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Letter to the Editor:

## State of skin antiseptic choices in UK NICUs in 2023

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In early 2023 two weaker-concentration chlorhexidine gluconate (CHG) antiseptic products Tisept® (0.015%CHG+0.15% cetrimide) and Unisept® (0.05%CHG) were discontinued, leaving a dilemma regarding alternatives for very preterm babies to minimise risk of chemical injury in the first postnatal days. We therefore surveyed current antiseptic choices in the wake of their withdrawal.

During October-December 2023 we telephoned all 54 UK NICUs. We asked a senior nurse/advanced neonatal nurse practitioner/doctor about type and concentration of skin antiseptic used to clean the skin prior to peripheral venous cannulation, umbilical catheterisation, and percutaneously-inserted central venous catheter (PCVC) insertion. We also asked whether local practices varied according to any gestational/postnatal age cut-offs.

We obtained responses from 54/54 (100%) units. **Table 1** summarises the antiseptic/cleansing agents in term and preterm neonates prior to venous cannulation, umbilical catheter, and PCVC insertion. Complete data, anonymised by NICU, are provided in <u>Supplementary\_File\_S1</u>.

For PCVC insertion in preterm neonates 21/54 (39%) units used 2% CHG with (n=17) or without (n=4) isopropyl alcohol (IPA); 33/54 (61%) used weaker CHG concentrations (0.05-1%) with (n=5) or without (n=28) IPA. We found that 18/54 (33%) units washed off antiseptic post application, a practice that may limit antiseptic efficacy; one centre was using a licensed cosmetic product, Octenisan® wash mitts, for all procedures - this is a nonmedicinal product and untested in any clinical trial in neonates; four units (7%) reported now using sterile water or 0.9% saline in lieu of antiseptic solution for skin cleansing prior to PCVC insertion in extremely preterm neonates since Unisept/Tisept withdrawal; and 6/54 (11%) units reported ad hoc self-diluting CHG solutions cot-side with sterile water to achieve lower concentrations.

Our survey found wide disagreement in antiseptic choices for PCVC insertion among UK NICUs, with practices even more disparate than shown in previous national surveys of 2007,[1] 2013,[2] and 2015-16.[3] Wide variation persists despite the 2021 publication of a position statement by the Neonatal and Paediatric Pharmacy Group, endorsed by the British Association of Perinatal Medicine, which recommended using aqueous 0.5% CHG for skin disinfection in babies of birth gestation <34 weeks in

the first postnatal week, and 2%CHG in 70%IPA otherwise.[4] Our data indicate only a single centre had adopted this recommendation.(<u>Supplementary\_File\_S1</u>)

An ideal antiseptic would provide effective, long-lasting disinfection and would be suitable for all NICU procedures, at all gestations, without causing skin injury. In Germany there is almostunanimous use of Octenidine dihydrochloride for pre-procedural skin antisepsis in premature neonates, following official recommendations.[5] Octenidine may represent a safer antiseptic choice: unlike CHG, it is not systemically absorbed and may carry a much lower risk of chemical burns.[5,6] Yet it has not yet been tested in any randomised controlled trial in neonates, and is unavailable for use as an antiseptic solution in medicinal product form in the UK. Clinical trials of Octenidine are urgently needed to inform its safety, effectiveness, biofilm and antimicrobial resistance profiles in preterm babies. Such data could assist a UK marketing authorisation application that could eventually make this promising newer antiseptic available for use in UK neonates.

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**Author contributions:** EA and CK conducted the survey and gathered the data. EA analysed the data and wrote the first manuscript draft. All authors contributed to manuscript revision and approved the final version. PC is guarantor.

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**Table 1.** Skin antiseptic/cleaning agent used prior to peripheral venous cannulation, percutaneous central venous catheterisation, and umbilical catheterisation in preterm and term neonates in 54 tertiary-level UK NICUs

Cleaning agent	Venous Cannulation		PCVC		UVC/UAC	
	Preterm	Term	Preterm	Term	Preterm	Term
2% CHG/70% IPA	42	52	17	40	17	38
2% CHG aqueous	1	-	4	1	3	2
1% CHG aqueous	-	-	-	2	-	2
0.5% CHG/ 70% IPA	-	-	5	2	4	1
0.5% CHG aqueous	5	-	17	4	17	6
0.1% CHG aqueous	-	-	1	1	1	1
0.05% CHG aqueous	2	-	10	3	10	2
70% IPA	3	2	-	-	-	-
Octenisan® wash mitts*	1	1	1	1	1	1
0.9% saline/sterile water	2	-	4	-	5	1

Data are numbers of neonatal units. Percentages are not shown because some units reported using more than one agent, depending upon gestational and/or postnatal age cut-offs or antiseptic agent availability: 42/54 (78%) centres had different practices or used different antiseptic strengths according to gestational age thresholds (varying from 24-37 weeks), postnatal age threshold (ranging from 2-14 days), or birthweight threshold (<1000g).

PCVC, percutaneously-inserted central venous catheter; UVC/UAC, umbilical venous catheter/umbilical arterial catheter; CHG, chlorhexidine gluconate; IPA: Isopropyl Alcohol

\* Octenidine concentration unspecified because licensed as a cosmetic product only.