



## Early View

Research letter

### **Complications of nasal and pharyngeal swabs – a relevant challenge of the COVID-19 pandemic?**

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## **Complications of nasal and pharyngeal swabs – a relevant challenge of the COVID-19 pandemic?**

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#shared first authorship, equal contributions

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Running head: Complications of nasal and pharyngeal swabs

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Summary:

Although swab procedures during SARS-CoV-2 testing are generally safe (3 adverse events in 11,476 swab procedures; 0.026%), increased awareness of complications is necessary, considering approximately 5.1 million tests conducted worldwide daily.

## TEXT

### *To the Editor:*

The coronavirus disease 2019 (COVID-19) pandemic comprises approximately 50 million confirmed cases and over 1.2 million deaths as of November 10, 2020 [1], affecting health care systems worldwide in an unprecedented way. In the absence of effective treatments or preventive measures, all attempts to control the pandemic are based on reliable diagnostic procedures, particularly RT-PCR of upper respiratory specimens, which is considered the diagnostic gold standard [2]. A previously unimaginable number of these diagnostic procedures has been performed since the beginning of the pandemic and there is a clear trend towards further expanding the number of tests [3]. Although specimens are frequently obtained by semi-skilled temporary staff, the collection is generally considered safe. However, possible adverse events (AEs) of the procedure have largely escaped systematic recording and reporting to date. A Pubmed search, performed on October 10, 2020, using every possible combination of the search terms “complications”, “adverse events”, “adverse effects” and “nasal swab”, “oral swab”, “nasopharyngeal swab”, “oropharyngeal swab”, revealed only three publications relevant for the question of AEs caused by pharyngeal swab procedures. The first one represents a case report describing the break of a nasal swab by triggering the swab’s breakpoint mechanism during the examination of an uncooperative patient [4]. The second publication compared commercially available swabs with three-dimensional printed nasopharyngeal swabs, reporting different mild complications in several individuals, and one individual with severe epistaxis needing medical help [5]. Lastly, one case of cerebrospinal fluid leak requiring endoscopic surgical repair was reported after a nasal COVID-19 test [6]. Of note, even the second study investigated AEs in only 176 individuals [5].

Here, we evaluated complications caused by deep nasal and oropharyngeal swabs requiring immediate medical attention in a large, representative cohort from Northern Germany and estimated the number of tests for SARS-CoV-2 involving swab procedures during the pandemic worldwide.

Within our population-based SARS-CoV-2 monitoring study (ELISA Cohort), 11,476 deep nasal and oropharyngeal swabs were taken in 3083 individuals from May to August 2020. Swab collection followed a clinically approved protocol as performed at the University Hospital Schleswig-Holstein, Campus Lübeck, Germany, and consisted of combined deep nasal (mid-turbinate) and oropharyngeal swabs in each participant. The deep nasal swab was performed by inserting the swab 2 - 3 cm into one nostril (until resistance was felt at the turbinates), while gently rotating. The same swab was then inserted through the mouth and rubbed between the tonsillar pillars over the posterior oropharynx avoiding the tongue, teeth, and gums. CE-marked PROBACT Transport Swabs (Technical Service Consultants Ltd., United Kingdom) and CITOSWAB Transport Swabs (Citotest Scientific, China) were used throughout the study. Specially trained medical students performed the swabs under the on-site supervision of a medical doctor.

AEs were documented in a standardised manner and classified as situations requiring immediate medical diagnosis or treatment, whereas severe adverse events (SAEs) were considered study-related complications causing permanent damage.

We observed a total of three AEs (0.026 % [95% CI: 0.007-0.077 %]). In two individuals, a 53-year-old and a 55-year-old male, the swab's tip broke off. In both cases, the swab tip was not visible by inspection. While the first person had a foreign body sensation, the second person did not report any similar complaints. Both individuals were immediately transferred to an otorhinolaryngology clinic, where the swab tip was retrieved without complications by nasal endoscopy in the first individual. The swab tip was no longer detectable in the second person despite a thorough examination by an

otorhinolaryngologist, suggesting that the tip had been swallowed without further complications. Third, a 29-year-old female developed a spontaneous anterior dislocation of the left temporomandibular joint when opening her mouth for the oropharyngeal swab. Exhibiting relevant pain, she was admitted to a hospital by ambulance for external jaw repositioning. Notably, no individual developed epistaxis that would have required medical care, nor were there any SAEs.

According to WHO data, at least 645 million tests involving swab procedures have been performed since the beginning of the pandemic until November 13, 2020. In the first half of November 2020, the total number of daily tests amounted to 5.1 million (**Table 1**). Of note, the observed occurrence of adverse events in 0.026 % of swab procedures is possibly still an underestimate, as we performed a combination of deep nasal and oropharyngeal swabs that yield comparable virus detection rates [7] but are less invasive than nasopharyngeal swabs.

Our results from a well-monitored, large cohort demonstrate that the combination of deep nasal and oropharyngeal swabs is generally safe. AEs are very rare, SAEs are unlikely, but cannot be entirely ruled out. However, given the exceptionally high number of SARS-CoV-2 tests performed worldwide that involve an increasing number of healthy, asymptomatic individuals with very low a priori probabilities for acute infections [8, 9], AEs of the diagnostic procedure require appropriate attention, as is common practice in SARS CoV-2 drug and vaccine development.

In conclusion, we would like to encourage i) increased awareness for AEs during the standard medical procedure for SARS CoV-2 testing; ii) the provision of appropriate diagnostic and therapeutic measures in case of AEs; iii) further research addressing AEs including the need to implement appropriate informed consent in clinical as well as in research settings.

**Table 1.** Number of swab procedures for detection of SARS-CoV-2 until November 13, 2020, based on WHO data (source: <https://github.com/owid/covid-19-data/tree/master/public/data/> [accessed 2020 Nov 16, 2020]).

Continent	Countries included	Population included (million)	Tests total (million)*	Tests daily‡
Africa	18	731	15.0	74,584
Asia	25	2,742	219.8	1,806,250
Europe	32	642	213.2	1,989,026
North America	9	546	175.9	1,085,027
Oceania	3	31	10.4	46,852
South America	6	110	10.9	75,013
Total	93	4,807	645.2	5,076,752

Abbreviations: AE, Adverse event.

\* Cumulative number of tests since March 2020, latest value period November 2-13.

‡ Daily number of tests, latest value period November 2-13, 2020, smoothed (7 days).

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