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Epidemiology of Histopathologically Diagnosed Mycoses: The Ibadan 37 Years Experience

B. A. F. Ngwu[1*], A. O. Oluwasola[2], F. E. Iyare[3], J. O. Ogunbiyi[2] and E. E. Akang[2]

[1]Department of Medical Microbiology, Faculty of Clinical Medicine, College of Health Sciences, Ebonyi State University, PMB 077, Abakaliki, Nigeria.
[2]Department of Pathology, University College Hospital, Ibadan, Nigeria.
[3]Department of Histopathology/Morbid Anatomy, Ebonyi State University Teaching Hospital, Abakaliki, Nigeria.

Authors' contributions

This work was carried out in collaboration between all authors. Authors BAFN and EEA designed the study, wrote the protocol, and wrote the first draft of the manuscript. Authors AOO and FEI managed the literature searches and histopathological diagnosis of the archival materials. Authors BAFN and JOO revised the original manuscript and harmonized the entire study. All authors read and approved the final manuscript.

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ABSTRACT

Background: Recent studies suggest that the occurrence of mycotic infections is increasing worldwide, due to predisposing factors such as immunosuppression from chemotherapy, surgery, HIV/AIDS and debilitating diseases, but there is paucity of information regarding fungal infections in our environment.
Aim: This study aimed to characterise mycoses diagnosed histopathologically in the Department of Pathology, University College Hospital (UCH), Ibadan between 1970 and 2006.
Methods: The surgical pathology and autopsy records of all mycoses diagnosed during the study period were retrieved and analysed. One hundred and eighty-six mycoses were recruited.
Results: There was a progressive decline in the annual occurrence of mycoses from 19.7% to

**Corresponding author: Email: bethfrancis5@yahoo.com;*

1.1%. The cases comprised 121 males and 65 females, whose ages ranged from 6 weeks to 80 years, with 68.3% being less than 40 years of age. The mean age of the male patients (29.9±18.4 years) was not significantly different from that of the females (27.4±18.2 years), t = 0.867, df = 186, p = 0.387. The most common mycotic infections were African histoplasmosis (28%), aspergillosis (12.4%), mycetoma (9.7%), candidiasis (8.6%) and actinomycosis (7%). Systemic mycoses accounted for 62%, followed by subcutaneous mycoses (21%), cutaneous mycoses (11%) and superficial mycoses (6%). The most common sites involved were the skin (23.7%), upper and lower limbs (15.6%), nose (11.3%) and lungs (7%).

Conclusion: The present study has demonstrated that fungal infections are common and account for significant morbidity and disease burden in our environment.

Keywords: Histopathological diagnosis; fungal infections; epidemiology of mycosis; Ibadan experience; Nigeria.

1. INTRODUCTION

Fungal infections occur throughout the world [1-10], but some of them are more predominant or endemic in certain geographic areas; e.g. *Histoplasma capsulatum var. capsulatum* infections occur along the Mississippi River Valley, *Coccidioides immitis* in the southwest, and *Blastomyces dermatitidis* in the central and southeastern states of USA [7,11]. In a population based laboratory active surveillance study of invasive mycotic infections in California USA [4]; candidiasis was the most common followed by cryptococcal infection, coccidioidomycosis, aspergillosis, and then histoplasmosis in that order. The low prevalence of histoplasmosis they observed may be due to geographical differences in the occurrence of histoplasmosis which is endemic in Africa and southern USA but not in California. In a meta-analysis of deep mycosis in India, Mishra and Sandhu [12], observed that cryptococcosis is the most common mycosis in India 28.6%, followed by nocardiosis 19.8%, candidiasis 17.6%, histoplasmosis 9.9%, actinomycosis 9.9%, and aspergillosis 8.8%. The variation in the observed prevalence in this study and those of USA, may be as a result of geographical variation in the occurrence of the causative organisms for these mycoses.

In Africa, histoplasmosis by *Histoplasma duboisii*, aspergillosis, sporotrichosis, mycetoma, and cryptococcosis are common [2,13-16]. In Nigeria fungal infections have been reported from all part of the country; from south western Nigeria, [17-24], from south eastern Nigeria: [25-31]; from the south southern Nigeria: [32,33]; from Northern Nigeria: [34]. However, most of these reports were done in the 1960s and 1970s and therefore need up dating. Majority of these cases are case reports and review articles and only represent incidental finding in the clinical practice.

Fungi are eukaryotic organisms that grow as yeasts, moulds or a combination of both (i.e. dimorphism) [5,35-38]. The moulds, are characterized by filamentous, vegetative cells called hyphae. Yeasts are unicellular organisms, which reproduce vegetatively by budding. The dimorphic fungi grow as mycelial hyphae in nature and as yeasts in the human body. Examples include *Histoplasma capsulatum,* and *Coccidioides immitis.* They grow as moulds at 25°C, and as yeasts at 37°C [39,40].

Clinically fungal infections are classified as: a. superficial mycoses b. subcutaneous mycoses c. systemic mycoses [41-44] and d. opportunistic mycoses.

The superficial mycoses also called cutaneous mycoses are fungal diseases that are confined to the outer layers of the skin, nail, or hair**,** (keratinised layers) rarely invading the deeper tissue or viscera. The fungi involved are called dermatophytes, including *Epidermophyton, Trichophyton* and *Microsporum* species, which are responsible for ringworm [7,35,45].

The subcutaneous mycoses are confined to the subcutaneous tissue and only rarely spread systemically. They usually form deep, ulcerated skin lesions or fungating masses, most commonly involving the lower extremities. The causative organisms are soil saprophytes, which are introduced through trauma to the feet or legs. Examples include *Sporothrix schenckii* and *Madurella mycetomi*, which are responsible for sporotrichosis and mycetoma, respectively [28,39].

The systemic mycoses may involve deep viscera and become widely disseminated. Each fungus type has its own predilection for various organs, which will be described as we discuss the individual diseases. Examples of causative organisms include *Histoplasma* species (histoplasmosis) and *Coccidioides immitis* (coccidioidomycosis) [26,31] (Table 1).

The Opportunistic mycoses are caused by ubiquitous saprophytes and occasional pathogens that invade the tissues of those patients who have: 1) Predisposing disease (diabetes, cancer, leukaemia) or 2) Predisposing conditions (agammaglobulinaemia, steroid or antibiotic therapy). Examples of opportunistic mycoses include systemic candidiasis, mucormycosis and cryptococcosis [27,44].

The aims and objectives of this study are to review all the cases of mycoses diagnosed in the Department of Pathology, University College Hospital (UCH), Ibadan in the last thirty seven years from 1970 to 2006 since recent studies suggest that the occurrence of mycotic infections are increasing worldwide, due to predisposing factors such as immunosuppression, chemotherapy, surgery, HIV/AIDS and other debilitating diseases; and also to provide information regarding fungal infections that are diagnosed histopathologically in our environment.

2. MATERIALS AND METHODS

2.1 Data Collection and Analysis

This study analysed mycoses histopathologically diagnosed in the Department of Pathology University College Hospital, Ibadan, Nigeria over a thirty-seven year period from January 1970 to December 2006. The slides of all the patients with fungal infections recorded in the surgical daybooks and autopsy reports of the department were retrieved and reviewed. Where the original slides had faded or could not be found, their paraffin blocks were retrieved and fresh slides made from them. Special stains such as Gomori's methenamine silver stain and periodic acid Schiff stains were done where necessary to confirm the diagnosis.

The following data were obtained from the request forms accompanying the surgical specimens and the surgical day book of the department: Age, sex, site of the lesion and clinical diagnosis. The same data were also extracted from autopsy records.

2.2 Statistical Analysis

The data was statistically analysed using the SPSS 14.0 software programme.

2.3 Ethical Issues

Ethical approval for the study was obtained from the joint University of Ibadan-University College Hospital, Ibadan Ethical Review Committee.

2.4 CONSENT

Approval and consent was granted by the institutional ethics committee on behalf of the hospital and archival material of the patients since no direct contact with the patients, only hospital records and materials were used for this study.

3. RESULTS

A total of 186 cases of mycoses were observed during the 37-year period covered by the study. During this same period, a total number of 166,857 cases were received in the Department of Pathology, comprising 153,916 (92.2%) surgical biopsy specimens and 12,941 (7.8%) autopsy cases. Thus, mycoses accounted for 0.11% of all cases (Table 1). The yearly occurrence of mycoses as observed in this study ranged from 1-12 cases with a mean yearly occurrence of 5 cases. There was a progressive decline in the annual percentage occurrence of mycoses from 19.7% between 1970 and 1974 to 1.1% between 2005 and 2006.

The 186 patients consisted of 121 males and 65 females, giving a male to female gender ratio of 1.86:1. The ages of the patients ranged from 10 weeks to 80 years, with a mean age of 29±18.3 years. One hundred and twenty-seven (68.3%) of the patients were below 40 years of age. There was a progressive decline in the occurrence of mycotic infections after the fifth decade of life in both sexes. The mean age of the male patients (29.9±18.4 years) was not significantly different from that of the females (27.4±18.2 years), $t = 0.867$, $df = 186$, $p = 0.387$.

As is shown in Table 2, the most common mycotic infection encountered in the present study was African histoplasmosis caused by *Histoplasma capsulatum var. duboisii*, (28%), Figs. 1A&B.

Other fungal infections in descending order of frequency included aspergillosis (12.4%), Fig. 1d; mycetoma (9.7%) Fig. 1c; candidiasis (8.6%) and actinomycosis (7%). mucormycosis (1.6%), cryptococcosis (1.6%), rhinosporidiosis (0.5%) and botryomycosis were the least common fungal infections encountered.

Table 1. Source of specimens and yearly occurrence of mycoses

Year	Total surgical specimens	Total autopsies	Total specimen reviewed	Yearly occurrence of mycosis	(%)
1970-1974	24,938	2,499	22,023	37	(19.9)
1975-1979	24,830	1,628	26,458	29	(15.6)
1980-1984	21,502	1,707	23,209	26	(14.0)
1985-1989	26,520	1,829	28,349	24	(12.9)
1990-1994	16,483	1,646	18,129	22	(11.8)
1995-1999	14,648	1,673	16,321	36	(19.4)
2000-2004	18,167	1,504	19,671	10	(5.4)
2005-2006	6,727	455	7182	2	(1.1)
Total	153,916	12,941	166,857	186	(100)

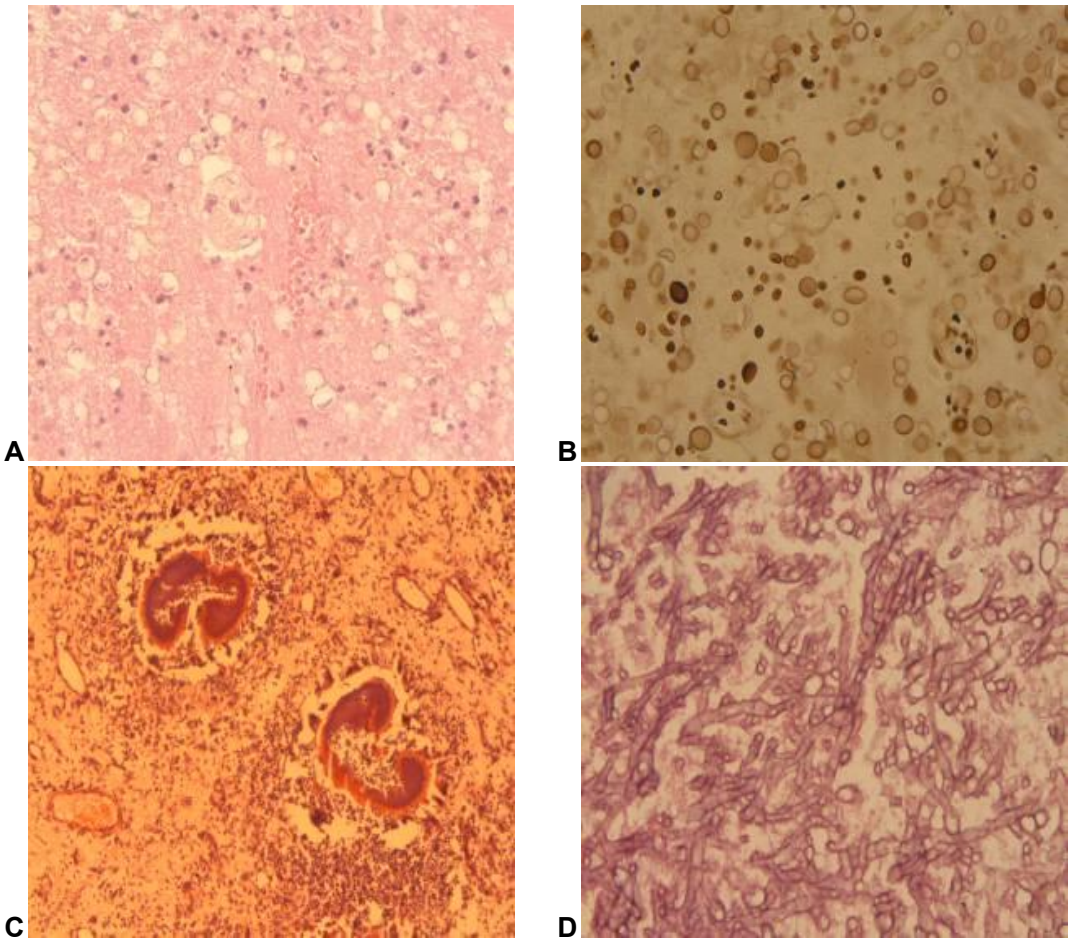

Fig. 1. Some of the observed fungal organisms

A. Histoplasma duboisii from caseous epidural spinal mass in a five-year old female. Haematoxylin and eosin, X400, B. Histoplasma duboisii from right thigh mass in a 10-year old female. Gomori's Methenamine silver stain X400, C. Actinomycotic mycetoma from a chronic leg ulcer in a 42-year-old female. Haematoxylin and eosin, X100, D. Aspergilloma from right nasal mass of a 52-year-old female. Haematoxylin and eosin, X400

The classification of the various types of mycoses, which is based on the level of tissue affected. Systemic (deep) mycoses had the highest prevalence of 115 cases (62%), followed by 39 subcutaneous mycoses (21%), 21 cutaneous mycoses (11%) and 11 superficial mycoses (6%), Fig. 2. The various sites of the body affected are shown in Table 3. The most common site involved was the skin, accounting for 44 cases (23.7%). The second most common site affected was the upper and lower limbs, accounting for 29 cases (15.6%). The third most common location for mycotic infections was the nose, accounting for 21 cases (11.3%), as shown in Table 3. Pulmonary mycoses accounted for 13 cases (7%). Other sites of fungal infection in descending order of frequency included the gastrointestinal tract (6.5%), nasopharynx (4.3%), liver (4.3%), brain (3.2%) and bone (3.2%) as shown in Table 3.

4. DISCUSSION

In the present study, mycotic infections accounted for 0.11% of all surgical biopsy and autopsy specimens reviewed in the Department of Pathology during the study period. The yearly occurrence of mycoses as observed in this study range from 1-12 cases with a mean yearly occurrence of 5 cases. This indicates that mycotic infections are relatively common in our environment. In a review of deep mycoses from Calabar, South Eastern Nigeria, fungal infections accounted for 0.35% of all surgical biopsy specimens, which is higher than the prevalence observed in our study [29]. The difference in the prevalence rates may be due to the fact that they used only surgical biopsy specimens (6,500 cases), without autopsies and that they studied only three years, while we studied both autopsies and surgical biopsy specimens (166,857 cases) received over a period of thirty-seven years, Table 1.

We also observed that there was a progressive decline in the occurrence of fungal infections during the 37-year period of the study. This decline may be the result of improved medical services and health education, with improvement of living standards in the local population. This observation does not agree with the expected rise in occurrence of fungal infection and the observations in other parts of the world where HIV/AIDS and chronic debilitating illnesses such as diabetes mellitus and tuberculosis have increased the occurrence of fungal infections [37-40]. Secondly, this study predates HIV/AIDS era by at least 10 yrs (1970-1980), the yearly occurrence of mycoses diagnosed histopathologically in pre HIV/AIDS era are more than those observed during the HIV/AIDS era, even though there was an isolated increase between 1995-1999.

The male to female ratio in this study was 1.86:1. This male predominance is most probably due to greater male exposure to the causative organisms than occurs in females. Traditionally, in Nigeria, farming is the major occupation and according to Gugnani, in a study from Enugu, Nigeria, mycotic infections tend to be relatively common in farmers [23]. Interestingly however, for the 43 patients whose case notes were retrieved, only one patient was a farmer, majority of these patients were students and traders. This observation is most likely due to accessibility to hospital services.

Table 2. Sex distribution and histological diagnosis of mycotic infections

No	Histological diagnosis	Male	Female	Total	%
1	Histoplasmosis	33	19	52	28.0
2	Aspergillosis	13	10	23	12.4
3	Mycetoma	16	2	18	9.7
4	Candidiasis	9	7	16	8.6
5	Actinomycosis	8	5	13	7.0
6	Phycomycosis	7	3	10	5.4
7	Pityriasis versicolor	8	2	10	5.4
8	Rhinophycomycosis	5	3	8	4.3
9	Chromoblastomycosis	6	0	6	3.2
10	Dermatophytosis	2	4	6	3.2
11	Mucormycosis	0	3	3	1.6
12	Cryptococcosis	1	2	3	1.6
13	Rhinosporidiosis	0	1	1	0.5
14	Botryomycosis	1	0	1	0.5
15	Unspecified fungal infections	12	4	16	8.6
Total		**121**	**65**	**186**	**100**

Table 3. Site distribution of specific mycotic infections

Sites	Ac	As	Ca	Ch	De	Hi	Mu	My	Ph	Rph	NS	Pv	Rsp	Bo	Cry	Total	%
Skin	1	-	-	3	5	14	-	3	3	-	5	1-	-	-	-	44	23.7
Upper and lower limbs	2	-	1	3	-	6	-	13	3	-	1	-	-	-	-	29	15.6
Nose	1	8	-	-	-	-	3	1	-	6	1	-	1	-	-	21	11.3
Lung	-	10	3	-	-	-	-	-	-	-	-	-	-	-	-	13	7
Gastrointestinal tract	1	-	6	-	-	2	-	-	-	-	3	-	-	-	-	12	6.5
Nasopharynx	5	-	2	-	-	-	-	-	-	1	-	-	-	-	-	8	4.3
Liver	-	-	-	-	-	8	-	-	-	-	-	-	-	-	-	8	4.3
Brain	-	1	-	-	-	3	-	-	-	-	-	-	-	-	2	6	3.2
Bone	-	-	-	-	-	1	-	1	1	-	2	-	-	1	-	6	3.2
Lymph node	1	-	-	-	-	3	-	-	-	-	-	-	-	-	-	4	2.2
Chest wall	-	-	1	-	-	3	-	-	-	-	-	-	-	-	-	4	2.2
Female genital tract	2	-	1	-	-	-	-	-	-	-	-	-	-	-	1	4	2.2
Ear	-	2	-	-	1	-	-	-	-	-	-	-	-	-	-	3	1.6
Face	-	1	-	-	-	2	-	-	-	-	-	-	-	-	-	3	1.6
Neck	-	-	-	-	-	3	-	-	-	-	-	-	-	-	-	3	1.6
Hip	-	-	-	-	-	1	-	-	1	-	1	-	-	-	-	3	1.6
Upper and lower jaws	-	-	-	-	-	3	-	-	-	-	-	-	-	-	-	3	1.6
Eye	-	1	-	-	-	-	-	-	-	-	1	-	-	-	-	2	1.1
Kidney	-	-	1	-	-	-	-	-	1	-	-	-	-	-	-	2	1.1
Spinal cord	-	-	-	-	-	2	-	-	-	-	-	-	-	-	-	2	1.1
Muscle	-	-	-	-	-	-	-	-	1	-	1	-	-	-	-	2	1.1
Omentum and retroperitoneum	1	-	-	-	-	1	-	-	-	-	-	-	-	-	-	2	1.1
Mouth	-	-	-	-	-	-	-	-	-	1	-	-	-	-	-	1	0.5
Heart	-	-	1	-	-	-	-	-	-	-	-	-	-	-	-	1	0.5
Total	**13**	**23**	**16**	**6**	**6**	**52**	**3**	**18**	**10**	**6**	**16**	**10**	**1**	**1**	**3**	**186**	**100**

KEY- Ac- Actinomycosis, As- Aspergillosis, Ca- Candidiasis, Ch- Chromoblastomycosis, De- Dermatophytosis, Hi- Histoplasmosis, Mu- Mucormycosis, My- Mycetoma, Ph- Phycomycosis, Rph- Rhinophycomycosis, NS- Not specified, Pv- Pityriasis versicolor, Rsp- Rhinosporidiosis, Bo- Botryomycosis, Cry- Cryptococcosis

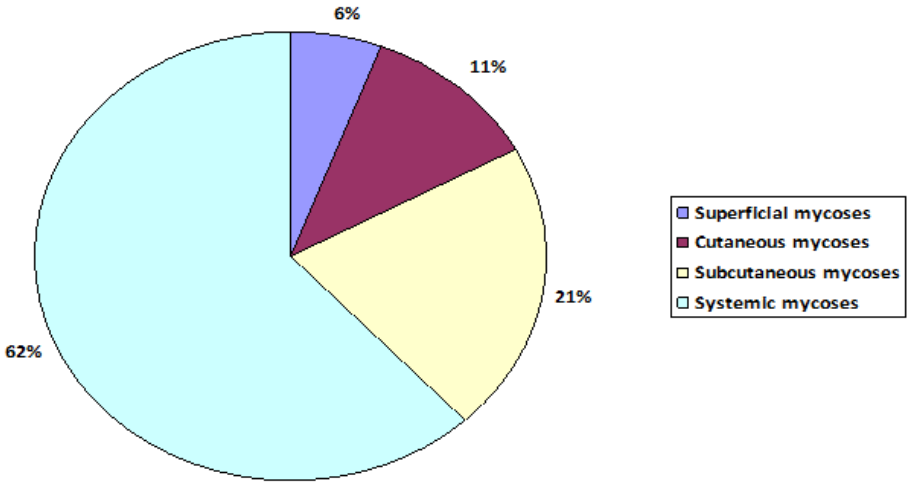

Fig. 2. Clinical classification of mycosis

Most patients with mycotic infections in the present study were below 40 years of age. Fungal infections can occur at all ages ranging from infancy to elderly age, as demonstrated by the present study and by other workers [4,22,29]. The predominance of fungal infection in patients less than 40 years of age suggests that there may be early exposure to the causative agents of mycoses, which are endemic in some areas and could infect individuals early in life or during early adult life from occupation or following travel to endemic areas.

By the age of 40 years and above, enough immunity has been developed and proper means of preventing the diseases learnt and applied hence the reduced incidence above 40 years of age. The most prevalent mycosis encountered in this study was African histoplasmosis, which occurred in 28%, followed by aspergillosis in 12.4%, mycetoma in 9.7%. In a surgical biopsy study of deep mycoses in Calabar, Nigeria by Khalil et al. [33], it was observed that African histoplasmosis was the most prevalent deep mycoses in the area studied, followed by mycetoma and actinomycosis, which agrees with our findings in Ibadan, Nigeria.

This study shows that systemic (deep) mycoses had the highest prevalence of 62%, followed by subcutaneous mycoses (21%), cutaneous mycoses (11%) and superficial mycoses (6%). This distribution is largely due to the bias of the study for histopathological biopsy material. Superficial and cutaneous mycoses are usually diagnosed using microbiological methods, which might explain the relatively low occurrence of dermatophyte infections and mucocutaneous candidiasis in the present study [35,45].

The most common site of the body affected by mycoses was the skin (23.7%), followed by the limbs (15.6%), the nose (11.3%), and the lungs (7%). In a study by Ikpatt from Calabar, it was observed that the skin, bone and lymph nodes were the most common sites affected [46].

5. CONCLUSION AND RECOMMENDATION

In conclusion, the present study has demonstrated that various fungal infections are common in our environment and account for significant morbidity in males and young adults. African histoplasmosis is the most common infection and the skin the most common site. It is therefore important that clinicians should have a high index of suspicion for mycotic infections and institute appropriate histopathological and microbiological investigations in all patients.

6. TAKE HOME MESSAGES

Mycoses especially deep mycoses are diagnosed using histopathological methods. The epidemiology shows that males and females of all age groups are affected if exposed to the causative organisms. There is a decline in annual incidence of mycoses diagnosed histopathologically as opposed to anticipated increase due to improved living conditions. The common mycoses are: Histoplasmosis; Aspergillosis; Mycetoma; Candidiasis; and Actinomycosis. These mycoses cause severe

morbidity and increased disease burden in our environment.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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