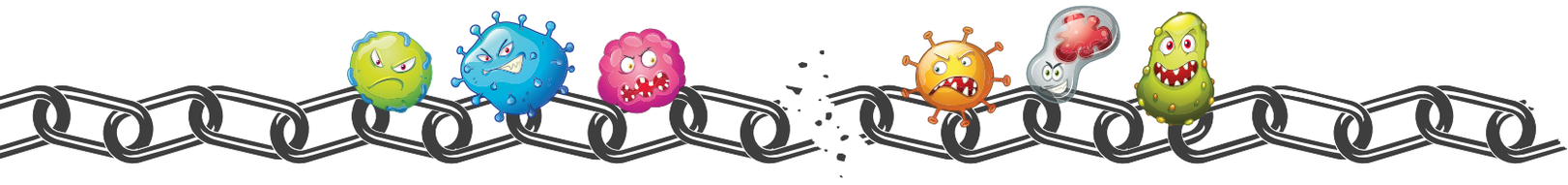


Featured this month:

PROTEUS SPECIES

Consummate opportunistic pathogens!

15-minute read + QUIZ

Hello readers!

Microbe of the Month aims to provide a concise clinical resource, to help you keep up to date about pathogens of importance, in an easy-to-read and understand format. Each issue covers the aetiology (sources) and epidemiology of topical bacteria, viruses, or fungi - their mode/s of transmission and the infections they cause; alerts on any antimicrobial resistance (AMR) capability they may have, and the relevant Infection Prevention and Control measures which should be routinely implemented for the safety of patients and healthcare personnel.

There is a quick quiz at the end of the newsletter to test your grasp of the content – please use this newsletter as a teaching tool in your workplace and start an 'infectious dialogue' about topical issues in infection control!

Proteus species are a member of the **Enterobacterales** (previously termed *Enterobacteriaceae*) – an order of Gram-negative, non-spore forming, facultatively anaerobic, rod-shaped bacteria. Proteus species are present in the human intestinal tract as part of the normal **human intestinal flora**, along with *Escherichia coli* and *Klebsiella* species, of which *E. coli* is the predominant resident.

Refer to Microbe of the Month newsletters for September 2018 and March 2022 for more information on these pathogens.

Proteus is also found in multiple environmental habitats – for example, it can be readily isolated from sewage or polluted soil and water sources. **Proteus *mirabilis* and Proteus *vulgaris* account for most of the Proteus isolates cultured by clinical laboratories.**

These bacteria do not usually pose a problem for healthy individuals, but given a debilitated host, they are notorious for causing catheter-associated urinary infections, wound infections, pneumonia and septicaemia.

Key words: *commensal flora, Gram-negative facultative anaerobe, swarming motility, opportunistic pathogen, healthcare-associated infections (HAIs), sepsis, SIRS.*

FAST FACT!

The name 'Proteus' has its origins in Greek mythology (Homer's Odyssey). Proteus was a prophetic sea god and the son of Poseidon. His special powers came from his ability to assume different shapes and forms, depending on the circumstances. Wikipedia

PATHOGENESIS AND VIRULENCE: Proteus *vulgaris* and Proteus *mirabilis*

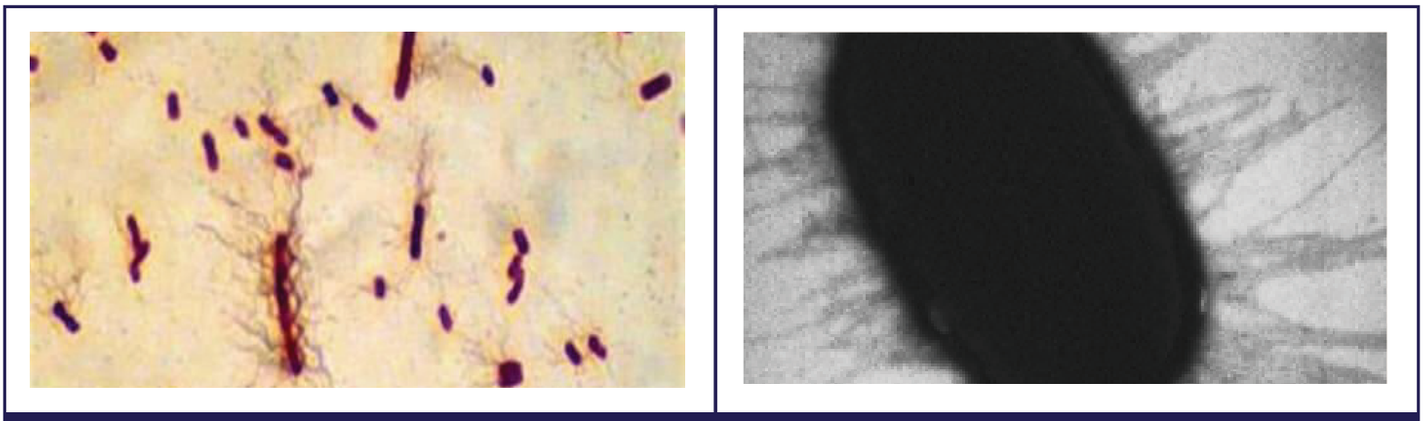
Specific virulence factors have been identified in bacteria.

The first step in the infectious process is adherence of the microbe to host tissue, which enhances the capacity of the organism to produce disease.

Proteus species express large numbers of **pili** (also known as **fimbriae**) and **flagellae** (refer to Figure 1 below).

Fimbria (from the Latin for 'fringe', plural *fimbriae*) is the term used for a short pilus which the bacterium uses to attach itself to a surface. **Pili are associated with increased adhesive qualities and virulence** – transforming the bacteria into elongated rods that move rapidly across the surface of agar plates, resulting in a characteristic "*swarming*" motility. This motility produces a characteristic pattern on growth plates **(refer to Figure 2)** and can overwhelm other microorganisms which are present.[1]

Figure 1



Scanning electron microscopy image of Proteus *vulgaris*.
Note the flagellae used for motility and swarming, while the tiny hair-like projections (pili or fimbriae) are used for adhesion to tissues and for biofilm formation.

Figure 2

When two different strains of P. *mirabilis* swarm on the same blood agar plate, a visible demarcation forms at the intersection – this is known as a *'Dienes line'*.

These striking concentric rings are formed during intermittent and repeated periods of swarming, multiplication and growth.

The 'Dienes phenomenon' is useful for differentiating between strains of Proteus for epidemiological studies.[1]

MODES OF TRANSMISSION

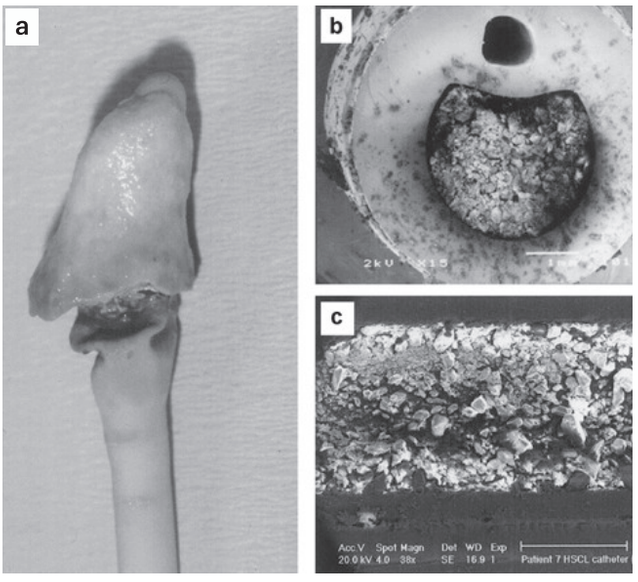
P. *vulgaris* and P. *mirabilis* are mainly spread via **contact transmission** ('direct' and 'indirect contact'; i.e., through contact with unwashed hands, breaches in aseptic technique or contaminated equipment and surfaces). Less commonly, these opportunistic pathogens may also be ingested via contaminated foodstuffs.[2]

THE SPECTRUM OF INFECTIONS CAUSED BY Proteus species [2,3]

Complicated urinary infection:

- Patients may present with **urethritis, cystitis, prostatitis or pyelonephritis**. Chronic, recurring kidney stones may also be an indication of chronic infection.
- Because Proteus is a bowel commensal (part of the natural flora), it gains access to the urinary tract either via the perineum (in females) or contamination of urinary catheters / instrumentation, during breaches in aseptic technique.
- Individuals with multiple prior episodes of urinary tract infection (UTI), multiple courses of antibiotic therapy, urinary tract obstruction, or infection developing after urinary instrumentation or catheterisation frequently become infected with Proteus bacteria.
- Signs and symptoms are usually sudden in onset, and include dysuria, increased frequency / passing small volumes of cloudy urine, urgency, suprapubic pain, back pain, concentrated appearance and haematuria. (Note: These symptoms may not be present if the patient has an indwelling catheter.)
- **Confusion, hypotension and pyrexia may be a sign of bacteraemia and impending sepsis.**
- **UTIs are the second most common infection responsible for hospital admission in long-term care residents (after pneumonia).**
- **Bacteriuria occurs in 10-15% of hospitalised patients with indwelling catheters** (the risk for infection is 3-5% per day of catheterisation).
- Interestingly, in the neonatal population, UTIs are more common in males than females – this is due to congenital abnormalities which are seen more often in male infants.
- **Failure to treat a complicated urinary tract infection, or a delay in treatment, can result in sepsis and SIRS (systemic inflammatory response syndrome), which carries a mortality rate of 20-50%.**

Figure 3



Examples of crystalline biofilms on blocked catheters removed from patients with Proteus-related urinary infections.

(a) An indwelling suprapubic catheter removed after 6 months.

(b) Cross-section of a silicone catheter in situ for 8 weeks.

(c) A longitudinal section of a silver/hydrogel-coated latex catheter which blocked after 11 days in situ.

Large struvite (or 'staghorn') kidney stone caused by chronic urinary infection with Proteus *mirabilis*.

WOUND INFECTION:

- **Proteus species thrive in moisture; therefore, venous stasis ulcers, stage 2-4 pressure injuries and deep burn wounds are vulnerable to infection if exudate levels are not actively managed.**
- **Continuous biofilm formation and elevated pro-inflammatory cytokines in the exudate** (e.g., bacterial exotoxins and MMPs) **disrupt the delicate balance of granulation and repair, leading to wound breakdown.**
- Dressings for moderate to highly exuding wounds should have proven fluid handling capacity, be hydroconductive (promote the vertical 'wicking' of exudate) and ideally, be able to retain the exudate within the dressing even when under compression.
- Dressings which can sequester (contain or isolate) microorganisms and harmful proteases away from the wound bed are useful to hinder the cyclical inflammatory process, which delays healing.

Figure 4

Chronic and heavily exuding wounds (such as venous stasis ulcers and full thickness burns) are prone to infection with P. *vulgaris* and P. *mirabilis*.

PRACTICE POINTS FOR INFECTION PREVENTION

- 'Dipstick' urinalysis is a valuable patient screening tool and may pick up an asymptomatic urinary infection.
- The pH of healthy urine should be acidic; however, once inside the bladder, Proteus species hydrolyse (break down) urea in the urine to ammonia, making the urine alkaline.
- An alkaline pH (e.g., 7.1-9.0) and the odour of 'rotten eggs' should trigger an alert for possible urinary tract infection with Proteus species.
- An undiagnosed urinary infection may be a cause of delayed wound healing or an unexpected deterioration in a previously healing wound.
- Wound cleansing with a topical antiseptic such as hypochlorous acid is useful under these circumstances to disrupt the microbial biofilm and promote a more acidic wound environment, which is less conducive to the growth and multiplication of faecal species.
- In conjunction with an antimicrobial wound cleanser, first-line topical antimicrobial dressings (e.g., DACC™-coated, PHMB, cadexomer iodine or medical-grade Manuka honey) should be used to control the wound bioburden.

FAST FACT!

Proteus *vulgaris* produces the gas hydrogen sulfide (H_2S) which gives off a 'fishy' odour or that of rotten eggs! [4]

TREATMENT and ANTIMICROBIAL STEWARDSHIP (AMS)

Cultures with susceptibility data are recommended to guide antimicrobial therapy.

Proteus species are naturally resistant to antibiotics, such as benzylpenicillin, oxacillin, tetracycline and the macrolides, and acquire resistance to ampicillin through the production of plasmid mediated ***beta-lactamases*** – enzymes which destroy the structure of penicillin-based antibiotics.

Proteus *vulgaris* is inherently resistant to polymyxins (colistin), nitrofurantoin, tigecycline and tetracycline. Inducible beta-lactamase production occurs in at least 30% of P. *vulgaris* strains, making them resistant to ampicillin and first-generation cephalosporins as well. Based on antibiotic resistance data, trimethoprim or cotrimoxazole may no longer be viable treatment options for P. *mirabilis* infections. Quinolone resistance is also increasing, and P. *mirabilis* is almost always resistant to nitrofurantoin, tetracycline and polymyxins. The most appropriate treatment may be amoxycillin with clavulanate (Augmentin®), piperacillin/tazobactam, aminoglycosides, carbapenems (except imipenem), and third generation cephalosporins.

The use of third generation cephalosporins should be restricted as part of an antimicrobial stewardship (AMS) programme, to reduce selective pressure leading to mutations which may contribute to ESBL (extended spectrum beta-lactamase) production.

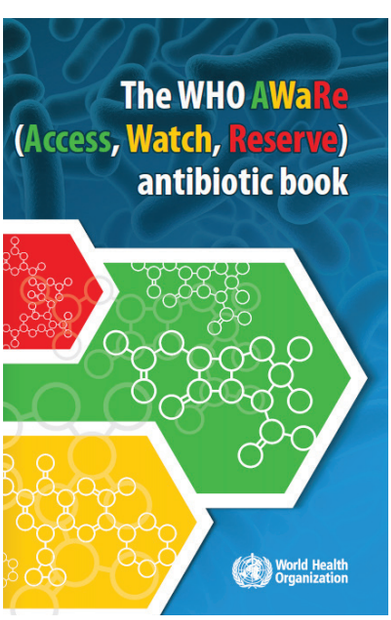
Currently, imipenem, fourth generation cephalosporins, aminoglycosides, TMP/SMZ (trimethoprim- sulfamethoxazole) and quinolones have good activity.[3,5,6]

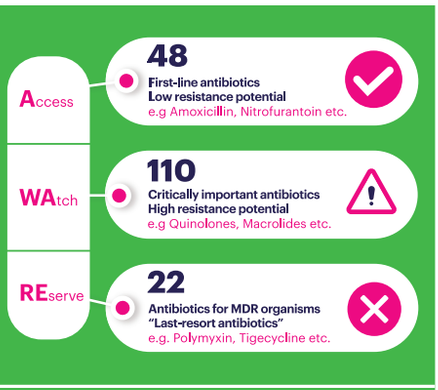
For complicated UTIs in hospitalised patients or individuals with long-term urinary catheters, it is important to consider whether the isolate is clinically significant. *Isolates which are not accompanied by pyuria or symptoms should not be treated.* [3]

In general, complicated urinary infections are treated with intravenous agents until fever has resolved. **In the case of recalcitrant urinary infections, consultation with a medical microbiologist, removal of the urinary catheter, and referral to a specialist urologist is usually necessary.** [2,3]

BREAKING NEWS

1. The World Health Organisation (WHO) has published **The WHO AWaRe (Access, Watch, Reserve) Antibiotic Book** as an adjunct to WHO's Essential Medicines List (EML). This comprehensive document provides concise, evidence-based guidance for more than 30 of the most common clinical infections in children and adults in both primary healthcare and hospital settings.[5]





The AWaRe system groups the hundreds of different antibiotics used globally into three simple categories – '**Access, Watch and Reserve**' – based on their clinical importance and the risk of their use promoting resistance. Clear guidance is provided on the choice of antibiotic, formulation, dose and duration for essential antibiotics for hospital and primary healthcare settings, including guidance on when not to use antibiotics.[5]

2. KZN Specialist Network Antimicrobial Stewardship Initiative [6]

Carbapenem-Resistant Enterobacterales (CRE) Blood Stream Infections in KZN (Private Sector): Guideline For Targeted Antimicrobial Therapy (endorsed by the KZN Branch of the Critical Care Society of Southern Africa [CCSSA] and the KZN Branch of the SA Society of Clinical Pharmacy [SASOCP]).

Carbapenem-resistant Enterobacterales (CRE) are a serious threat to public health. Infections with CRE are difficult to treat and have been associated with mortality rates of up to 50% for hospitalised patients. Enterobacterales that produce metallo-beta-lactamases (e.g., NDM – New Delhi metallo-beta- lactamase) are a growing problem worldwide, making effective antibiotic therapy very challenging. Private laboratory surveillance in KwaZulu-Natal has indicated a concerning and steady increase in CRE isolates – **with NDM-1 carbapenemase accounting for two thirds of all clinical isolates in the region.**

The KZN Specialist Network's Antimicrobial Stewardship Initiative (KZNSN ASI) committee convened a panel of clinicians, microbiologists and pharmacists to consider appropriate therapeutic guidelines for the treatment of **blood culture positive carbapenemase-producing Enterobacterales.**

The objectives were to:

- Optimise patient outcomes in settings where there have been increasing dependence on colistin as salvage therapy.
- Avoid the redundant and inappropriate use of Ceftazidime-Avibactam from an AMS and cost-containment perspective.
- Ensure the longevity of existing broad-spectrum and new antibiotics.
- These guidelines have taken into consideration by both the Infectious Diseases Society of America, and the European Society of Clinical Microbiology and Infectious Diseases guidelines. A table of dosage recommendations, as well as extensive references, have also been included.[6]

THE BOTTOM LINE... [2,3,5,6,7]

- Scrupulous hand hygiene, the use of standard and contact precautions (e.g., gloves, disposable aprons) for potential exposure to body fluids and wound exudate, and maintaining a hygienic environment will prevent the transmission of Proteus species.
- Glove use is NOT a substitute for hand hygiene – always wash or sanitise your hands after removing gloves.
- Practice strict aseptic techniques for invasive procedures such as urinary catheterisation, uroscopy and wound care.
- Avoid unnecessary urinary catheterisation and implement catheter-associated UTI (CAUTI) infection prevention bundles.
- Urinary catheters and drainage bags should be treated as a 'closed system'; bladder instillations and washouts should not be used to prevent urinary infection.
- Remove urinary catheters as soon as they are no longer required.
- Actively manage heavily exuding wounds with antimicrobial dressings which have good fluid handling capacity (even under compression therapy) to prevent maceration of the peri-wound skin and wound breakdown.
- All instrumentation and equipment should be scrupulously cleaned after use with an enzymatic detergent and sterilisation by autoclaving.
- Disinfectants with proven efficacy against Gram-negative pathogens should be used for the routine cleaning of environmental surfaces – with 'high touch' points disinfected at least twice daily.
- Used linen and textiles should be carefully handled (i.e., not placed on the floor, held close to the body, carried through clinical areas, or manually sluiced) and washed at a minimum temperature of 80°C (SANS 10146:2020 Laundry Standard - Process Management).
- Without the implementation of aggressive stewardship measures for last-line, potentially life-saving antibiotics, we will likely rapidly lose their efficacy, with few to no treatment options in the near-future.

Supply the correct answer!

1. Proteus _____ and Proteus _____account for most of the Proteus isolates cultured by clinical laboratories.

2. Microorganisms which cause infection in debilitated individuals are termed _____ pathogens.

3. _____ and _____ on the surface of Gram-negative bacteria are associated with increased adhesion and virulence.

4. Proteus species are spread by _____ transmission.

5. An _____ pH and the odour of '_____or_____ ____ 'should trigger an alert for possible urinary tract infection with Proteus species.

ANSWERS: 1.P. *mirabilis* and P. *vulgaris* **2.** Opportunistic **3.** Pili and fimbriae **4.** Contact **5.** Alkaline and fish or rotten eggs.

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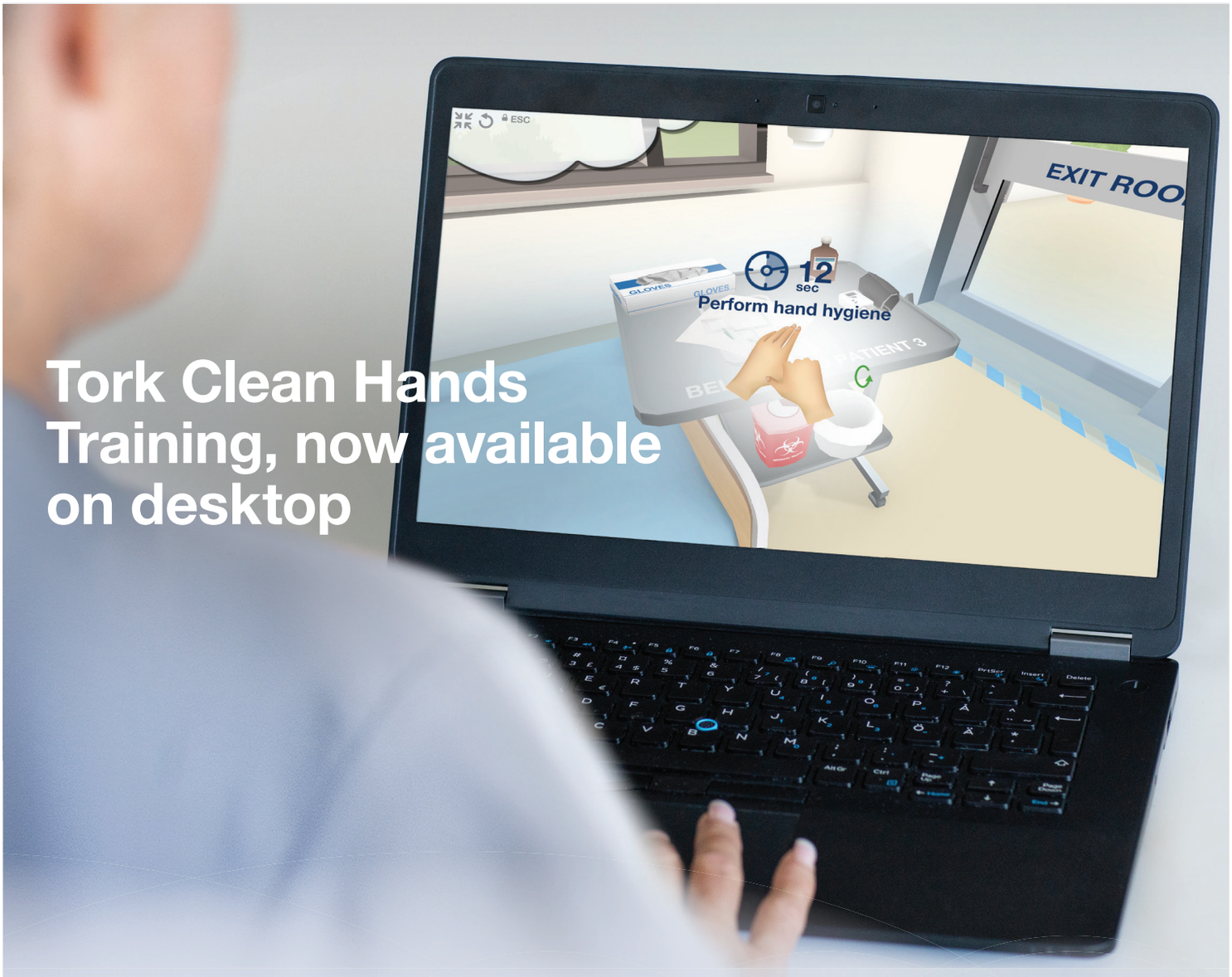

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