ipac pci
Infection Prevention and Control Canada
Prévention et contrôle des infections Canada
EDITORIAL

The use of dogs for the detection of infectious diseases; an emerging diagnostic option

James Ayukekbong, BMLS, MSc, Ph.D., CIC[1 *] and Adenike Oguntimehin, BMLS, MPH, LTC-CIP[2]

[1]Editor-in-Chief, Canadian Journal of Infection Control, Winnipeg, Manitoba, Canada
[2]Department of Public Health, Walden University, Minneapolis, Minnesota, USA

*Corresponding Author
J. Ayukekbong
Editor-in-chief, CJIC
Winnipeg, Manitoba, Canada
Email: editor-in-chief@ipac-canada.org

BACKGROUND

Accurate and timely diagnosis are important aspects of infection prevention and control as reliable testing for the identification of both symptomatic and asymptomatic infected persons may reduce the spread of infection. Common infectious disease-testing strategies require the collection of specimens through often invasive procedures, e.g., venous blood collection, nasopharyngeal swabs, urethra swab, rectal swab, etc. Besides the invasiveness of these procedures, they also require trained laboratory personnel and specialized laboratories for testing. In addition, the collection, transportation, storage, and analysis of samples is time consuming and also costly. These challenges necessitate the need for alternative strategies which are faster, reliable, and non-invasive for screening of both asymptomatic and symptomatic individuals for diseases.

Canines have been shown to have extraordinary olfactory acuity and for a long time, trained dogs (e.g., Labrador retrievers, Golden retrievers, German shepherds, Belgian malinois, and many other mixed breeds) have been used for varying purposes, e.g., in search and rescue to find victims of all sorts of events: avalanches, earthquakes, floods, landslides, plane crashes (Kokocińska-Kusiak et al., 2021). Sniffer dogs have also been used for explosive detection to combat terrorism, stop the flow of illegal narcotics or contraband, detect unreported currency, concealed humans, or smuggled agriculture products. Increasingly, the usefulness of sniffer dogs has been studied for the detection of viral, bacterial, and parasitic infections, as well as non-infectious diseases and disorders such as epilepsy, diabetes, and cancer (McCulloch et al., 2006; Cambau et al., 2020; Hardin et al., 2015; Catala et al., 2019).

CURRENT FINDINGS

In a paper published in The Lancet Infectious Diseases, the authors suggested that dogs can distinguish between the smell of asymptomatic malaria-infected and uninfected individuals. The authors collected foot odours from Gambian children aged five to 13 years with and without falciparum malaria infection and using two dogs, they found that the sensitivity of the first dog was 73.3% (95% CI 54.1 – 87.7) and specificity of 91% (85.2 – 95.1); the sensitivity of second dog was 70% (50.6-85·3), with a specificity of 90.3% (84.3 – 94.6%) (Guest et al., 2019). At the end of the study, the authors concluded that dogs could be used to screen individuals infected with malaria, which, in turn, may prove useful at ports of entry. In another study, the authors evaluated the operating characteristics of two comparably trained dogs as a "point-of-care" diagnostic tool to detect toxin gene-positive Clostridioides difficile. Each dog was able to detect toxin gene-positive C. difficile in stool specimens with sensitivities of 77.6% (67.3 – 86.0) and 92.6% (84.6 – 97.2) and specificities of 85.1% (79.6 – 89.6) and 84.5% (79.0 – 89.0) respectively (Taylor et al., 2018).

Canines have also been used for the detection of urinary tract infections. In this study, samples were obtained from 687 individuals (34% culture-positive and 66% culture-negative controls). The canines detected urine samples positive for 100,000 colony-forming units/mL Escherichia coli (n = 250, sensitivity 99.6%, specificity 91.5%). The diagnostic accuracy was similar to Enterococcus sp. (n = 50; sensitivity 100%, specificity 93.9%), Klebsiella sp. (n = 50; sensitivity 100%, specificity 95.1%), and Staphylococcus aureus (n = 50; sensitivity 100%, specificity 96.3%). Overall, the sensitivity was about 100%, and specificity was above 90%. The results prompted authors to suggest that canine scent detection is an accurate and feasible method for the detection of bacteriuria (Maurer et al., 2016).

Also, in the Auburn University Canine Performance Sciences Breeding Program, two dogs were trained to detect cell cultures infected with bovine viral diarrhea virus (BVDV) and to discriminate BVDV-infected cell cultures from uninfected cell cultures and from cell cultures infected with bovine herpes virus 1 (BHV 1) and bovine parainfluenza virus 3 (BPIV 3). The detection of BVDV-infected cell cultures by Dog 1 had a diagnostic sensitivity of 0.850 (95% CI: 0.701 – 0.942) and the sensitivity of Dog 2 was

0.967 (95% CI: 0.837–0.994). Both dogs exhibited very high diagnostic specificity 0.981 (95% CI: 0.960–0.993) and 0.993 (95% CI: 0.975–0.999), respectively (Angle et al., 2016).

Most recently, during the COVID-19 pandemic, dogs were trained to detect SARS-CoV-2 infection by smell from sweat. At a concert in Germany, dogs correctly identified individuals with active infections with a specificity of nearly 100% and a sensitivity of 82%. It took about 1 to 2 seconds for the dogs to smell each sample. As a result, the authors suggested that dogs may provide a fast and reliable screening option for public events at which mass screening is required (Larkin et al., 2022). In a similar study, dogs were able to discriminate between samples of COVID-19-infected (positive) and non-infected (negative) individuals with a sensitivity of 82.63% (95% CI: 82.02 – 83.24%) and a specificity of 96.35% (95% CI: 96.31 – 96.39%) (Jendrny et al., 2020). Also, in a paper recently published in the Canadian Journal of Infection Control, the authors reported that two canines that were previously trained and validated to differentiate COVID-19 positive and negative PCR samples from breath, sweat, and gargle clinical samples from scent stands, were subsequently taught to screen pillowcases for COVID-19 infection. The overall sensitivity was 100% and the specificity was 100% for the first canine and 82.6% for the second canine. The agreement between the two canine teams was 98.4% on room alerts (Charles et al., 2023).

Beside the use of canines in infectious disease diagnosis, sniffer dogs have also been used in chronic disease diagnosis such as cancer. In an article by McCulloch et al., 2006, dogs were used for screening for lung and breast cancers. The authors found that among lung cancer patients and controls, the overall sensitivity of canine scent detection compared to biopsy-confirmed conventional diagnosis was 0.99 (95% CI, 0.99–1.00) and overall specificity 0.99 (95% CI, 0.96 – 1.00). Among breast cancer patients and controls, sensitivity was 0.88 (95% CI, 0.75–1.00) and specificity 0.98 (95% CI, 0.90–0.99). Sensitivity and specificity were remarkably similar across all four stages of both diseases (McCulloch et al., 2006).

The World Health Organization (WHO) recommends the thresholds for diagnostic specificities and sensitivities for point-of-care antigen tests of more than 97% and 80% respectively (WHO, 2020). The predictive values of the studies cited above, as well as many others, are within the WHO threshold for specificity and sensitivity of point-of-care testing, suggesting that the use of sniffer canines as an alternative diagnostic strategy deserves further investigation for routine medical use.

MECHANISM OF DISEASE DETECTON BY SNIFFER DOGS

In this editorial, we look at some of the physiological factors that make dogs suitable for disease diagnosis. Both infectious and non-infectious diseases can trigger complex metabolic processes which result in the release of volatile organic compounds from the body (Shirasu et al., 2011; Issitt et al., 2022). With appropriate sensory ability, sniffer dogs can detect these volatile biochemical fingerprints as biomarkers for specific diseases (Jendrny et al., 2021). Although, the mechanisms, properties of olfactory receptors, and the interplay of olfactory sensory neurons in the identification of specific odorants are still not fully understood, the sense of smell of dogs is thought to be a thousand times more sensitive than that of humans. In fact, a dog has more than 220 million olfactory receptors in its nose, while humans have only 5 million (Alabama A&M, 2011). Dogs' enhanced sense of smell allows them to not only gather both current and historical information about their surrounding environment, but also to find the source of the smell. The olfactory receptor cells in the nose of a dog extend throughout the entire layer of specialized olfactory epithelium found in the nasal cavity, which contains a rich supply of olfactory nerves. These nerves ultimately connect with a highly developed olfactory lobe in the dog's brain. The mucous gland within the nasal cavity enables the nose to be moist. This moisture helps the nasal cavity to easily dissolve molecules in the air and brings them into contact with the specialized olfactory epithelium.

It is the sniffing action, however, that enhances odour detection in dogs. This sniffing action is the result of a disruption of the normal breathing pattern, and is accomplished through a series of rapid, short inhalations and exhalations. During the process, air is forced through the olfactory epithelium. Odour molecules in the olfactory epithelium are absorbed into the mucous layer and diffuse to the cilia of receptor neurons. This interaction generates nerve impulses which are transmitted by the olfactory nerves to the dog's brain, which has a well-developed olfactory lobe. This allows the dog to recognize a scent and follow a trail. But in general, the massive number of neurons, including the size of the olfactory epithelium, has a significant effect on olfactory acuity in dogs (Issel-Tarver et al., 1996).

Despite this enhanced olfactory acuity of dogs, adequate training is still required for canines to effectively detect odours, including the physical mechanics of searching for and responding to odour in the testing environment. Through this, trained dogs are able to appreciate the difference between background scent (healthy people) and the target scent present in only diseased individuals. Therefore, defining the correct target scent in advance is crucial during training for reliable subsequent testing. Unfortunately, there is lack of standardization of canine training methods for disease recognition, and training protocols differ depending on the materials, settings, and learning approaches that are used.

CONCLUSION

Publications in the field to-date suggest that medical sniffer dogs can become an affordable rapid diagnostic option for disease screening, especially where mass testing is necessary as part of contact tracing during outbreaks, or in areas where test infrastructure is limited. Most importantly, early during a pandemic, dogs can be trained quickly before specific laboratory methods are available, thus helping with isolation or quarantine of infected patients to mitigate the risk of further spread.

Although the use of sniffer canines for disease diagnostics is a promising option, the deployment and routine use of this strategy will require clear regulatory guidelines.

REFERENCES

1. McCulloch., M., Jezierski, T., Broffmann, M., Hubbard, A., Turner, K., Janecki T. (2006). Diagnostic accuracy of canine scent detection in early- and late-stage lung and breast cancers. Integrative Cancer Therapies, 5:30–9.
2. Cambau, E., Poljak, M. (2020). Sniffing animals as a diagnostic tool in infectious diseases. Clinical Microbiology and Infection, 26:431–5.
3. Hardin, D.S., Anderson, W., Cattet, J. (2015). Dogs can be successfully trained to alert to hypoglycemia samples from patients with type 1 diabetes. Diabetes Therapy, 6:509–17.
4. Catala, A., Grandgeorge, M., Schaff, J-L., Cousillas, H., Hausberger, M., Cattet, J. (2019). Dogs demonstrate the existence of an epileptic seizure odour in humans. Scientific Reports, 9:4103. doi: 10.1038/s41598-019-40721-4.
5. Guest, C., Pinder, M., Doggett, M., Squires, C., Affara, M., Kandeh, B., et al. (2019). Trained dogs identify people with malaria parasites by their odour. The Lancet Infectious Diseases, 19:578–80.
6. Taylor, M., McCready, J., Broukhanski, G., Kirpalaney, S., Lutz, H., Powis, J. (2018). Using dog scent detection as a point-of-care tool to identify toxigenic Clostridium difficile in stool. Open Forum Infectious Diseases, 5, 1–4.
7. Angle, T.C., Passler, T., Waggoner, P.L., Fischer, T.D., Rogers, B., Galik, P.K., et al. (2016). Real-time detection of a virus using detection dogs. Frontiers in Veterinary Science, 2:1–6.
8. Larkin, H. (2022). Dogs May Reliably Detect SARS-CoV-2 Infections at Mass Events. Journal of the American Medical Association, 328(23):2294. doi:10.1001/jama.2022.20040.
9. Jendrny, P., Schulz, C., Twele, F. et al. (2020). Scent dog identification of samples from COVID-19 patients – a pilot study. BMC Infectious Diseases, 20, 536. https://doi.org/10.1186/s12879-020-05281-3.
10. Charles, M., Zurberg, T., Woznow, T., Eckbo, E., Asku, L., Pescador, R., Gomez, L.N., O'Neill, R., Thompson, E., and Bryce, E. (2023). Deployment of canine scent detection for the screening of COVID-19 on pillowcases of residents in a long-term care setting – a pilot study. Canadian Journal of Infection Control, 38(43), 128-133.
11. World Health Organization. SARS-CoV-2 antigen-detecting rapid diagnostic tests: an implementation guide, 2020. Available: https://www.who.int/publications/i/item/9789240017740 [Accessed 30 Jul 2023].
12. Shirasu, M., Touhara, K. (2011). The scent of disease: volatile organic compounds of the human body related to disease and disorder. Journal of Biochemistry, 150:257–66.
13. Issitt, T., Wiggins, L., Veysey, M., Sweeney, S.T., Brackenbury, W.J., Redeker, K. (2022). Volatile compounds in human breath: critical review and meta-analysis. Journal of Breath Research, 16:024001. doi: 10.1088/1752-7163/ac5230.
14. Issel-Tarver, L., Rine, J. (1996). Organization and expression of canine olfactory receptor genes. Proceedings of the National Academy of Sciences of the United States of America, 93:10897–902.
15. Maurer, M., McCulloch, M., Willey, A. M., Hirsch, W., & Dewey, D. (2016). Detection of bacteriuria by canine olfaction. In Open Forum Infectious Diseases, 3(2), p. ofw051). Oxford University Press.
16. Alabama A&M and Auburn universities. (2011). The Dog's Sense of Smell. UNP-0066. Ava https://ourdogssavelives.org/wp-content/uploads/2012/02/Dogs-Sense-of-Smell.pdf.
17. Kokocińska-Kusiak, A., Woszczyło, M., Zybala, M., Maciocha, J., Barłowska, K., Dzięcioł, M. (2021). Canine Olfaction: Physiology, Behavior, and Possibilities for Practical Applications. Animals (Basel), 21, 11(8):2463.
18. Jendrny, P., Twele, F., Meller, S. et al. (2021). Canine olfactory detection and its relevance to medical detection. BMC Infectious Diseases 21, 838. https://doi.org/10.1186/s12879-021-06523-8.