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CHEMICAL PATHOLOGY

Are your hands clean enough for point-of-care electrolyte analysis?

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Aim: To investigate clinically significant analytical interference in point-of-care electrolyte analysis caused by contamination of blood specimens with hand disinfectant.

Methods: Six different hand hygiene products were added separately to heparinised blood samples in varying amounts as contaminant. The contaminated samples were analysed by three different blood gas and electrolyte analysers for assessing interference on measured whole blood sodium and potassium concentrations.

Results: There were significant analytical interferences caused by hand hygiene product contamination that varied depending on the combination of disinfectant and analyser. Small amounts of Microshield Antibacterial Hand Gel contamination caused large increases in measured sodium concentration. Such effect was much greater compared with the other five products tested, and started to occur at much lower levels of contamination. There was a trend towards lower sodium results in blood samples contaminated with Hexol Antiseptic Lotion (Hexol), the hand hygiene product that we used initially. Apart from AiE Hand Sanitizer, all the other hand disinfectants, especially Hexol, significantly elevated the measured potassium concentration, particularly when a direct ion-selective electrode method was used for measurement.

Conclusions: Hand disinfectant products can significantly interfere with blood electrolyte analysis. Proper precautions must be taken against contamination since the resultant errors can adversely affect the clinical management of patients.

Key words: Point-of-care (POC), blood gas analyser, alcoholic hand disinfectant, infection control, interference, ion-selective electrode.

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INTRODUCTION

The availability of point-of-care (POC) blood gas and electrolyte analysis has assisted clinicians in managing acutely ill patients. It enables a rapid turnaround time for obtaining test results. This is often critically important to the neonatologist or intensivist who is managing unstable patients such as those on assisted ventilation or intravenous fluid therapy that require close monitoring and therapeutic adjustments.

After the outbreak of severe acute respiratory syndrome (SARS) in Hong Kong in March 2003,^{1–3} we observed

abnormally high whole blood sodium concentrations (>150 mmol/L) collected in heparinised syringes from a Rapidpoint 400 analyser (RP400; Bayer Healthcare, USA) for POC blood gas and electrolyte analysis located in our neonatal unit. These abnormal test results did not correlate with the clinical condition of the corresponding patients. Upon cross checking, the sodium concentrations of these patients were found to be normal when venous blood samples were analysed in our main chemical pathology laboratory, where electrolytes are measured in heparinised plasma by the DP Modular analyser (Roche Diagnostics, USA) using an indirect ion-selective electrode (ISE) method. A malfunction of the RP400 analyser was suspected initially. However, quality control records showed no evidence of instrument failure. All POC blood gas and electrolyte analysers in our hospital are networked and connected centrally to the main chemical pathology laboratory, with automatic daily monitoring of performance (internal quality control) and subscription to the monthly external quality assurance program (QAP) organised by the Royal College of Pathologists of Australasia (RCPA) and the Australasian Association of Clinical Biochemists (AACB). This POC connectivity system has been accredited by the National Association of Testing Authorities, Australia (NATA) and RCPA. Table 1 illustrates some of the abnormal results.

Although strict infection control had already been implemented in our neonatal unit, the SARS outbreak necessitated further upgrade measures.⁴ Our hand hygiene protocol was introduced in 1996.⁵ This protocol was considered adequate even during the SARS epidemic, and was used in combination with other upgraded infection control procedures.⁴ Part of the protocol required that health care workers disinfect both gloved hands by rubbing with an alcohol-based antiseptic agent before any kind of direct patient contact, including blood-sampling procedures such as heel-prick, venepuncture, and direct withdrawal of arterial blood via an *in situ* arterial catheter. During the SARS epidemic there was an inadequate supply of our usual hand hygiene product Hexol Antiseptic Lotion (Hexol; Sigma Pharmaceuticals, Australia) due to simultaneous upgrading of infection control measures in many other departments of nearly all hospitals in Hong Kong. Microshield Antimicrobial Hand Gel (MAH gel; Johnson & Johnson Medical, Australia) and some other products were provided as substitute (Table 2). The abnormal and discrepant sodium results began to emerge after we changed to MAH gel. Furthermore, the erroneous results

TABLE 1 Examples of abnormal electrolyte results

Specimen type		Capillary whole blood (mmol/L)	Heparinised venous plasma (mmol/L)
Patient A	Sodium	179	140
	Potassium	4.8	4.7
Patient B	Sodium	164	137
	Potassium	6.4	4.7
Patient C	Sodium	187	133
	Potassium	5.1	4.6

Electrolytes in capillary whole blood specimens were analysed by the point-of-care Rapidpoint 400 analyser using direct ion-selective electrodes (ISE); heparinised venous plasma specimens were taken within 10 min of the capillary samples and analysed in the main chemical pathology laboratory by the DP Modular analyser using indirect ISE.

were noted to occur much more frequently with capillary blood sampling. Therefore, contamination of blood samples by MAH gel was suspected to be the cause of the spuriously high sodium results.

This study was initiated to investigate the analytical interference of POC electrolyte analysis caused by contamination of blood specimens with hand hygiene products, producing clinically significant errors that can adversely affect patient care.

MATERIALS AND METHODS

Six disinfectants that were commonly used in hospitals in Hong Kong (Table 2) were analysed for sodium and potassium concentrations in the main chemical pathology laboratory using inductively coupled plasma mass spectrometry (ICP-MS; Agilent 7500c mass spectrometer; Yokogawa Analytical Systems, Japan).

Two capillary tubes were prepared for further investigation of analytical interference. The first tube was filled with normal saline, while the second tube contained normal saline contaminated with a small drop of MAH gel. Both tubes were analysed by our POC RP400 analyser.

Three different POC blood gas and electrolyte analysers were included in this study. At our hospital, the Rapidpoint 400 and Rapidlab 865 analysers (RP400, RL865; Bayer Healthcare) are used at POC sites and the

main chemical pathology laboratory, respectively. The i-STAT 1 analyser (i-STAT; Abbott Diagnostics, USA) is used at POC sites in other hospitals in Hong Kong. Both the RP400 and RL865 analysers use direct ion-selective electrode (ISE) technology to measure whole blood sodium and potassium concentrations, while the i-STAT employs a biosensor technology.

Six different hand disinfectant products (Table 2) were tested for interference of electrolyte analysis. The test samples were prepared by mixing 500 μ L of heparinised whole blood with varying amounts of each hand disinfectant (0, 5, 10, 15, 20, 25 μ L), except for MAH gel, where 1000 μ L of heparinised whole blood was used with the same varying amounts of gel. The reason for this was because all three analysers produced substantially greater errors with MAH gel. The sodium and potassium concentrations of each contaminated sample were measured in duplicate and mean values were used for statistical analysis. The coefficients of variation (CV) of the measurements were within the previously established precision limits of the analysers. Student's *t* test was applied for assessing any significant difference between various measurements and analysers. A *p* value <0.05 was considered to be statistically significant. All probabilities were two tailed.

RESULTS

The measured sodium concentration of the saline-filled capillary tube was 146 mmol/L, and that of the MAH gel contaminated tube was >180 mmol/L. On the other hand, the sodium concentrations of all six disinfectants were found to be <5 mmol/L, while their potassium concentrations were <0.5 mmol/L using ICP-MS. These findings showed that MAH gel significantly interfered with sodium analysis on the RP400 analyser.

Figures 1 and 2 show that contamination of blood specimens with any of the six hand disinfectants can interfere with sodium and potassium analyses on all three POC analysers.

MAH gel contamination at concentrations $\geq 1\%$ (10 μ L per 1000 μ L whole blood) caused marked increases in measured sodium concentration on the RP400 analyser. The RL865 and i-STAT analysers were also affected, but to a much lesser extent. For potassium analysis, all three analysers had similar interference showing progressive

TABLE 2 The six hand disinfectant products used in Hong Kong hospitals during the SARS epidemic

Brand (Supplier)	Active ingredients	Other constituents
Microshield Antibacterial Hand Gel (Johnson & Johnson Medical Pty Ltd, North Ryde, NSW, Australia)	Ethanol 61.5%	Methyl hydroxybenzoate 0.011% Propyl hydroxybenzoate 0.003% Diazolidinyl urea 0.125% Benzalkonium chloride 0.1% Iodopropynyl butylcarbamate 0.001% Phenoxyethanol 0.5%
Microshield Handrub (Johnson & Johnson Medical Pty Ltd, North Ryde, NSW, Australia)	Ethanol 70%	'Emollient' 'Moisturiser'
Hexol Antiseptic Lotion (Sigma Pharmaceuticals Pty Ltd, Clayton, Vic, Australia)	Chlorhexidine gluconate 0.5% (per 100 mL): Ethanol 26.5 mL Chlorhexidine gluconate 1 g Isopropyl alcohol 42 mL	'Skin conditioners'
Swashes Handrub – Topical Antiseptic Lotion (Swashes Chemical Co Ltd, Shenzhen, People's Republic of China)	Ethanol Chlorhexidine	'Emollient' 'Moisturiser'
Avagard Antiseptic Handrub (3M Pharmaceuticals Pty Ltd, Thornleigh, NSW, Australia)	Ethanol 58% Chlorhexidine gluconate 0.5%	Not listed
AiE Hand Sanitizer (DeVos Cosmetics Asia Ltd, Hong Kong, People's Republic of China)	Ethanol 70%	Water Glycerin Carbomer Fragrance Aloe vera Glycol

increases in measured potassium concentration with increasing contamination (Fig. 1a, 2a).

Contamination with Microshield Handrub did not affect sodium measurement on any analyser, but caused marked increases in measured potassium concentrations on the RP400 and RL865 analysers (Fig. 1b, 2b).

Hexol Antiseptic Lotion did not affect sodium measurement using the i-STAT, but significantly decreased sodium results from the RP400 and RL865 analysers. On all three analysers, potassium concentration started to falsely elevate from 1% contamination (Fig. 1c, 2c).

At $\geq 4\%$ contamination, Swashes Handrub (Swashes Chemical Co., China) caused small but statistically significant negative and positive interferences with sodium measurements on the RL865 and i-STAT analysers, respectively. However, potassium results were significantly increased on all analysers (Fig. 1d, 2d).

Avagard Antiseptic Handrub (3M Pharmaceuticals, Australia) at low concentrations did not cause significant changes in measured sodium concentrations, but resulted in markedly increased measured potassium concentrations on all analysers (Fig. 1e, 2e).

Compared with the other five disinfectants, *AiE Hand Sanitizer* (DeVos Cosmetics Asia, China) caused the smallest interference in sodium and potassium measurements on all analysers. While sodium concentrations

tended to decrease, there were no consistent changes in potassium measurement (Fig. 1f, 2f).

Tables 3 and 4 summarise the test statistics for the measurements of both sodium and potassium concentrations by RL865, RP400 and i-STAT, respectively, comparing the absence and the presence of varying amounts of different brands of hand disinfectants as contaminant.

In summary, of the six products tested, MAH gel caused the greatest and most clinically important changes in measured sodium concentrations on the RP400 analyser. Apart from *AiE Hand Sanitizer*, all of the other products significantly increased the measured potassium concentration, especially on the RP400 and RL865 analysers, both of which use a direct ISE method for electrolyte measurement.

DISCUSSION

POC testing is an integral part of patient management in many clinical departments, including intensive care units, accident and emergency departments, and many other acute wards. The provision of rapid and reliable analysis of blood samples allows important clinical decisions to be made in a timely fashion. It is of great importance that potential sources of interference with POC analysers are recognised and avoided. Previous studies have identified

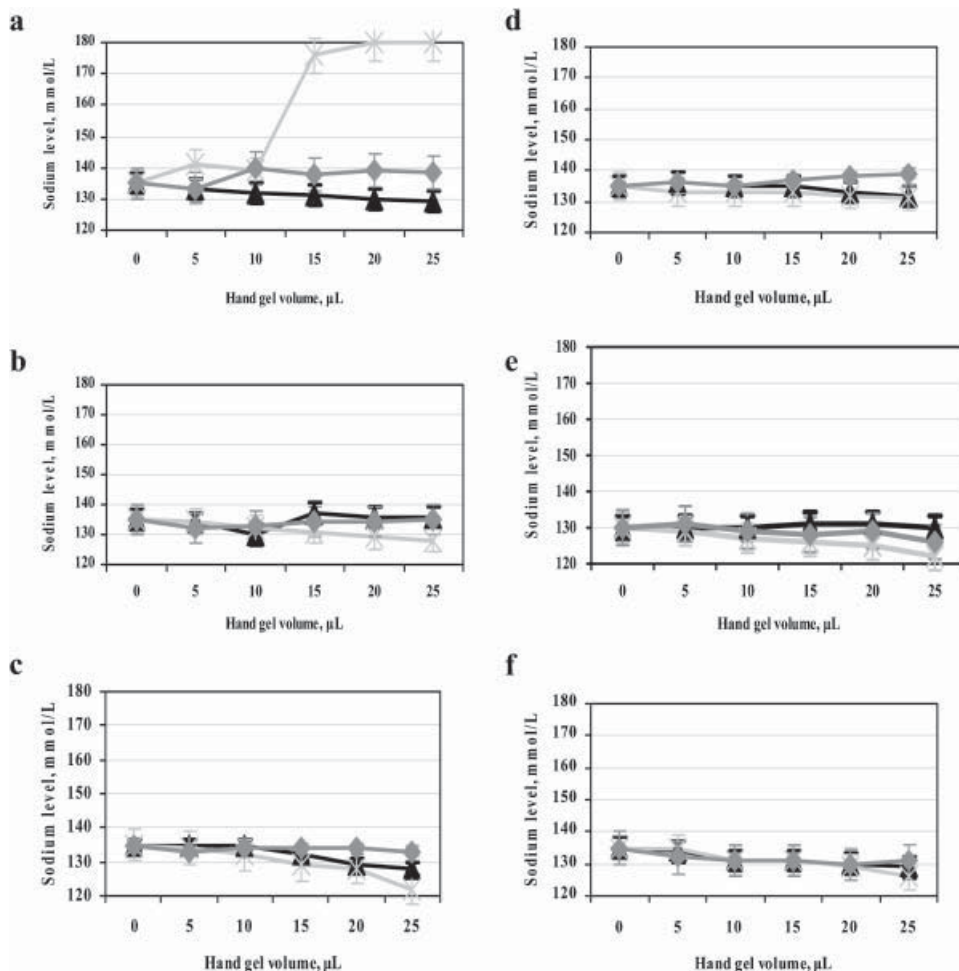


Fig. 1 (a) Microshield Antibacterial Hand Gel; (b) Microshield Handrub; (c) Hexol Antiseptic Lotion; (d) Swashes Topical Antiseptic Lotion; (e) Avagard Antiseptic Handrub; (f) *AiE Hand Sanitizer*. (▲) Rapidlab 865; (×) Rapidpoint 400; (◆) i-STAT 1.

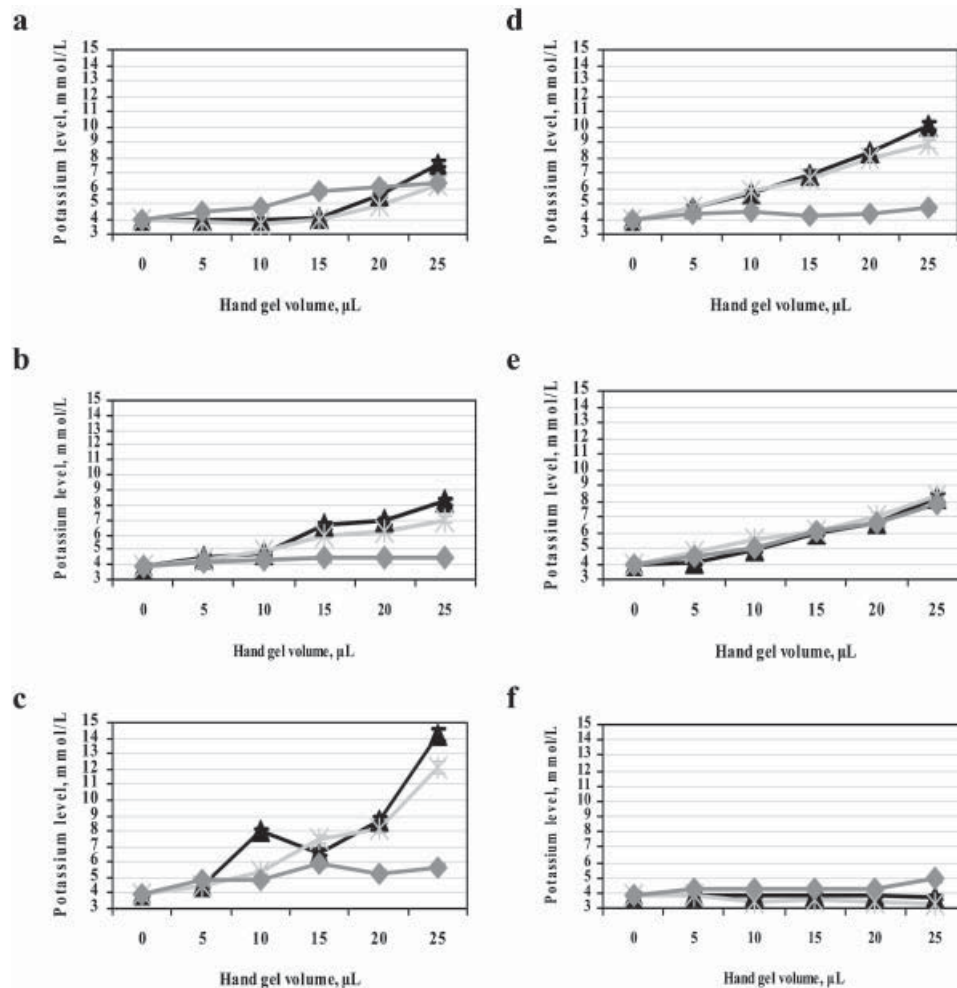


Fig. 2 (a) Microshield Antibacterial Hand Gel; (b) Microshield Handrub; (c) Hexol Antiseptic Lotion; (d) Swashes Topical Antiseptic Lotion; (e) Avagard Antiseptic Handrub; (f) AiE Hand Sanitizer. (▲) Rapidlab 865; (×) Rapidpoint 400; (◆) i-STAT 1.

several potential causes of interference of electrolyte analysis with ISE-based instruments.⁶⁻¹⁰ These problems include contamination of samples,⁶ difference in electrode design,^{6,8-10} variations in salt bridge solution,^{6,8,10} and interfering substances in the blood specimen itself.^{6,8,9}

To the best of our knowledge, the interference effects of hand disinfectants on electrolyte measurements by ISE-based analysers have not been previously reported. From our study, the effects of contamination on electrolyte measurements are not only statistically significant, but also clinically important in that they may result in serious errors in patient management if not recognised. These interferences are not due to the electrolyte content of the hand disinfectants, since their sodium and potassium concentrations are very low. It seems that the effects are due to substances in the disinfectants that interfere with the measuring process of the analyser. In particular, it has been previously reported that benzalkonium chloride, one of the constituents of MAH gel, can grossly affect sodium measurement by ISE-based analysers.⁷ Further investigation to identify the interfering substance(s) is required. Whether altering the design of the electrodes or salt bridge solution can reduce or eliminate the interference effects should be explored by the manufacturing industry.

Grossly abnormal sodium and potassium results can easily be detected due to incompatibility with the clinical conditions of the patients. Taking the within-individual biological variations for sodium and potassium concentrations to be 0.7% and 4.8%,¹¹ respectively, a clinically significant change would be approximately 2.5 mmol/L for sodium and 0.5 mmol/L for potassium. Therefore, intermediate interference changes within 2-3 times the biological variations would be most dangerous because such changes may be considered genuine, thereby affecting patient management.

Clinicians and chemical pathologists should interpret electrolyte results with care and caution, especially those of capillary blood sampled by inexperienced personnel. In the past, erroneously elevated capillary blood potassium concentration was always attributed to haemolysis or tissue injury caused by poor blood-sampling technique. Retrospectively, this may not have been the only interpretation, as some degree of interference from Hexol contamination may have been the contributing cause in some cases. Biochemical results that are incompatible with the clinical condition of the patient should prompt careful re-sampling by a different route or analysis by a different method if necessary.

TABLE 3 Summary of test statistics of hand disinfectant interference on sodium measurements

Product	Microshield Antibacterial Hand Gel			Microshield Handrub			Hexol Antiseptic Lotion			Swashes Topical Antiseptic Lotion			Avagard Antiseptic Handrub			AiE Hand Sanitizer						
	RL865	RP400	i-STAT	RL865	RP400	i-STAT	RL865	RP400	i-STAT	RL865	RP400	i-STAT	RL865	RP400	i-STAT	RL865	RP400	i-STAT				
Volume (µL)	5	0.036	0.021	0.039	0.021	0.039	0.248	0.654	0.002	1.000	0.654	0.019	0.248	0.379	0.188	1.000	0.654	0.188	1.000	0.248	1.000	0.002
	10	0.005	0.097	<0.001	0.198	0.019	<0.001	0.198	0.188	1.000	0.198	0.188	1.000	0.379	1.000	1.000	0.198	0.188	1.000	<0.001	0.097	<0.001
	15	<0.001	<0.001	0.003	0.036	0.097	0.188	0.005	0.021	0.188	0.005	0.188	1.000	0.379	0.019	0.248	0.097	0.019	<0.001	0.097	<0.001	<0.001
	20	<0.001	<0.001	<0.001	0.248	0.021	0.248	<0.001	0.010	0.188	<0.001	0.188	0.036	0.198	0.002	0.248	0.046	0.046	0.188	<0.001	0.021	<0.001
	25	<0.001	<0.001	<0.001	0.248	0.010	0.248	<0.001	<0.001	1.000	<0.001	0.019	0.005	0.097	<0.001	1.000	0.005	<0.001	<0.001	<0.001	0.002	<0.001

TABLE 4 Summary of test statistics of hand disinfectant interference on potassium measurements

Product	Microshield Antibacterial Hand Gel			Microshield Handrub			Hexol Antiseptic Lotion			Swashes Topical Antiseptic Lotion			Avagard Antiseptic Handrub			AiE Hand Sanitizer						
	RL865	RP400	i-STAT	RL865	RP400	i-STAT	RL865	RP400	i-STAT	RL865	RP400	i-STAT	RL865	RP400	i-STAT	RL865	RP400	i-STAT				
Volume (µL)	5	1.000	0.100	<0.001	<0.001	0.013	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.045	<0.001	<0.001	<0.001	<0.001	1.000	1.000	0.001
	10	1.000	0.005	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.045	<0.001	<0.001
	15	0.001	0.100	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	1.000	<0.001	0.001
	20	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.045	<0.001	<0.001
	25	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.001	<0.001	<0.001

In the light of the results of this study, special care must be taken with regard to blood-sampling technique and the interpretation of spurious results. To minimise contamination of blood samples, the alcoholic hand rub should be allowed to dry completely before blood sampling. Health care workers should avoid rubbing or pressing the site where blood is to be sampled, or touching the tip of the capillary tube with contaminated fingers. The choice of hand disinfectant is also important. As shown, MAH gel causes significant interference even at low concentrations, takes longer to dry and is stickier than the other disinfectants, thus increasing the risk of contamination and subsequent analytical errors. Therefore, its use in the neonatal intensive care unit is not recommended. In fact, after reverting from MAH gel to the original brand of hand disinfectant, Hexol, we no longer observed such spurious sodium results.

In conclusion, it is apparent that clinically significant interference of POC electrolyte analysis can be caused by contamination of blood specimens with hand hygiene products. Careful blood sampling and interpretation of spurious test results are crucial in avoiding errors in clinical management. Good communication and cooperation between clinicians and chemical pathologists will facilitate the identification and investigation of such problems.

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