The global burden of chromoblastomycosis

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Abstract

Background
Chromoblastomycosis (CBM), represents one of the primary implantation mycoses caused by melanized fungi widely found in nature. It is characterized as a Neglected Tropical Disease (NTD) and mainly affects populations living in poverty with significant morbidity, including stigma and discrimination.

Methods and findings
In order to estimate the global burden of CBM, we retrospectively reviewed the published literature from 1914 to 2020. Over the 106-year period, a total of 7,740 patients with CBM were identified on all continents except Antarctica. Most of the cases were reported from South America (2,619 cases), followed by Africa (1,875 cases), Central America and Mexico (1,628 cases), Asia (1,390 cases), Oceania (168 cases), Europe (35 cases), and USA and Canada (25 cases). We described 4,022 (81.7%) male and 896 (18.3%) female patients, with the median age of 52.5 years. The average time between the onset of the first lesion and CBM diagnosis was 9.2 years (range between 1 month to 50 years). The main sites involved were the lower limbs (56.7%), followed by the upper limbs (19.9%), head and neck (2.9%), and trunk (2.4%). Itching and pain were reported by 21.5% and 11%, respectively. Malignant transformation was described in 22 cases. A total of 3,817 fungal isolates were cultured, being 3,089 (80.9%) Fonsecaea spp., 552 (14.5%) Cladophialophora spp., and 56 Phialophora spp. (1.5%).

Conclusions and significance
This review represents our current knowledge on the burden of CBM world-wide. The global incidence remains unclear and local epidemiological studies are required to improve these
Chromoblastomycosis (CBM), represents one of the primary implantation mycoses caused by melanized fungi widely found in nature. It is characterized as a Neglected Tropical Disease and mainly affect populations living in poverty with significant morbidity, including stigma and discrimination. The global incidence of CBM remains unclear because this mycosis is not a mandatory notifiable disease and most of the literature consists of case reports or small series incompletely characterized. Although several authors suggest that the CBM global burden may be comparable to mycetoma, its geographic distribution and incidence rates in different endemic areas have never been widely characterized in the medical literature. We retrospectively conducted a comprehensive systematic review of all medical literature published between 1914 and 2020 to better characterize the prevalence rates, geographic distribution, and clinical aspects of CBM in all continents. All reviewed data were not a substitute for high quality epidemiological study or comprehensive surveillance but do provide an approximation of the burden by country. Information generated corroborate the WHO recognition of CBM as a NTD and provides helpful support for all local governments interested in developing specific policies and actions for preventing, diagnosing and assisting patients with CBM.

Introduction
Chromoblastomycosis (CBM), together with mycetoma, represents one of the primary implantation mycoses caused by melanized or black fungi widely found in nature that may infect agricultural workers after transcutaneous inoculation during their daily activities [1–4]. Chromoblastomycosis is primarily an occupational disease associated with a considerable social stigma and severe personal and family socioeconomic consequences [1,3,5,6]. It is mainly caused by Fonsecaea spp., followed by Cladophialophora, Phialophora, and Rhinocladiaella. The genera Fonsecaea includes three closely related siblings represented by F. pedrosoi, F. monophora, and F. nubica. The genus Cladophialophora spp. contains two related siblings: C. carrionii that may be found in clinical samples and nature, whereas C. yegresii is exclusively found in the environment [1,7–12]. These agents present some peculiarities in terms of geographic distribution and ecological niches. The clinical manifestations and therapeutic response of the patients differs by infecting fungus.

CBM is nowadays characterized as a Neglected Tropical Disease (NTD) because (a) it mainly affects populations living in poverty causing significant morbidity and mortality–including stigma and discrimination; (b) it is mostly found in tropical and sub-tropical areas; (c) it may be controlled or eradicated by applying one or more of the five public health strategies adopted by the Department for Control of NTDs; (d) it has been neglected by research when it comes to developing new diagnostics, medicines, and other control tools [1,3–5]. The process of recognizing CBM as NTD began at the meeting held in São Luís, state of Maranhão, Brazil, in 2011, when the disease’s centenary was celebrated. After an application by the Global
Action Fund for Fungal Infections with support from the governments of Brazil and Madagascar, World Health Organization (WHO) incorporated CBM into the NTD portfolio in category B in 2017, together with mycetoma and other deep mycoses [1,7].

In most endemic areas, health services do not have professionals trained in the early diagnosis and clinical management of CBM. Skills in skin biopsy, direct microscopy, histopathology with fungal stains fungal culture is often lacking. Effective antifungal treatment rarely included in universal health coverage and government insurance. Long term itraconazole at 400mg daily or variable terbinafine dose are not be available in many countries and is expensive and requires monitoring [1,3,6–9]. Patients are usually diagnosed after several years of clinical manifestations, and medication is unavailable or unaffordable, two factors that may increase the risk of sequelae and further social stigma [1,3]. In addition, CBM in some patients is complicated by continuous bacterial co-infection and later neoplastic transformation of the CBM lesions into epidermoid carcinoma may occur [1,3].

The global incidence of CBM remains unclear. Only a few population epidemiology studies have been done. This mycosis is not a mandatory notifiable disease and most of the literature consists of case reports or small series incompletely characterized. Although several authors suggest that the CBM global burden may be comparable to mycetoma, its geographic distribution and incidence rates in different endemic areas have never been widely characterized in the medical literature.

We conducted a comprehensive systematic review of all medical literature published between 1914 and 2020 to characterize better the prevalence rates and geographic distribution of CBM in all continents. Data generated in this paper corroborate the WHO recognition of CBM as a NTD and provides helpful support for all local governments interested in developing specific policies and actions for preventing, diagnosing, and assisting patients with CBM [1,5–7,13,14].

Methods

Our plan for literature review included the selection of all articles addressing the epidemiology of chromoblastomycosis in the world that were published in four different languages (English, Spanish, French and Portuguese) between 1914 and 2020 and listed in the PubMed (https://www.ncbi.nlm.nih.gov/pubmed/) and Bireme (http://portal.revistas.bvs.br/) with access to “LILACS”, “IBECS”, “MEDLINE”, “Cochrane Library” and “SciELO” databases. The terms used to select papers included “chromoblastomycosis”, “chromomycosis”, “neglected mycoses”, “subcutaneous mycoses” or “implantation fungal infections”. Letters to the editor and abstracts available published in congress or conferences were also searched and identified. The literature review was complemented by reviewing the reference lists of all studies selected to be sure that we did not miss any relevant references. Due to the large number of single case reports published in some highly endemic countries, papers from Mexico, Brazil, Venezuela, Colombia, Madagascar, India, China, Japan, and Australia were only included if they reported at least 5 patients. Review papers were selected only to find references to original papers to avoid case duplication [2,15]. All papers in this comprehensive review were able to meet the main diagnostic criteria of CBM: presence of dark pigmented and thick-walled muriform cells in a biological sample. Whenever there was doubt about this finding, the paper was excluded from the analysis.

Epidemiological and clinical data of all cases of CBM were collected using a standard clinical form. The variables that were systematically assessed along the literature review included year and country of publication, the number of cases, the period of cases collection, age, gender, history of cutaneous trauma and previous agricultural work, time from onset of symptoms to diagnosis (years), symptoms, clinical pattern of the lesions and severity of the disease,
malignant transformation and clinical management (physical methods such as surgery, ther-motherapy, laser therapy, and photodynamic therapy; antifungal drugs with itraconazole, ter-binafine, iodide, flucytosine) [1,3].

To determine the prevalence rate of CBM in each country, we used the method described by Van de Sande [2]. The number of reported cases along each year in all countries was divided by the total population of each country in the selected period. Population data for each country in each collection period was extracted from the website www.indexmundi.com/facts/ indicators/SP.POP.TOTL/compare#country=ma) [2]. As an example 71 cases of CBM were reported between 1978 and 1993 in Sri Lanka, with a mean of 4.73 cases/year. The average population of this country in this period was 16,283,921 inhabitants. In this case, the prevalence of CBM in Sri Lanka was defined as 0.29 cases per 1 million inhabitants.

**Results**

Our review identified a total of 208 articles that were published in English (119 articles), Spanish (42 articles), French (39 articles), and Portuguese (8 articles), accounting for 7,740 cases of CBM on all continents except Antarctica. The main characteristics of CBM are illustrated by countries and continents, as summarized in Tables 1 and S1. The worldwide distribution and prevalence of CBM cases are shown in Fig 1.

Table 1. Epidemiology and main clinical aspects of 7,740 cases of chromoblastomycosis documented in 5 different continents.

| Variables                  | South America (n = 2,619) | Central America, The Caribbean, and Mexico (n = 1,628) | Africa (n = 1,875) | Asia (n = 1,390) | Europe (n = 35) | USA and Canada (n = 25) | Oceania (n = 168) | Total (n = 7,740) |
|----------------------------|---------------------------|--------------------------------------------------------|--------------------|-----------------|-----------------|------------------------|-----------------|-----------------|
| Age (years), (mean, range) | 57.1 (12y-93y)            | 53.3 (9y-90y)                                          | 47.9 (2y-73y)      | 49.7 (7y-90y)   | 60.9 (17y-85y) | 55.7 (19y-79y)         | 53.8 (19y-91y)  | 52.5 (2y-93y)   |
| Male/Female n (%)          | 1,237 (87.4%) / 178 (12.6%) | 802 (76.7%) / 243 (23.3%)                              | 1,338 (83.6%) / 263 (16.4%) | 463 (71.6%) / 183 (28.4%) | 27 (77.2%) / 8 (22.8%) | 22 (88%) / 3 (12%) | 133 (88%) / 18 (12%) | 4,022 (81.7%) / 896 (18.3%) |
| Rural occupation           | 927                       | 642                                                    | 129                | 162             | 2               | 13                     | 20              | 1,895           |
| History of trauma          | 276                       | 117                                                    | 20                 | 116             | 18              | 3                      | 18              | 568             |
| Delay between onset and diagnosis (mean, years) | 10.8 (1mo-50y) | 13.4 (2mo-28y)                                          | 8.7 (4mo-31y)      | 8.3 (1mo-40y)   | 13.6 (3mo-31y) | 4.8 (2m-20y)          | 8.02 (1mo-30y) | 9.2 (1mo-50y)  |
| Sites of lesions           |                           |                                                        |                    |                 |                 |                        |                 |                 |
| Lower limbs                | 1,021                     | 472                                                    | 1,340              | 308             | 16              | 6                      | 34              | 1,917           |
| Upper limbs                | 301                       | 288                                                    | 196                | 214             | 11              | 16                     | 94              | 1,120           |
| Face, head, neck           | 47                        | 13                                                     | 20                 | 73              | 1               | 2                      | 2               | 158             |
| Trunk                      | 54                        | 42                                                     | 32                 | 50              | 2               | 0                      | 0               | 180             |
| Unusual sites              | 11                        | 2                                                      | 4                  | 39              | 4               | 1                      | 0               | 61              |
| Types of lesions           |                           |                                                        |                    |                 |                 |                        |                 |                 |
| Plaque                     | 248                       | 39                                                     | 153                | 109             | 4               | 11                     | 1               | 565             |
| Verrucous                  | 329                       | 162                                                    | 131                | 76              | 0               | 7                      | 5               | 710             |
| Tumoral                    | 87                        | 6                                                      | 558                | 9               | 1               | 0                      | 2               | 663             |
| Nodular                    | 84                        | 46                                                     | 117                | 24              | 1               | 5                      | 8               | 285             |
| Scarring                   | 37                        | 1                                                      | 32                 | 2               | 2               | 0                      | 2               | 75              |
| Ulcer                      | 47                        | 7                                                      | 27                 | 16              | 1               | 7                      | 0               | 105             |
| Etiologic agents           | 864                       | 703                                                    | 1,406              | 750             | 30              | 21                     | 43              | 3,817           |
| Fonseca spp.               | 759 (87.9%)               | 676 (96.2%)                                            | 1,017 (72.3%)      | 569 (75.8%)     | 24 (80%)        | 15 (71.5%)              | 29 (67.4%)      | 3,089 (80.9%)   |
| Cladophialophora spp.      | 82 (9.5%)                 | 11 (1.6%)                                              | 376 (26.8%)        | 68 (9%)         | 1 (3.3%)        | 0                      | 14 (32.6%)      | 552 (14.5%)     |
| Phialophora spp.           | 12 (1.4%)                 | 5 (0.7%)                                               | 8 (0.6%)           | 24 (3.2%)       | 1 (3.3%)        | 6 (28.5%)               | 0               | 56 (1.5%)       |
| Rhinocladiella spp.        | 5 (0.6%)                  | 1 (0.1%)                                               | 0                  | 2 (0.3%)        | 1 (3.3%)        | 0                      | 0               | 9 (0.2%)        |
| Other and not identified agent | 6 (0.6%)                 | 10 (1.4%)                                              | 4 (0.3%)           | 87 (11.7%)      | 3 (10.1%)       | 0                      | 0               | 110 (2.9%)      |

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A  Total reported cases of chromoblastomycosis

B  Chromoblastomycosis cases per 1 million inhabitants

Prevalence:
- <0.03 cases/1M
- 0.03–0.15 cases/1M
- 0.16–0.30 cases/1M
- 0.31–1.34 cases/1M
- 1.35–4.70 cases/1M
- No data

Absolute number:
- 1–2 cases
- 3–7 cases
- 8–24 cases
- 25–155 cases
- 156–1323 cases
- No data
Chromoblastomycosis in Central America, the Caribbean and Mexico

A total of 26 articles were identified which described 1,628 patients who were documented in Mexico (603 cases) [16], Dominican Republic (450 cases) [17], Cuba (319 cases) [18–25], Costa Rica (153 cases) [26–30], Honduras (52 cases) [31–34], Jamaica (31 cases) [35], Panama (8 cases) [36–39], Puerto Rico (7 cases) [40], and Guadalupe Islands (5 cases) [41]. Data from the Dominican Republic relies on a single publication from Isa-Isa, who mentioned 450 cases since 1966 without further details [17].

The authors described 802 male and 243 female patients, with Mexico the country with the lowest male:female ratio (1.95:1). They mention exposure to rural activities and history of trauma for 61.5% (642 out 1,043 cases) and 48% (117 out 244 cases), respectively. Histological findings were described for 269 (16.5%) patients. Cultures from the patient’s lesions allowed the isolation of 703 clinical isolates, being Fonsecaea spp. (676; 96.2%) the most frequent isolated agent with geographic distribution throughout Central America [16,19,20,30,35,40–42]. Cladophialophora spp. was found only in Mexico, Cuba, and Costa Rica [16,20,21,30]. A molecular identification study conducted in Mexico found only F. pedrosoi in all nine samples of Fonsecaea spp. isolated in culture [42]. The highest prevalence rates of CBM per 1 million inhabitants were observed in Costa Rica, Dominican Republic, Panama, and Guadalupe Island [16–41]. The primary epidemiologic and clinical data of all CBM cases reported in the region were summarized in Tables 1 and S1.

Chromoblastomycosis in South America

A total of 51 articles described 2,619 patients that were reported in Venezuela (1,167 cases) [43–49], Brazil (1,143 cases) [50–70], Colombia (167 cases) [71–76], Paraguay (82 cases) [77–81], Ecuador (34 cases) [82,83], French Guiana (11 cases) [84–86], Peru (7 cases) [87–89], Argentina (4 cases) [90,91], Bolivia (3 cases) [92], and Uruguay (1 case) [93]. In Brazil, most cases came from the Amazon region (states of Pará, Rondonia, and Amazon), Maranhão state (northeast region), in addition to the Central-West Region (Mato Grosso) and South Regions (states of Paraná and Rio Grande do Sul) [50–54,56–58,62,68–70]. Venezuela is an important endemic area in South America, and the disease is found throughout the country, with the states of Falcón, Lara, and Zulia standing out [44,45,48]. The Falcón region is responsible for 55% of the cases described in the country [48]. Data from Peru, Bolivia, Argentina, and Uruguay are scarce, as most cases were divulgated only in local meetings and conferences or published in non-indexed publications [87–93]. Biagini et al. (1982) reported that from 1929 to 1982, 11 cases of the disease were recorded in Argentina. According to Ricardo Negroni (personal communication), there were 2 to 3 cases per year in most medical centers in Buenos Aires [91].

The authors described 1,237 male and 178 female patients. Venezuela, as mentioned in several publications, had the lowest male:female rate [43,44,47]. They mentioned the previous exposition to rural activities and history of trauma for 74.5% (927 out 1,244 cases) and 53.1% (276 out 520 cases), respectively. Histological findings were described for 555 (21.2%) patients. Cultures from the patient’s lesion allowed the isolation of 864 isolates. Fonsecaea spp. (759; 87.9%) was the most frequently found agent, followed by Cladophialophora spp. (82; 9.5%). The latter agent is typical of semi-arid rural areas of Venezuela and has been found sporadically in Brazil, Paraguay, Ecuador, and Peru [43–46,48,49,60,63,77,83,89]. The report by Richard-Yegres and Yegres, accounted for 900 cases of CBM in Venezuela, with 490 (54.5%) in the state of Falcón, caused almost exclusively by C. carrionii [48]. Thus, the real number of cases...
caused by *C. carrionii* in Venezuela is underestimated in the indexed literature, specially in Falcon state, and it should be greater than 500. The highest prevalence rates of the disease per 1 million inhabitants were observed in Venezuela, French Guyana, Colombia, and Paraguay. The primary epidemiologic and clinical data of all CBM cases reported in the region were summarized in Tables 1 and S1.

**Chromoblastomycosis in Africa**

A total of 65 articles were selected between 1947 and 2018 describing 1,875 patients distributed between Madagascar (1,323 cases) [94–99], South Africa (156 cases) [100–106], Republic of the Congo and Democratic Republic of the Congo (121 cases) [107–115], Gabon (64 cases) [116], Zimbabwe (35 cases) [117], Uganda (34 cases) [118], Kenya (33 cases) [119], Cameroon (23 cases) [120–123], Morocco (18 cases) [124–132], Tanzania (17 cases) [133,134], Ethiopia (14 cases) [135,136], Angola (7 cases) [115,137,138], Nigeria (5 cases) [138–141], Tunisia (5 cases) [142–146], Reunion Island (5 cases) [147–149], Libya (4 cases) [150–153], Comoro Island (4 cases) [154,155], Sierra Leone (3 cases) [156], Senegal (2 cases) [157,158], Botswana (1 case) [159] and Djibouti (1 case) [160]. There are descriptions of CBM in Chad and the Ivory Coast. Madagascar and other islands located in the Indian Ocean (Comoro and Reunion Islands) had the highest prevalence of the disease. Madagascar had 1,323 cases described in some case series published before the 1990s. New cases of CBM continue to be reported on the island, but a recent population survey has not been conducted. Data simulated by mathematical models suggest that Madagascar should have close to 2,745 cases spread throughout the country, many of them without diagnosis [161–164]. CBM is widely distributed in the central region of the continent (Democratic Republic of Congo and Republic of Congo—Congo Brazzaville), part of West Africa (Gabon), South Africa, and part of the east coast (Kenya and Tanzania) [105–116,119,133]. The disease is rarely described in desert areas.

The authors described 1,338 male and 263 female patients. Kenya, Ethiopia, Gabon, and Cameroon showed the highest male: female rates [116,119,122,135]. They mentioned the previous exposition to rural activities and history of trauma for 74.6% (129 out 173 cases) and 30.8% (20 out 65 cases), respectively. Histological findings were described for 854 (45.5%) patients. Cultures obtained from the patient’s lesion yielded 1,406 fungal agents, being *Fonsecaea* spp. the most frequently found etiological agent (1,017; 72.3%), followed by *Cladophialophora* spp. (376; 26.8%). *Fonsecaea* spp. is widely distributed throughout the African continent, while *Cladophialaphora* spp. is found especially in the semi-arid zones of Madagascar (366 cases) and in other countries, such as Morocco, South Africa, Lybia, and Nigeria [99,100,102,110,112,113,116,122–124,127,130,131,155]. *Phialophora* spp. was also found in some African countries at a high frequency, such as Libya, Madagascar, Kenya, South Africa, Morocco, and Djibouti [95,104,119,130,132,150,153,160].

The highest prevalence rates of CBM per 1 million inhabitants were observed in Mayotte Island, Madagascar, Gabon, and Reunion Island. The primary epidemiologic and clinical data of all CBM cases reported in the region were summarized in Tables 1 and S1.

**Chromoblastomycosis in Asia**

A total of 38 articles published between 1930 and 2019 were selected. They reported 1,390 patients distributed among China (589 cases) [165], Japan (450 cases) [166–169], India (169
cases) [170], Sri Lanka (71 cases) [171], Taiwan (33 cases) [172–175], Malaysia (20 cases) [176,177], Nepal (15 cases) [178,179], Thailand (14 cases) [180–183], Indonesia (13 cases) [184–187], South Korea (9 cases) [188–196], Pakistan (2 cases) [197,198], and Philippines, Bangladesh, Laos, Vietnam and Iraq each one with 1 case [199–202]. In India, the main provinces reporting cases of CBM were Kerala, Karnataka, Assam, Himachal Pradesh, and Maharashtra [170]. In Mainland China, most of the cases came from the southern provinces of Guangdong, Shandong, and Hebei [165].

The authors described 463 male and 183 female patients. Japan, Thailand, and Nepal the countries with the lowest male: female rates among patients with CBM [166–168,177,179,181,182]. They mentioned rural activities and a history of trauma for 20.3% (162 out 799 cases) and 14.3% (116 out 811 cases), respectively. Histological findings were described for 369 (26.5%) patients. Cultures from the patient’s lesion allowed the identification of 750 fungal pathogens, with *Fonsecaea* spp. the most frequent etiologic agent (569; 75.8%), followed by *Cladophialophora* spp. (68; 9%) and *Phialophora* spp. (24; 3.2%) [165,167–171,174]. *Cladophialophora* spp. was found only in China, India, Thailand, and Nepal [165,170,179,182]. Less common agents, such as *Exophiala* spp., *Bipolaris* spp., *Rhinocladiella* spp., and *Rhizidiomyces* spp. were reported, especially in Japan, India, Thailand, and South Korea [167–170,183,196].

Fig 3. The chromoblastomycosis lesion site. A- The percentage of cases reported from a certain body site is shown. For lower limbs, lesions were described in 3,197 (56.7%) out of 5,639 patients; for upper limbs in 1,120 (19.9%) out of 5,634 patients; for the face and neck in 238 (4.3%) out of 5,555 patients; for the trunk in 180 (3.3%) out of 5,476 patients described; and finally for the buttocks in 89 (1.6%) out of 5,639 patients described. Unusual sites such as ear, breast, inguinal region were reported in 61 cases. B—Percentage of lesion severity.
Some authors describe the latter cases are doubtful because these genera do not belong to known agents of CBM and may concern misidentifications [1,3]. Some strains of Fonsecaea spp. (27 strains) were subjected to molecular identification, showing F. monophora in 21, F. pedrosoi in 5, and F. nubico in 1 case [165,175,201]. The highest prevalence rates of CBM per 1 million inhabitants were observed in Sri Lanka, Laos, Taiwan, Japan, Malaysia, and Nepal. The primary epidemiologic and clinical data of all CBM cases reported in the region were summarized in Tables 1 and S1.

Chromoblastomycosis in Oceania

A total of 9 articles published between 1947 and 2013 were selected, describing 168 patients from Australia (158 cases) [203–208], New Caledonia (5 cases) [209], New Zealand (4 cases) [210], and Solomon Islands (1 case) [211]. There are some reports of patients who probably acquired the disease in Samoa and the Cook Islands [209–211]. In Australia, CBM occurred predominantly in rural areas of Queensland, northern New South Wales, and the Northern Territory, including the northern part of Western Australia [205,206,209].

The authors described 133 male and 18 female patients, exhibiting one of the highest male:female rates in all studies analyzed. They mentioned the previous rural activities or a history of trauma in 40.8% (20 out 49 cases) and 42.9% (18 out 42 cases), respectively. Histological findings were described for 23 (13.7%) patients. Cultures from the lesions yielded 43 fungal agents represented by Fonsecaea spp. (29; 67.5%) and Cladophialophora spp. (14; 32.5%). Cladophialophora spp. was found only in Australia. Fonsecaea spp. was widely distributed throughout Oceania, especially in the southeast coastal area of Queensland, Australia [203,205,208–211]. The highest prevalences of CBM per 1 million inhabitants were observed in New Caledonia and the Solomon Islands. The primary epidemiologic and clinical data of all CBM cases reported in the region were summarized in Tables 1 and S1.

Chromoblastomycosis in Europe

Excluding two publications from Russia and Finland that were written in their native languages, which precludes our analysis of data, we were able to evaluate only 35 cases of CBM published on the European continent.

The 35 European cases (24 autochthonous) were documented in the following countries: Finland (9 cases), Poland (5 cases), United Kingdom (5 cases), Czech and Slovakia (3 cases), Germany (3 cases), France (3 cases), Ukraine (2 cases), Russia (1 case), Belgium (1 case), Spain (1 case), Portugal (1 case) and Netherlands (1 case). All cases of CBM diagnosed in the UK and Netherlands, in addition to 2 cases from Germany and 1 case from France, were imported [212–218].

The authors described 27 male and 8 female patients. They mentioned the previous exposition to rural activities and history of trauma for 66.6% (2 out 3 cases) and 56.3% (18 out 32 cases), respectively. Histological findings were described for all 35 (100%) patients. Cultures from the patient’s lesion yielded 30 fungal agents represented by Fonsecaea spp. (24; 80.1%), followed by Exophiala spp. (2; 6.7%), Phialophora spp. (1; 3.3%), Rhinocladiella spp. (1; 3.3%), and Cladophialophora spp. (1; 3.3%) [212,214–218]. The primary epidemiologic and clinical data of all CBM cases reported in the region were summarized in Tables 1 and S1.

Chromoblastomycosis in the US and Canada

A total of 13 articles between 1915 and 2018 were selected, with 25 patients distributed between the United States (24 cases) and Canada (1 case) [219–231]. In the USA, most CBM cases were published before the 50s, and the disease is supposed to be rare nowadays. In the
USA, most CBM reports came from Massachusetts (Boston), Texas, Missouri, Georgia, Louisiana (New Orleans), and Pennsylvania (Philadelphia) [219–230]. The single case published in Canada was probably imported once the patient had a previous history of trauma in Sri Lanka [231].

The authors described 22 male and 3 female patients. They mentioned the previous exposure to rural activities and history of trauma for 56.5% (13 out 23 cases) and 100% (3 out 3 cases), respectively. Histological findings were described for 20 (57.1%) patients. Cultures from the patient’s lesion yielded 21 etiological agents, including Fonsecaea spp. (15; 71%), and Phialophora spp. (6; 29%). Cladophialophora spp. was not reported in any case from the USA [219–231]. The primary epidemiologic and clinical data of all CBM cases reported in the region were summarized in Tables 1 and S1.

Consolidated worldwide CBM data

A total of 7,740 cases of CBM was described in five continents. The authors described 4,022 (81.7%) male and 896 (18.3%) female patients. The median age was 52.5 years (range between 2–93 years), and the average time between the onset of the first lesion and CBM diagnosis was 9.2 years (range between 1 month to 50 years). The authors mentioned exposure to rural activities and history of trauma for 56.8% (1,895 out 3,334 cases) and 33.1% (568 out 1,717 cases), respectively. Histological findings were described for 2,125 (27.8%) patients.

The presence of immunosuppressive diseases at the time of diagnosis of CBM was reported in only 16 (0.2%) cases, with solid organ transplantation the most common condition (kidney, heart transplantation), followed by HIV infection, rheumatoid arthritis, systemic lupus erythematosus, bladder neoplasia, celiac disease, pernicious anemia, and non-Hodgkin lymphoma [66,68,92,148,170,229]. Concomitant infection diseases were reported in 19 cases of CBM, including mycetoma (5 cases), leprosy (5 cases), cutaneous filariasis (3 cases), paracoccidioidomycosis (2 cases), cutaneous histoplasmosis (1 case), syphilis (1 case), actinomycosis (1 case) and visceral leishmaniasis (1 case) [19,50,54,56,60,65,68,108,121,157,158,170].

CBM lesions were present in only one body segment in 1,313 out 1,472 cases (89.2%) and in more than one body segment in 159 out 1,472 cases (10.8%). Itching and pain were reported by 21.5% (281 out 1,309 cases) and 11% (145 out 1,313 cases), respectively.

The main sites involved were the lower limbs (3,197 out 5,639 cases; 56.7%), followed by the upper limbs (1,120 out 5,634 cases; 19.9%), head and neck (158 out 5,555 cases; 2.9%), trunk (180 out 7,568 cases; 2.4%), buttocks (89 cases) and unusual sites such as ear, breast, inguinal region (61 cases).

The main patterns of dermatological lesions were verrucous (710 cases), followed by tumorous (663 cases), plaque (565 cases), nodular (285 cases), ulcers (105 cases), and scarring (75 cases) lesions. Approximately 63.2% (470 out 743) of the patients had only 1 pattern of dermatologic lesions, while polymorphisms of lesions were observed in 36.8% (273 out 743) of patients. Regarding the severity of the disease by Carrió’s criteria, 83 out 338 patients (24.5%) had mild, 148 out 338 patients (43.8%) moderate, and 107 out 338 patients (31.7%) severe forms. Malignant transformation diagnosed by histopathology of CBM lesions was described in 22 cases. Except for one case of melanoma, all others were described as squamous and basal cell carcinomas. A total of 3,817 fungal isolates were cultured, being 3,089 (80.9%) Fonsecaea spp., 552 (14.5%) Cladophialophora spp., and 56 Phialophora spp. (1.5%). The primary epidemiologic and clinical data of all CBM cases reported in the world were summarized in Figs 1–3 and Tables 1 and S1.

Data about the treatment of CBM were scarcely documented, with incomplete information in most papers. In this regard, the management of lesions solely by surgical excision or
physical methods (cryotherapy, thermotherapy, and photodynamic therapy) was documented in 133 cases. Surgical debridement as adjuvant therapy was described in additional 191 cases [35,37,39,47,50,100,110,113,165,170,182,204,212]. Itraconazole was the antifungal therapy mostly used in all continents, being reported in 318 patients, followed by treatment with terbinafine that was used by 87 patients, especially in India, China, and Madagascar [18,65,67,70,77,99,165,170]. The use of fluconazole, ketoconazole, flucytosine, and systemic or intralesional amphotericin were only sporadically reported. Curiously, the administration of iodides as pharmacological therapy was described in 103 cases, and it was a common practice in India, Cuba, and Australia [19,170,204,212,228]. Unfortunately, clinical and laboratory follow up data were not available to check for the clinical response (complete or partial cure) in the mentioned articles. A total and partial cure were described in 302 and 188 cases, respectively. Amputation of the affected limb was observed in 14 cases [56,67,68,76,99,103,116,119,167,181].

Discussion

The true burden of CBM is not known. A lack of national surveillance systems checking for CBM in sentinel centers does not exist [1,2,232,233]. This paper represents the most comprehensive review of CBM cases published between 1914 and 2020, providing data to partially characterize the relative burden of this neglected implantation mycosis in different countries and the main clinical and mycological characteristics of the affected patients.

Our review showed that CBM has been widely described on all continents over the last eight decades and thrives in areas where access to adequate sanitation, clean water, and healthcare is limited. Regardless of the country considered, CBM is diagnosed in people who live in remote and rural areas and affects some of the world’s poorest and most marginalized communities, predominantly in Africa, Asia, and America [1,2,232]. Rural areas in developing countries highly endemic for CBM generally present high informal employment arrangements, low human development index, and lack of appropriate social protection systems for agriculture workers. In most countries, surveillance practices for personal protective equipment (PPE) in agriculture are unknown, and their use in rural areas is woefully inadequate and requires more attention. The lack of protective shoes, gloves, or garments associated with poor hygienic habits and insufficient nutrition may favor development of CBM after infection by implantation [1–7,14,234–236]. It is not known if there are other factors affecting the development of CBM in particular individuals or disease expression and severity. For example, an inability of toll like receptor 7 (TLR7) to recognize and respond appropriately to the causative fungi could underly the progressive nature of CBM in some patients [237].

Although the route of acquisition of CBM agents is by traumatic inoculation, most of the series did not track the source of infection once clinical manifestations as several years usually elapse after trauma when the patients and the lesion(s) grows very slowly. We were not capable to analyze data related to trauma or characterization of rural jobs as this information were not available in most papers [1,3,6,18,19,27,35,56,70,116,165,238,239].

Rarely CBM is described simultaneously with other NTDs (mycetoma, leprosy, filariasis and leishmaniasis). This occurrence reflects areas of co-endemicity, with common environmental exposure in populations under conditions of poverty [1,3,54,56,57,60,108,121].

Although the diagnosis of CBM does not rely on expensive and sophisticated laboratory tools, the disease remains neglected by all health systems, making the time of diagnosis too long (mean of 9 years). This aspect certainly impacts in morbidity, including disease progression, risk of superinfection and malignant transformation [8,56,68,99,167,175,240,241,242].
Considering the insidious progression of the fungal disease, patients continue their labor and social activities for many years before having the diagnosis made [1,3,5,48,176].

Notably, the disease is mostly observed in males probably due to different environmental exposition and possible protection of women by endogenous steroids [1,5]. This hypothesis needs further investigation and validation. However, in some countries the prevalence in women is high probably due to their involvement in agricultural activities [16,43,44,116,122,166–168,199]. Lower limbs are the most common site affected, although some countries frequently reported lesions in upper limbs due to local practice of carrying wood or other agricultural materials in arms or shoulders [16,19,20,165,180,182,204,205,228,229].

In the present review, we adopted the CBM Carrión classification for skin lesions considered the most consistent and comprehensive description of dermatological lesions with updated nomenclature [1,3,65,68]. As expected, warty lesions (29%), tumors (27%), infiltrative plaques (23%), and nodules (12%) were the most common pattern of CBM, but polymorphic lesions may also be found, especially in patients with a long history and chronic evolution of the process [52,56,65,67,68,99,165,169,175]. The main symptoms were itching (21%) and pain (11%), with local edema rarely reported by most authors [6,7,9,21,28,30]. Of note, the pattern of skin lesions is not linked to the etiological agent of CBM.

Some series have shown that secondary bacterial infections and lymphedema are concerns. Uncommonly, malignant transformation may occur, especially in patients with a long history of CBM diagnosis [1,3,54,67,68,76,99,103,116,119,167,240–242]. CBM progresses slowly, produces fibrotic changes and lymphatic stasis. Secondary recurrent bacterial infection exacerbates the involvement of lymphatic vessels, resembling elephantiasis. Severe forms of CBM disable and disfigure patients much more frequently than they kill, and are multifactorial [243,244]. Affected people live decades with disability, stigma and social withdrawal. Disability Adjusted Life-Years (DALY) lost due to CBM has not been comprehensively evaluated in endemic areas [1,3–5,7,14,15].

Laboratory diagnosis of CBM requires only the visualization of single or clustered muriform cells by direct mycological examination or histopathology. Most diagnoses in North American and European countries are provided by histological examination. In contrast, in Asian, African, and Latin American countries where CBM is endemic, less than 30% of all cases required biopsy for the diagnosis [8,16,25,49,51,56,68,99,169]. Direct mycological examination with potassium hydroxide solution of skin scrapings containing crusts or cellular debris is a fast and straightforward tool frequently useful in low-income countries to diagnose patients with CBM [56,68,99,170].

Although the different agents of CBM have certain ecological features, there is no apparent impact of the diversity of species on clinical manifestations or therapeutic management. Molecular characterization of different species has mostly been used to characterize this ecology and epidemiological aspects of the various etiological agents of CBM [1,11–13,238,239].

Fonsecaea spp. is the main genus causing CBM worldwide [16,18–25,50–56,68,99,116,165,169,170,189–191]. Molecular studies showed that Fonsecaea pedrosoi is the main species within this genera, and it is found practically in all countries where CBM has been reported. This species causes almost exclusively subcutaneous disease, with rare visceral involvement [11,12,16,68]. Disseminated forms of the disease have also been reported but without unambiguous muriform cells in tissue (44), and thus, they may be considered phaeohyphomycosis. Fonsecaea monophora is widely distributed, with high prevalence, especially in Asia and subtropical or temperate countries. F. monophora, together with F. pugnacius, can cause disseminated CBM or phaeohyphomycosis with visceral impairment [165,245,246].
Finally, *Fonsecaea nubica* is also widely distributed in Asia, but current studies showed that Madagascar might be the country with the highest number of CBM caused by this species [239].

The second main etiological agent of CBM is *C. carrionii*, with Venezuela, Madagascar, Australia, India, and China the countries most affected [44,45,48,49,99,165,170,203–208]. This agent is typically found in arid and semi-arid climates, with average yearly temperatures of 24°C, scarce rainfall (up to 600 annual mL) and is located at moderate altitude (up to 500 m) [43,48,99,208]. Finally, *Phialophora* spp. (*P. verrucosa*) is an uncommon agent, responsible for almost 30% of cases in the USA [166–170,219–221,228,230]. *Rhinocladiella* spp. is the etiologic agent of less than 1% of CBM cases [16,68,212].

Treatment of CBM is difficult, and several different therapeutic regimens have been tried, including physical methods. Most of small initial lesions in mild disease can be excised surgically, but clinical data and follow-up of these patients are incompletely characterized. CBM lesions are refractory, and healing is almost impossible to achieve, especially in its moderate to severe clinical presentations [19,21,22,30,52,95,99]. Although there are no randomized clinical trials to define the best choice for its treatment, itraconazole is the main antifungal drug used, specially 400 mg per day in moderate and severe cases, based on observational studies [65,66,68]. Terbinafine is the second most frequently used antifungal drug, especially in some countries as Madagascar and China, based on open and non-comparative clinical trials [163,240]. Voriconazole, posaconazole, and isavuconazole are used only in refractory disease [1,247,248]. Interestingly, some therapies have been abandoned, such as cholecalciferol, thiabendazole, intravenous amphotericin, ketoconazole, and topical 5-fluorouracil. Due to the low cost, potassium iodide has been used in some countries, especially in Cuba and India [19,23,170]. Adjuvant therapy for improve the cellular immune response with topical imiquimod or intramuscular glucan was used mostly in more severe and refractory cases [249–251].

Conclusions

Despite all limitations, our study provides a comprehensive review of clinical and therapeutic aspects of CBM and an estimate of the prevalence of the disease in each country. Our maps have shown CBM to be widespread in five different continents, specially in Latin America, Africa and Asia. Countries such as Madagascar, Gabon, Indian Ocean Islands (Comoros and Reunion), Costa Rica, Dominican Republic, Venezuela, French Guiana, and Island of Oceania (New Caledonia) are the countries with the highest incidence densities in the world. CBM in world is probably more common than expected. The disease especially affects men (81.7%), with an average delay of 9.2 years between onset and diagnosis. The mean age was 57.1 years (range 2–93 years), being the lower and upper limbs the most compromised sites. Verrucous, tumoral and plaque represent the main dermatological patterns. *Fonsecaea* spp. is the main etiological agent, being widely distributed on all continents and responsible for more than 80% of cases. This review allows the understanding of a gap in epidemiological, diagnostic and therapeutic data. There is an urgent need to create and implement social protection policies for vulnerable populations and national programs for the diagnosis and treatment of the disease.

Supporting information

S1 Table. Rate of occurrence, clinical and demographic data of chromoblastomycosis cases stratified by countries.

(DOCX)
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References

1. Queiroz-Telles F, de Hoog S, Santos DW, Salgado CG, Vicente VA, Bonifaz A et al. Chromoblastomycosis. Clin Microbiol Rev. 2017 Jan; 30(1):233–276. https://doi.org/10.1128/CMR.00032-16 PMID: 27856522

2. Van de Sande W. Global burden of human mycetoma: A systemic review and metanalysis. PLoS Negl Trop Dis. 2013; 7: https://doi.org/10.1371/journal.pntd.0002556 PMID: 24244780

3. Queiroz-Telles F, Fahal AH, Falcí DR, Caceres DH, Chiller T, Pasqualotto AC. Neglected endemic mycoses. Lancet Infect Dis. 2017 Nov; 17(11):e367–e377. https://doi.org/10.1016/S1473-3099(17)30306-7 PMID: 28774696

4. Watts C. Neglected tropical diseases: A DFID perspective. PLoS Negl Trop Dis. 2017 Apr 20; 11(4): e0005492. https://doi.org/10.1371/journal.pntd.0005492 PMID: 28426686

5. Hotez PJ, Aksoy S, Brindley PJ, Kamhawi S. World neglected tropical diseases day. PLoS Negl Trop Dis. 2020 Jan 29; 14(1):e0007999. https://doi.org/10.1371/journal.pntd.0007999 PMID: 31995572

6. Hay R, Denning DW, Bonifaz A, Queiroz-Telles F, Beer K, Bustamante B et al. The Diagnosis of Fungal Neglected Tropical Diseases (Fungal NTDs) and the Role of Investigation and Laboratory Tests: An Expert Consensus Report. Trop Med Infect Dis. 2019 Sep 24; 4(4). pii: E122. https://doi.org/10.3390/tropicalmed4040122 PMID: 31554262
7. GAFFI. Available from: https://www.gaffi.org/poor-farmers-fungal-skin-condition-gets-approval-from-who-as-neglected-after-lobbying-by-gaffi/

8. Kneale M, Bartholomew JS, Davies E, Denning DW. Global access to antifungal therapy and its variable cost. J Antimicrob Chemother. 2016 Dec; 71(12):3599–3606. https://doi.org/10.1093/jac/dkw325 Epub 2016 Aug 10. PMID: 27516477.

9. GAFFI. Available from: https://www.gaffi.org/antifungal-drug-maps/.

10. de Hoog GS, Attili-Angelis D, Vicente VA, Van Den Ende AH, Queiroz-Telles F. Molecular ecology and pathogenic potential of Fonsecaea species. Med Mycol. 2004; 42:405–416. https://doi.org/10.1080/1369378041000166146 PMID: 15552642

11. Najafzadeh MJ, Gueidan C, Badali H, van den Ende AH, Xi L, de Hoog GS. Genetic diversity and species delimitation in the opportunistic genus Fonsecaea. Med Mycol. 2009; 47:17–25. https://doi.org/10.1080/13693780902814603 PMID: 19107635

12. Najafzadeh MJ, Sun J, Vicente VA, Klaassen CH, Bonifaz A, Gerrits van den Ende AH et al. Molecular epidemiology of Fonsecaea species. Emerg Infect Dis. 2011 Mar; 17(3):464–9. https://doi.org/10.3201/eid1703.100555 PMID: 21392438

13. Queiroz-Telles F, Santos DW. 2013. Challenges in the therapy of chromoblastomycosis. Mycopathologia 175:477–488. https://doi.org/10.1007/s11046-013-9648-x PMID: 23636730

14. WHO Department of Control of Neglected Tropical Diseases. Sustaining the drive to overcome the global impact of neglected tropical diseases: second WHO report on neglected tropical diseases. Geneva: World Health Organization, 2013. Available from: https://www.who.int/neglected_diseases/9789241564540/en/

15. Bongomin F, Gago S, Oladele RO, Denning DW. Global and Multi-National Prevalence of Fungal Diseases-Estimate Precision. J Fungi (Basel). 2017; 3(4):57 https://doi.org/10.3390/jof3040057 PMID: 29371573

16. Navarrete MR, Arenas R, Estrada VFM, Diáez CEA, Mayorga J, Bonifaz A et al. 2014. Cromoblastomicosis in México. Revisión de 603 casos en siete décadas. Dermatol Clin 12:87–93

17. Maleck D, Amaya-Araujo M, Cochón M, Isa Isa R. Cromoblastomicosis facial y esporotricide. A propósito de un caso. Revista Dominican de Dermatología. 2010; 37(1):28–30.

18. Larrondo Muguerza RJ, Gray Lovio O, Abreu Daniel A, Bonito Lovio D. Cromomicosis. Estudio de un decenio. Hospital Universitario Comandante Manuel Fajardo. 1996–2005. Folia Dermatol Cubana. 2009; 3(2):1–7.

19. Pardo-Castello V, Leon R, Trespacios F. Chromoblastomycosis in Cuba. Arch Dermatol Syphilograph. 1942; 45:19–32.

20. Daniel Simón R, Moya Duque S, Abreu García M. Cromomicosis: Hongos dematiáceos que intervienen en su etiología. Rev Cubana Med. 1998; 37(3), 136–140.

21. Pastrana Fundora F, Ramírez Albañés C, Naranjo Lorenzo M, Galiano Audvert O. Cromomicosis: quince años de incidencia / Chromomycosis: 15 years incidence. Rev Cuba Hig Epidemiol. 1989; 27(3):285–92

22. Díaz JGD, Taboas Gonzalez M, Dube A. Cromoblastomicosis in Cuba, estudio retrospectivo clínico y epidérmico de 72 enfermos. Rev Cubana Med Trop. 1978; 30(2):95–108. PMID: 368916

23. Alfonso-Armenteros J. Micología Medica. Micosis observadas en Cuba. Ministerio de Salud Publica. Capítulo XIX. Chromomycosis (Cromomycosis–Dermatitis verrucosa). Editorial Científica. 34 pp. 1965.

24. Olano SM, Rodríguez Gonzalez DP, D’escouet EF, Leon GV, Perez AB. Cromomicosis, estudio de cinco años. Rev Cub Med Trop. 1984; 36:102–109

25. Manzur-Katrib J, Alvarez-Mesa M, Hernandez Z Bitor MA. Cromomicosis. Estudio Retrospectivo de Junio de 1961 a Junio de 1978. Rev Cub Med Trop. 1979; 31:217–224.

26. Romero A, Trejos A. La cromoblastomicosis en Costa Rica. Rev Biol Trop. 1953; 1(2):95–115.

27. Trejos A. La cromoblastomicosis como problema micológico. 1954. Tesis de grado para optar por el título de licenciatura.

28. Astorga E, Bonilla E, Martinez C, Mora W. Cromomicosis. Nuevos casos de Cromomicosis tratados con Anfotericina B y 5 Fluorocitosina en forma simultánea Revista Médica de Costa Rica XLVII. 1980; 470:17–22.

29. Solano E. Cromomicosis. Acta Médica Cost. 1966; 9(2):77–85

30. Trejos LS, Viquez DJ. Cromoblastomicosis: Situación en Costa Rica. Revista Medica De Costa Rica Y Centroamerica LXXI. 2014; 613:737–44.

31. Velásquez-Montoya X, Herrera-Guzmán M, Wilkinson-Oberti O, Jeremias-Soto R, Alger J. Micosis subcutánea y profunda en el hospital escuela, Tegucigalpa. Rev Med Post Unah. 2001; 6(1):61–65.
32. Adan Cueva J. Cromoblastomicosis en Honduras. Revista Medica Hondureña. 1956; 24(4):112–117. PMID: 13454024
33. Corrales Padilla H. Cromoblastomicosis. Revista Medica Hondureña. 1955; 23(4):1030–6.
34. Corrales Padilla H. Cromomicosis. Revista Medica Hondureña. 1970; 38(2):55–63.
35. Bansal AS, Prabhakar P. Chromomycosis: a twenty-year analysis of histologically confirmed cases in Jamaica. Trop Geogr Med. 1989 Jul; 41(3):222–6. PMID: 2595799
36. Mugleston BJ, Usatine RP, Rosen T. Wide Morphologic Variability of Chromoblastomycosis in the Western Hemisphere. Skinmed. 2016 Dec 1; 14(6):423–427. eCollection 2016. Available from: https://skinmedjournal.com/2016-issues/#. PMID: 28031127
37. Calero C. Cromoblastomycosis in Panama: report of a new case and a new clinical form. Arch Derm Syphilol. 1948 Feb; 57(2):266–71. PMID: 18912488
38. Calero M. Chromomycosis. Arch Derm Syphilol. 1970; 38(2):55–63.
39. Bansal AS, Prabhakar P. Chromomycosis: a twenty-year analysis of histologically confirmed cases in Jamaica. Trop Geogr Med. 1989 Jul; 41(3):222–6. PMID: 2595799
40. Calero C. Cromoblastomycosis in Panama: report of a new case and a new clinical form. Arch Derm Syphilol. 1948 Feb; 57(2):266–71. PMID: 18912488
41. Levang J, Muller P, Marreel A, Nicolas M, Puzenat E, Aubin F et al. Chromomycosis en Guadeloupe. Annales de dermatologie et de vénéréologie (2008) 135, 111–115
42. Najafzadeh MJ, Sun J, Vicente VA, Klaassen CHW, Bonifaz A, Gerrits van den Ende AHG, et al. Molecular epidemiology of Fonsecaea species. Emerg Infect Dis 2011; 17(3): 464–469. doi:10.3201/eid1703.100555 PMID: 21392438
43. Barroeta S, Mejia de Alejos MA, Franco de Arias CM, Prado A, Zamora R. Cromomicosis en el estado Lara. Dermatol Venez. 1986; 24(2/4):134–7
44. Bopp C. Cromoblastomicose. Contribuição ao Estudo de Alguns de seus Aspectos. Thesis for Cathe- dratic Professor of Dermatology of Universidade Federal do Rio Grande do Sul. 1959. pp 01–315.
45. Silva NN. Cromoblastomicose no Rio Grande do Sul. Anais Brasileiros de Dermatologia e Sifilografia. 1949; 24(2):113–145.
46. Bopp C. Cromoblastomicosis: a review of 100 cases in the state of Rio Grande do Sul, Brazil. J Am Acad Dermatol. 2001; 44(4):585–92. doi:10.1067/mjd.2001.112220 PMID: 1259077
47. Avelar-Pires C, Simoes-Quresma JA, Moraes-de Macedo GM, Brasil-Xavier M, Cardoso-de Brito A. Revisiting the clinical and histopathological aspects of patients with chromoblastomycosis from the Brazilian Amazon region. Arch Med Res. 2013 May; 44(4):302–6. doi:10.1016/j.arcmed.2013.04.008 PMID: 23684532
58. Talhari S, Cunha MG, Schettini AP, Talhari AC. Deep mycoses in Amazon region. Int J Dermatol. 1988 Sep; 27(7):481–4. https://doi.org/10.1111/j.1365-4362.1988.tb00925.x PMID: 3220630

59. Silva JP, de Souza W, Rozental S. Chromoblastomycosis: a retrospective study of 325 cases in Amazon region (Brazil). Mycopathologia. 1999–2000; 143(3):171–5.

60. Mouchalouat Mde F, Gutierrez Galhardo MC, Zancopé-Oliveira RM, Monteiro Fialho PC, de Oliveira Coelho JM, Silva Tavares PM et al. Chromoblastomycosis: a clinical and molecular study of 18 cases in Rio de Janeiro, Brazil. Int J Dermatol. 2011 Aug; 50(8):981–6. https://doi.org/10.1111/j.1365-4632.2010.04729.x PMID: 21781072

61. Pérez Herrera MA, Martinez GC, MACHIN Villafranca MC. Diagnóstico histopatológico de 98 casos de Micosis Profunda en el Hospital Dom Orione, Brasil. In: VI Congresso Virtual Hispanoamericano de Anatomia Patológica. 2004. Cited 10 January 2020. Available from: http://www.conganan.org/6congreso/index-261.htm

62. Mate SM, Lopes JO, Melo IS, Espadim LE, Pinto MS. Chromoblastomycosis in Rio Grande do Sul: a report of 12 cases. Rev Soc Bras Med Trop. 1997 Jul-Aug; 30(4):309–11. https://doi.org/10.1590/s0037-86821997000400006 PMID: 9265226

63. Marques GF, Barreto JA, Masuda PY, Wachholz PA, Sousa JMP. Perfil clínico e demográfico da cro-moblastomicose em serviço de referência no centro-oeste do estado de São Paulo, Brasil. Anais Brasileiros de Dermatologia. 2015; 90(1):143–45 https://doi.org/10.1590/abd1806-4841.20142998e PMID: 25672319

64. Mattedi MGS, Palhano Junior L, Coelho CC, Mattêde AF. Dermatite verrucosa cromoparasítica (cro-momicose). Investigação de casos no estado do Espírito Santo. An Bras Dermatol. 1990; 65(2):7074

65. Queiroz-Telles F, Purim KS, Fillus JN. Itraconazol e in the treament of chromobl astomyco sis due to Fonsecaea pedrosoi. Int J Dermatol 1992; 31:805–812 https://doi.org/10.1111/j.1365-4362.1992.tb04252.x PMID: 1330949

66. Queiróz AJR, Pereira Domingos F, Antônio JR. Chromoblastomycosis: clinical experience and review of literature. Int J Dermatol. 2018 Nov; 57(11):1351–1355 https://doi.org/10.1111/ijd.14185 PMID: 30113072

67. Silva Pacheco A. Cromomicose em Santa Catarina. Monografia de conclusão do curso de medicina. 2003. Cited 10 January 2020. Available from: https://repositorio.ufsc.br/bitstream/handle/123456789/114294/201442.pdf?sequence=1&isAllowed=y

68. Santos DWCL, Vicente VA, Weiss VA, de Hoog GS, Gomes RR, Batista EMM et al. Chromoblastomycosis in an Endemic Area of Brazil: A Clinical-Epidemiological Analysis and a Worldwide Haplotype Network. J Fungi (Basel). 2020 Oct 3; 6(4):E204. https://doi.org/10.3390/jof6040204 PMID: 33022951

69. Londero AT, Ramos CD. Cromoblastomicose no interior do Estado do Rio Grande do Sul. Anais Brasileiros de Dermatologia 64:155–58, 1989.

70. de Andrade TS, de Almeida AMZ, Basano SA, Takagi EH, Szeszs MW, Melhem MSC et al. Chromoblastomycosis in the Amazon region, Brazil, caused by Fonsecaea pedrosoi, Fonsecaea nubica, and Rhinocladiella similis: Clinicopathology, susceptibility, and molecular identification. Med Mycol. 2020 Feb 1; 58(2):172–180. https://doi.org/10.1093/mmy/myz034 PMID: 31329924

71. López H, Hurtado H, Correa E. Las micosis profun das en el Hospital de San Juan de Dios. Publicaciones del Hospital de San Juan de Dios (Cali). 1964; 16:1–24.

72. Sánchez J. Micosis. Estudio etiológico de las diversas micosis admitidas em el Hospital de San Vicente de Paul durante 1964 y 1965. Tesis de grado. Facultad de Medicina, Universidad de Antioquia, pp. 68–85.

73. Duque O. Cromoblastomicosis. Revisión general y estudio de la enfermedad en Colombia. Ant Med. 1961; 1:499–521.

74. Pena C. Cromoblastomicosis. Rev Fac Med Univ Nal. 1966; 34:55–59.

75. Velasquez J, Restrepo A, Calle G. Cromomicosis. Experiencia de doce años. Acta Médica Colombiana. 1976; 1(3):165–171.

76. Rocha H, Guifiérez G. Cromomicosis: a propósito de 35 casos observados en el Hospital San Juan de Dios de Bogotá. Rev Fac Med. 1972; 38(1):50–65.

77. Wattiez V, García J, Aquino N, Insaurralde S, Mendoza G, Celias L et al. Rev Virtual Soc Parag Med Int. 2017; 4(2):27–33.

78. Rodríguez Mais M. Estudio clínico y epidemiológico de la paracoccidioidomicosis y otras micosis profundas. Anales de la Facultad de Ciencias Médicas de la UNA. 2004; 37:9–19.

79. Canese A, Da Silva D. Hongos aislados durante el año 1972, en la Cátedra de Bacteriología y Parasitología de la Facultad de Medicina. Rev Parag Microb. 1973; 8:53–6.

80. Canese A, Da Silva D. Micosis en el Paraguay. Rev Parag Microb. 1969; 4(1):12–4.
81. Maas LC. Aspectos Clínicos de las Micosis em el Paraguay. Thesis de Clinica Médica para la II Cátedra del Hospital Universitario. Asuncion, Paraguay. 1964. pp01-81.

82. Rodríguez M JD. Revisión Crítica de Investigaciones y literatura micológicas durante los años 1950–1960 em Ecuador. Mycopathologia et Mycologia Applicata. 1962; 17:185–202.

83. Ronquillo TF, Acosta Y, Almeida R. Cromoblastomicosis en el Ecuador. Rev Med FCM-UCSG. 2015; 19(4):246–251.

84. Silverie R, Ravisse P. On 2 cases of chromomycosis observed in French Guiana. Bull Soc Pathol Exot Filiales. 1962 Sep-Oct; 55:751–2. PMID: 13992936

85. Pradinaud R, Joly F, Basset M, Basset A, Grosshans E. Chromomycosis and Jorge Lobo disease in French Guiana. Bull Soc Pathol Exot Filiales. 1969 Nov-Dec; 62(6):1054–63. PMID: 5409181

86. Pradinaud R. Traitement de 6 chromomycoses par la 5 fluorocytosine em Guyane franç¨ase. Nouv Presse Med. 1974; 3(31):1955. PMID: 4444938

87. Ventura-Flores R, Failoc-Rojas V, Silva-Diaz H. Cromoblastomicosis: caracterı´sticas clı´nicas y micro-biolı´gicas de una enfermedad desatendida. Rev Chilena Infectol 2017; 34 (4): 404–407 https://doi.org/10.4067/s0716-10182017000400404 PMID: 29165523

88. Galarza C. Enfoque de las micoses profundas em el Peru´. Dermatol Peru. 1996; 6(1 suppl):39S–40S.

89. Cavero J, Delgado V. Cromoblastomicosis por Cladosporium sp. Folia Dermatol. 2004; 15(1):28–31.

90. Molina-Leguizamon EB, Casas JG, Perini GM. Cromomicosis de la nalga. Med Cut ILA. 1984; 12:430–438.

91. Biagini RE, Maza AL, Abulafia J, Museli A. Cromomycosis. Arch Argent Dermat. 1982; 32:93–100.

92. Escobar AY, Maldonando SE, Iriarte A, Rollano F. Revista Boliviana de Dermatologı´a. 2015; 5(8):32–36.

93. Vignale B, Montero ED, Tost JFr, Sanjines A. Cromoblastomicosis (Segundo caso descrito en el Uruguay). An Fac Med. 1955; 40(3–4):87–92

94. Brygoo ER. La chromoblastomicose à Madagascar. Sem Hop Paris. 1957; 33:774–791. PMID: 13421798

95. Brygoo ER, Coudurier J, Meyer G. La chromoblastomicose à Madagascar. Arch Inst Pasteur Madagascar. 1958; 26:11–22.

96. Brygoo ER, Destombes P. Epidémiologie de la chromoblastomycose humaine. Bull Inst Pasteur. 1976; 74:219–243.

97. Brygoo ER, Segrétain G. Etude clinique, epidemiologique et mycologique de la chromoblastomycose à Madagascar. Bull Soc Pathol Exot. 1960; 3:443–75.

98. Coulanges P, Locheron P. La chromomycose a Madagascar. Donnees epidemiologiques sur le foyer de plus importante actuellement connu dans le monde. Arch Inst Pasteur Madagascar. 1981; 48(1) 69–95. PMID: 7342901

99. Esterre P, Andriantsimahavandy A, Raharisoa C. Natural history of chromoblastomycosis in Madagascar and the Indian Ocean. Bull Soc Pathol Exot. 1997; 90(5):312–7. PMID: 9507759

100. Simson FW. Chromomycosis; some observations on the types of the disease in South Africa. Mycologia. 1946; 38(4):432–449. PMID: 2092395

101. Friedlander J, Moss C. Chromoblastomycosis. S Afr Med J. 1949; 23(36):736. PMID: 1319312

102. Martin PM, Berson SD. Fungus diseases in Southern Africa. Mycopathol Mycol Appl. 1973; 50(1):1–84. https://doi.org/10.1007/BF02050005 PMID: 4711932

103. Harwood-Nash DC. A case of chromoblastomycosis in a coloured male. S Afr Med J. 1962; 36:647–50. PMID: 13905116

104. Findlay GH. Chromomycosis caused by the Simson species of Hormodendrum. S Afr Med J. 1957; 31(22):538–40. PMID: 13442743

105. Lurie H. Fungal diseases in South Africa. S Afr Med J. 1955; 29(8):186–8 PMID: 14358886

106. Ninane G. Rev Med Liege. 1956; 11(21):601–3. PMID: 13390204

107. Banks IS, Palmieri JR, Lanoie L, Connor DH, Meyers WM. Chromomycosis in Zaire. Int J Dermatol. 1985; 24(5):302–7. https://doi.org/10.1111/j.1365-4362.1985.tb05789.x PMID: 4018979

108. Destombes P, Ravisse P, Nazimoff O. Summary of deep mycoses established in 20 years of histopathology in the Institut Pasteur de Brazzaville. Bull Soc Pathol Exot Filiales. 1970; 63(3):315–24. PMID: 5537809
110. Vanbreuseghem R, Vandepitte J, Thys A, Windey W. First case of chromoblastomycosis due to Phialophora pedrosoi in a Belgian Congo native. Ann Soc Belg Med Trop (1920). 1951; 31(4):495–9.

111. Rasson G, Thys A. Second case of chromoblastomycosis in the Belgian Congo. Ann Soc Belg Med Trop (1920). 1951; 31(5):547–50. PMID: 14915309

112. Defrenne P. Third case of chromoblastomycosis in the Belgian Congo. Ann Soc Belg Med Trop (1920). 1952; 32(5):417–9. PMID: 13031302

113. Thys A, Courtois G, Vanbreuseghem R, Baker DH, Bertrand M, De Muyncke A, Limbos P, Verselder R et al. Nine new cases of chromoblastomycosis in the Belgian Congo; trial and failure of treatment by pentamidine. Ann Soc Belg Med Trop (1920). 1952; 32(5):491–500. PMID: 13031302

114. Heuls J, Orio J. First case of chromoblastomycosis ever seen in French Equatorial Africa, with isolation of the causative organism. Bull Soc Pathol Exot Filiales. 1958; 51(6):887–91. PMID: 13662793

115. Ricossé PJ, Guélain J, Boudon A, Ogrièz M. New cases of chromoblastomycosis: importances of anatomo-pathologic examinations. Bull Soc Pathol Exot Filiales. 1983; 76(5):596–603. PMID: 6673852

116. Kombila M, Gomez de Diaz M, Richard-Lenoble D, Renders A, Walter P, Billiault X et al. Chromoblastomycosis in Gabon. Study of 64 cases. Sante. 1995; 5(4):235–44. PMID: 7582644

117. Ross MD, Gelfand M. Deep fungal infections in Rhodesia—a 10-year survey of histological material. Part I. Cent Afr J Med. 1978 Oct; 24(10):208–12 PMID: 7197350

118. Kwizera R, Bongomin F, Lukande R. Deep fungal infections diagnosed by histology in Uganda: a 70-year retrospective study. Med Mycol. 2020 Apr 3. pii: myaa018. https://doi.org/10.1093/mmy/mya018 PMID: 32242631

119. Cameron HM, Gatei D, Bremner AD. The deep mycoses in Kenya: A histopathological study. 3. Chromomycosis. East Afr Med J. 1973; 50(8):406–12. PMID: 4761210

120. Destombes P, Poirier A, Nazimoff O. Deep mycoses identified in 9 years’ histopathological practice in the Institut Pasteur du Cameroun. Bull Soc Pathol Exot Filiales. 1970; 63(3):310–5. PMID: 5537808

121. Ravisse P, Mariat F, Destombes P. Association of chromoblastomycosis (Fonsecaea pedrosoi) and histoplasmosis (Histoplasma capsulatum) in South Cameroon. Bull Soc Pathol Exot Filiales. 1973; 66(3):385–90. PMID: 4801858

122. Gamet A, Brottès H. Chromoblastomycosis in the Cameroons. Bull Soc Pathol Exot Filiales. 1963; 56:117–9. PMID: 14073518

123. Campourcy A. Chromoblastomycose au Cameroun. Bull Soc Pathol Exot Filiales. 1947; 40(7–8):252. PMID: 18903347

124. Samira Eddaoudi. Les mycoses profondes (à propos de 07 cas). 2016. Doctoral Thesis. Available from: http://scolarite.fmp-usmba.ac.ma/cdim/mediatheque/e_theses/239-16.pdf

125. Tlamcani Z, Figuigui S, Taghouiti A, El Loudi S, Mernissi FZ. Chromoblastomycosis due to Cladosporium carrionii: case report. Moldovan Journal of Health Sciences. 2016; 9:98–101

126. Lassir A, Chiheb S, Azzouzi S, Benchikh H. Chromomycoses intercostales. In: Congrès Maghrébin de Dermatologie, 3–4 November. Tunis. 2006. Tunis.

127. Kawtar I, Salim G, Mariame M, Fatimazahra M, Imane T, Salma B et al. Sporotrichoid chromomycosis. Dermatology Online Journal. 2013; 19(11):3. Available from: https://escholarship.org/uc/item/913521rt.

128. Ikhachineya Y, Elbenayea J, Er-Rami M, Sakkah A, Jakar A, Elhaouri M. Chromomycose cutanée étendue: efficacité de l’association terbinafine et cryothérapie. Annales de Dermatologie et de Vénérologie. 2018; 145:512–515. https://doi.org/10.1016/j.annder.2018.04.005 PMID: 29779858

129. Halli F, K. Khadir K, Zouhair K, Benchikh H, Azzouzi S. Suppurations périméatiques: étude étiologique de 60 cas. Annales de dermatologie et de vénérologie. 2010; 137:591–596. https://doi.org/10.1016/j.annder.2010.04.020 PMID: 20932437

130. Labbardi W, Halli F, Moundib H, Baline K, Chiheb S. Chromomycose cutanée: trois nouveaux cas marocains. Annales de Dermatologie et de Vénérologie. 2015; 142(12):S625.

131. Belarbi F, Ouadi Z, Hocar O, Akhdari N, Amal S, Zoughari B et al. Chromomycose cutanée diffuse. Annales de Dermatologie et de Vénérologie. 2016; 143:S37–S38. https://doi.org/10.1016/S0151-9638(16)30048-6 PMID: 29429508

132. Radouane N, Halli F, Khadir K, Soussi M, Ouakadi A, Marouane S et al. Chromomycose cutanée diffuse à Phialophora verrucosa. Annales de dermatologie et de vénérologie. 2013; 140:197–201. https://doi.org/10.1016/j.annder.2012.10.005 PMID: 23466152

133. van Raalte JA, Venkataramaiah NR. Chromomycosis in Tanzania. Trop Geogr Med. 1982; 34(1):39–42. PMID: 7080185
134. Savioli L, Bianco P. A case of chromomycosis from Pemba Island. J Trop Med Hyg. 1983 Jun; 86 (3):109–11. PMID: 6632031

135. Olafsson J, Lindtjorn B, Beiske K. Chromomycosis: a report of three cases from Ethiopia. Olafsson J, Lindtjorn B, Beiske K. Ethiop Med J. 1981 Jul; 19(3):91–6. PMID: 7285897

136. Gimbcl DC, Legesse TB. Dermatopathology practice in ethiopia. Gimbcl DC, Legesse TB. Arch Pathol Lab Med. 2013 Jun; 137(6):798–804. https://doi.org/10.5858/arpa.2012-0041-RA PMID: 23721275

137. Gatti F, Renoirte R, Vanbreuseghem R. African histoplasmosis and chromomycosis in Angolians. Ann Soc Belges Med Trop Parasitol Mycol. 1967; 47(3):249–56. PMID: 5619092

138. Des Marchais J, Vanderick F. A case of chromomycosis in Rwanda. Ann Soc Belges Med Trop Parasitol Mycol. 1970; 50(2):205–9 PMID: 5518951

139. Jacyk WK, Lawande RV, Tulpule SS. Deep mycoses in West Africa: a report of 13 cases and review of the Nigerian literature. J Natl Med Assoc. 1981; 73(3):251–6. PMID: 7009881

140. Ive FA, Clark BM. Chromoblastomycosis in Nigeria. J Trop Med Hyg. 1966; 69(8):184–6. PMID: 5920216

141. Grillo E, Mavura D, Jaén-Olasolo P. Chromomycosis. Rev Clin Esp (Barc). 2014; 214(3):e35. doi:10.1016/j.rce.2013.11.012 PMID: 24439668

142. Fenniche S, Zaraa I, Benmously R, Marrak H, Debbiche A, Ayed MB et al. Chromomycosis: a new Tunisian case report. Int J Infect Dis. 2005; 9(5):288–9. https://doi.org/10.1016/j.ijid.2004.10.005 PMID: 16098783

143. Marrak H, Mnajaa N, Fenniche S, Fourati M, Zghal M, Chaker E et al. Chromomycosis: a case report from Tunis. J Mycol Med 2003; 13:37–9.

144. Ezzine-Sebah N, Benmosly R, Chaker BFE, Zermani R, Kamoun MR. Chromomycosis arising in a Tunisian man. Dermatol Online J. 2005; 11(2):14. PMID: 26049906

145. El Amine El Hadj O, Msakni I, Lamine F, Laabidi B, Bouziane A. Chromomycosis: Report of a case from a non-endemic region. Our Dermatol Online. 2017; 8(1):100–101. Available from: http://www.oder matol.com/oder matology/20171/27.Chromoblas to-HadjA.pdf

146. Martin De Miranda P, Segretain G, Bataillard. A case of chromoblastomycosis in Réunion. Bull Soc Pathol Exot Filiales. 1958; 51(6):884–7. PMID: 13662792

147. Hofmann H, Choi SM, Wilsmann-Theis D, Horré R, de Hoog GS, Bieber T. Invasive chromomycosis and sinusitis due to Phialophora verrucosa in a child from northern Africa. Mycoses. 2005; 48 (6):456–61. https://doi.org/10.1111/j.1439-0507.2005.01150.x PMID: 16262887

148. Bhaktaviziam C, Shafi M, Mehta MC, Bhaktaviziam CA. Chromomycosis. Report of a case from Tripoli, Libya. Mycopathology. 1983; 82(2):111–3. https://doi.org/10.1007/BF00437340 PMID: 6884899

149. Miquel P. Trois observations de chromomycose à La Réunion. Médecine et Maladies Infe ctieuses. 1978; 8:398–403.

150. Hofmann H, Choi SM, Wilsmann-Theis D, Horré R, de Hoog GS, Bieber T. Invasive chromomycosis and sinusitis due to Phialophora verrucosa in a child from northern Africa. Mycoses. 2005; 48 (6):456–61. https://doi.org/10.1111/j.1439-0507.2005.01150.x PMID: 16262887

151. Bari AU, Khan MB. Pattern of skin infections in black Africans of Sierra Leone (West Africa). Indian Journal of Dermatology 2007; 52(1):361–368.

152. Develoux M, Dieng MT, Ndiaye B, Ndiaye B, Lepers JP. Chromomycose à Exophiala spinifera en Afrique sahélienne. Ann Dermatol Venereol 2006; 133:68–72. https://doi.org/10.1016/s0151-9638(06)70849-3 PMID: 16495858
158. Passeron T, Barberet P, Colbachini P, Hovette P, Lacour JP. Association d’un eumycétome et d’une chromomycose: une observation au Sénégal. Med Trop (Mars) 2003; 63(6):614–6.

159. Merriweather AM, Weir A, Murray JF. S Afr Med J. 1972 Nov 4; 46(44):1679–81. PMID: 4651722

160. Carteron B, Bruneau M, Morvan D, Rodhain- Reboug F, Destombes P, Francq JR. Human mycoses in the Republic of Djibouti. Bull Soc Pathol Exot Filiales. 1978 Jan-Feb; 71(1):63–70. PMID: 719848

161. Denning DW, Razanamparany VR, Rakotoarivelona RA. The burden of serious fungal diseases in Madagascar. Special Issue: 7th Trends in Medical Mycology, 9–12 October 2015, Lisbon, Portugal. Mycoses. 2015; 58(suppl.4):132.

162. Rasamoelina T, Rakotozandraindry N, Raberahonana M, Rapelano Rabenja F, Rakoto Andrianarivelona M, Andrianarison M et al. Chromoblastomycosis and sporotrichosis in Madagascar: epidemiology, molecular diagnostic and perspectives. Mycoses. 2015; 58(54):99–100.

163. Esterre P, Andriantsahavandy A, Ramarcel ER, Pecarrere JL. Forty years of chromoblastomycosis in Madagascar: a review. Am J Trop Med Hyg 1996; 55:45–47. https://doi.org/10.4269/ajtmh.1996.55.45 PMID: 8702021

164. Gauzère BA, Aubry P. History of human epidemic and endemic diseases in the southwest Indian Ocean. Med Sante Trop. 2013 May 1; 23(2):145–57. https://doi.org/10.1684/mst.2013.0183 PMID: 2379783

165. Lu S, Lu C, Zhang J, Hu Y, Li X, Xi L. Chromoblastomycosis in Mainland China: a systematic review on clinical characteristics. Mycopathologia. 2013; 175(5–6):489–95 https://doi.org/10.1007/s11046-012-9586-z PMID: 23086329

166. Harada S, Fumimori M, Honda M, Ueda T, Murakami M, Hattori S et al. Chromomycosis of the skin: report of five cases. Int J Dermatol. 1971; 10(2):118–25. https://doi.org/10.1111/j.1365-4362.1971.tb03721.x PMID: 5105128

167. Fukushiro R. Chromomycosis in Japan. Int J Dermatol. 1983; 22(4):221–9. https://doi.org/10.1111/j.1365-4362.1983.tb03371.x PMID: 6345416

168. Tanuma H, Hiramatsu M, Mukai H, Abe M, Kume H, Nishiyama S et al. Case report. A case of chromoblastomycosis effectively treated with terbinafine. Characteristics of chromoblastomycosis in the Kitasato region, Japan. Mycoses. 2000; 43(1–2):79–83. https://doi.org/10.1046/j.1439-0507.2000.00548.x PMID: 10838854

169. Kondo M, Hiruma M, Nishioka Y, Mayuzumi N, Mochida K, Ikeda S et al. A case of chromomycosis caused by Fonsecaea pedrosi and a review of reported cases of dermatophagous fungal infection in Japan. Mycoses. 2005; 48(3):221–5 https://doi.org/10.1111/j.1439-0507.2005.01089.x PMID: 15842342

170. Agarwal R, Singh G, Ghosh A, Verma KK, Pandey M, Xess I. Chromoblastomycosis in India: Review of 169 cases. PLoS Negl Trop Dis. 2017 Aug 3; 11(8):e0005534. https://doi.org/10.1371/journal.pntd.0005534 PMID: 28771470

171. Attapattu MC. Chromoblastomycosis—a clinical and mycological study of 71 cases from Sri Lanka. Mycopathologia. 1997; 137(3):145–51. https://doi.org/10.1023/a:1006819530825 PMID: 9368408

172. Hsu Yung-Hsiang. Chromomycosis. Tzu Chi Medical Journal. 2009; 21(1):89.

173. Huang S, Lee S, Lee C, Ho H, Chang L. Coexisting Chromoblastomycosis and Mycobacterium fortuitum Skin and Subcutaneous Infection. Coexisting Chromoblastomycosis and Mycobacterium fortuitum Skin and Subcutaneous Infection. Journal of Internal Medicine of Taiwan. 2008; 19(4):365–370.

174. Yang SP, Liu CY, Cheng NC, Lee WS, Liu CE, Kuo BI. Successful treatment of subcutaneous mycoses with fluconazole: a report of two cases. Zhonghua Yi Xue Za Zhi (Taipei). 1995; 56(6):432–5. PMID: 8851486

175. Yang CS, Chen CB, Lee YY, Yang CH, Chang YC, Chung WH et al. Chromoblastomycosis in Taiwan: A report of 30 cases and a review of the literature. Med Mycol. 2018; 56(4):395–405. https://doi.org/10.1093/mmy/myx075 PMID: 29087525

176. Jeyalakshmi P, Looi LM, Soo-Hoo TS. Chromoblastomycosis in Malaysia. Mycopathologia 109: 27–31, 1990. https://doi.org/10.1007/BF00437003 PMID: 2325747

177. Yap FB. Chromoblastomycosis in Sarawak, East Malaysian Borneo. Trans R Soc Trop Med Hyg. 2010; 104(2):168–9. https://doi.org/10.1016/j.trstmh.2009.05.016 PMID: 19766279

178. Pradhan SV, Talwar OP, Ghosh A, Swami RM, Shiva Raj KC, Gupta S. Chromoblastomycosis in Nepal: a study of 13 cases. Indian J Dermatol Venereol Leprol. 2007 May-Jun; 73(3):176–8. https://doi.org/10.4103/0378-6233.32741 PMID: 17558050

179. Agarwalla A, Khanal B, Garg VK, Agrawal S, Jacob M, Rani S et al. Chromoblastomycosis: report of two cases from Nepal. J Dermatol. 2002 May; 29(5):315–9. https://doi.org/10.1111/j.1346-8138.2002.tb00270.x PMID: 12081165
180. McDaniel P, Walsh DS. Chromoblastomycosis in Western Thailand. Am J Trop Med Hyg. 2010; 83(3):448. https://doi.org/10.4269/ajtmh.2010.10-0210 PMID: 20810801

181. Ungpakorn R, Reangchaintam S. Pulse itraconazole 400 mg daily in the treatment of chromoblastomycosis. Clin Exp Dermatol. 2006; 31(2):245–7. https://doi.org/10.1111/j.1365-2230.2005.02024.x PMID: 16487103

182. Mahaisavariya P, Chaiprasert A, Sivayathorn A, Khemngern S. Deep fungal and higher bacterial skin infections in Thailand: clinical manifestations and treatment regimens. International Journal of Dermatology 1999, 38, 279–284. https://doi.org/10.1046/j.1365-4362.1999.00681.x PMID: 10321944

183. Kampirapap K, Reangchaintam S, Ornpaew P, Tresukosol P. Chromoblastomycosis masquerading as dermatophytosis, with the description of a new opportunistic species. Southeast Asian J Trop Med Public Health. 2015 Jan; 46(1):105–9. PMID: 26513911

184. Bonne C. Sur la presence de la chromoblastomycose aux Indes Orientales Néerlandaises. Bull Soc Path Exot. 1930; 23:765.

185. Haykal Ahmad, Kadir Dirmawi, Amin Safruddin. Chromoblastomycosis et causaphialophora verrucosa. Indonesian Journal of Dermatology and Venereology. 2013; 1(4):66–72.

186. Harahap M, Nasution MA. Dermatomycoses in Indonesia. Int J Dermatol. 1984; 23(4):273–4. https://doi.org/10.1111/j.1365-4632.1984.tb01247.x PMID: 6735554

187. Park SG, Oh SH, Suh SB, Lee KH, Chung KY. A case of chromoblastomycosis with an unusual clinical manifestation caused by Phialophora verrucosa on an unexposed area: treatment with a combination of amphotericin B and 5-flucytosine. Br J Dermatol. 2005; 152(3):560–4. https://doi.org/10.1111/j.1365-2133.2005.06424.x PMID: 15787829

188. Kim DM, Hwang SM, Suh MK, Ha GY, Choi GS, Shin J et al. Chromoblastomycosis Caused by Fonsecaea pedrosoi. Ann Dermatol. 2011; 23(3):369–74. https://doi.org/10.5021/ad.2011.23.3.369 PMID: 21909211

189. Ahn SK, Lee SN. A case of chromonycosis. Korean J Dermatol 1990; 28:345–348.

190. Suh MK, Sung YO, Yoon KS, Ha GY, Kim JR. A case of chromoblastomycosis caused by Fonsecaea pedrosoi. Korean J Dermatol 1996; 34:832–836.

191. Kim HU, Son GY, Ihm CW. A case of chromoblastomycosis showing a good response to itraconazole. Ann Dermatol 1997; 9:51–54.

192. Kim SW, Oh SH, Choi SK, Lee YH, Yoon JH, Bang YJ et al. Chromoblastomycosis treated with occlusive dressing of amphotericin B cream. Korean J Med Mycol 2000; 5: 144–149.

193. Kang NG, Suh MK, Park SG, Song KY, Kim TH. A case of chromomycosis showing ulcerative lesions on dorsa of hands. Korean J Dermatol 2002; 40:174–177.

194. Lee CW, Sim SJ, Song KH, Kim KH. A case of chromoblastomycosis treated with terbinafine. Korean J Med Mycol 2003; 8:26–29.

195. Jun JB, Park JY, Kim DW. Chromoblastomyosisis caused by Rhinocladiella aquaspersa. Korean J Med Mycol 2004; 9:117–122. https://doi.org/10.1080/13693780310001597700 PMID: 15283241

196. Khan S, Khan M, Khan F, Ahmad Z, Zia-Ur-Rehman A. A Rare Case of Chromoblastomycosis in a 12-year-old boy. J Pak Med Assoc. 2019; 69(9):1390–1393. PMID: 31511733

197. Hussain I, Rashid T, Haroon TS. Parenteral vitamin D(3) and oral terbinafine for refractory chromoblastomycosis. Br J Dermatol. 2002; 146(4):704. https://doi.org/10.1046/j.1365-2133.2002.04711.x PMID: 11966710

198. Simuangco SA, Halde C. Chromoblastomycosis: first case in the Philippines. J Philipp Med Assoc. 1955; 31(3):117–20. PMID: 14368538
203. Santos LD, Arianayagam S, Dwyer B, Lee KC, O’Kane G, Withnall K et al. Chromoblastomycosis: a retrospective study of six cases at the Royal Darwin Hospital from 1989 to 1994. Pathology. 1996; 28 (2):182–7. https://doi.org/10.1080/0031302960169843 PMID: 8743828

204. Leslie DF, Beardmore GL. Chromoblastomycosis in Queensland: a retrospective study of 13 cases at the Royal Brisbane Hospital. Australas J Dermatol. 1979; 20(1):23–30. https://doi.org/10.1111/j.1440-0960.1979.tb00120.x PMID: 475694

205. Weedon D, van Deurze M, Allison S, Rosendahl C. Chromoblastomycosis in Australia: an historical perspective. Pathology. 2013; 45(5):489–91. https://doi.org/10.1097/PAT.0b013e32836326a1 PMID: 23856839

206. Barrack BB. Chromoblastomycosis in Queensland. Aust J Dermatol. 1952; 1(4):207–13. https://doi.org/10.1111/j.1440-0960.1952.tb01429.x PMID: 13081515

207. Stevens FRT. Chromoblastomycosis. Med J Aust 1947; 2:93. https://doi.org/10.5694/j.1326-5377.1947.tb27572.x PMID: 20257951

208. Powell RE. A survey of chromoblastomycosis in Queensland. Aust J Dermatol. 1952 Oct; 1(4):214–22. https://doi.org/10.1111/j.1440-0960.1952.tb01430.x PMID: 13081516

210. Huerre M, Ravisse P, Dubourdieu D, Morillon M, McCarthy S, Bobin P. Les mycoses profondes observées en Nouvelle-Calédonie. Bull Soc Path Ex 1991; 84:247–256

211. Woodgyer AJ, Bennetts GP, Rush-Munro FM. Four non-endemic New Zealand cases of chromoblastomycosis. Australas J Dermatol. 1992; 33(3):169–76. https://doi.org/10.1111/j.1440-0960.1992.tb00113.x PMID: 1303079

212. Pindycka-Piasecka M, Krzyścik P, Piasecki M, Cieslicki S, Januszewski K, Izdebska-Straszak G et al. Chromoblastomycosis as an endemic disease in temperate Europe: first confirmed case and review of the literature. Eur J Clin Microbiol Infect Dis. 2014 Mar; 33(3):391–8 https://doi.org/10.1007/s10096-013-1969-7 PMID: 24048727

213. Knox J, Marshall C. Med J Aust. 2012 Sep 17; 197(6):350 https://doi.org/10.5694/mja12.10006 PMID: 22994835

214. Menezes N, Varela P, Furtado A, Couceiro A, Calheiros I, Rosado L et al. Chromoblastomycosis associated with Fonsecaea pedrosoi in a carpenter handling exotic woods. Dermatol Online J. 2008; 14 (2):9. PMID: 18700112

215. Buot G, Bachmeyer C, Benazera C, Bourrat E, Beltzer-Garrelly E, Binet O. Chromoblastomycosis: an unusual diagnosis in Europe. Acta Derm Venereol. 2005; 85(3):259–60. https://doi.org/10.1080/00015550410024508 PMID: 16040416

216. Chopinaud M, Bonhomme J, Comoz F, Barreau M, Morice C, Verneuil L. Chromomycosis in metropolitan France. Ann Dermatol Venereol. 2014; 141(5):396–8. https://doi.org/10.1016/j.annder.2014.01.009 PMID: 24835659

217. Ouédraogo MS, Vignon-Pennamen MD, Battistella M, Levy A, Feuillade de Chauvin M, Petit A. Chromomycosis acquired in a non-tropical area: A case report. Ann Dermatol Venereol. 2017 Jun—Jul; 144(6-7):438–42. https://doi.org/10.1016/j.annder.2017.02.006 PMID: 28396061

218. Richarz NA, Jaka A, Fernández-Rivas G, Bassas J, Bielsa I, Ferrándiz C. First case of chronic cutaneous chromoblastomycosis by Rhinocladiella similis acquired in Europe. Clin Exp Dermatol. 2018; 43 (8):925–927. https://doi.org/10.1111/ced.13659 PMID: 29885020

219. Lane CG. A cutaneous lesion caused by a new fungus Phialophora verrucosa. The Journal of Cutaneous Diseases. 1915; 33:1–8.

220. Wilson SJ, Hulsey S, Weidman FD. Chromoblastomycosis in Texas. Arch Derm Syphilol. 1933; 27 (1):107–122.

221. Moore M, Mapother P. Chromomycosis of the face: report of a case and a study of the causative organism, Phialophora verrucosa. Arch Derm Syphilol. 1940; 41(1):42–54.

222. Weidman FD, Rosenthal LH. Chromoblastomycosis: a new and important blastomycosis in north american acquired in a non-tropical area: A case report. Ann Dermatol Venereol. 2017 Jun—Jul; 144(6-7):438–42. https://doi.org/10.1016/j.annder.2017.02.006 PMID: 28396061

223. Emmons CW, Hailey H, Hailey H. Chromoblastomycosis: report of the sixth case from continental United States. JAMA. 1941; 116(1):25–28.

224. Moore M, Cooper ZK, Weiss RS. JAMA. 1943; 122(18):1237–1243.

225. Binford CH, Hess G, Emmons CW. Chromoblastomycosis: report of a case from continental united states, report of the classification of the causative fungus. Arch Derm Syphilol. 1944; 49 (6):398–402.

226. Barwasser NC. Chromoblastomycosis; thirteenth reported case in the United States. J Am Med Assoc. 1953; 153(6):556. https://doi.org/10.1001/jama.1953.02940230028006f PMID: 13084420
227. French AJ, Russell SR. Chromoblastomycosis; report of first case recognized in Michigan, apparently contracted in South Carolina. AMA Arch Derm Syphilol. 1953; 67(2):129–34. https://doi.org/10.1001/archderm.1953.01540020007002 PMID: 13029895

228. Howles JK, Kennedy CB, Garvin WH, Brueck JW, Buddingh GJ. Chromoblastomycosis: report of nine cases from a single area in Louisiana. AMA Arch Derm Syphilol. 1954; 69(1):83–90. https://doi.org/10.1001/archderm.1954.01540100805008 PMID: 13113726

229. Mugleston BJ, Usatine RP, Rosen T. Wide Morphologic Variability of Chromoblastomycosis in the Western Hemisphere. Skinmed. 2016; 14(6):423–427. eCollection 2016. Acesso https://skinmedjournal.com/2016-issues/# PMID: 28031127

230. Franco-Paredes C, Mathur S, Villamil-Gomez W, Henao-Martinez AF. A Man Who Harvest Peanuts With Verrucous Lesions In His Right Index Finger. Am J Med Sci. 2018; 355(3):e7. https://doi.org/10.1016/j.amjms.2017.11.010 PMID: 29549935

231. Burns RE. Chromoblastomycosis in a Canadian airman serving in Ceylon. Can Med Assoc J. 1950; 63(6):595–6. PMID: 14792443

232. Poverty Home—World Bank Group. In: The World Bank: Countries and Economies. Cited 26 April 2020 [Internet]. Available from: https://data.worldbank.org/country

233. Rural Population—World Bank Group. In: World Bank staff estimates based on the United Nations Populations Division’s World Urbanization Prospects: 2018 Revision. Cited 26 April 2020 [Internet]. Available from: https://data.worldbank.org/indicator/SP.RUR.TOTL.ZS

234. Santmyire A. The Effectiveness of a Multifocal Training to Improve the Treatment of Chromoblastomycosis in Rural Madagascar. J Health Care Poor Underserved. 2016; 27(3):993–1010. https://doi.org/10.1353/hpu.2016.0146 PMID: 27524747

235. Al-Hamdani M, Salmo NA, Hadi AW. Chromomycosis of the skin: first case report in Iraq. Int J Dermatol. 1973 Nov-Dec; 12(6):354–7. https://doi.org/10.1111/j.1365-4362.1973.tb00220.x PMID: 4797015

236. Grandizio LC, Wagner B, Graham J, Klena JC. Upper Extremity Trauma Resulting From Agricultural Accidents: Mechanism and Severity for Patients With and Without Upper Extremity Injury. Hand (N Y). 2018; 13(4):384–390. https://doi.org/10.1177/1558944717715140 PMID: 28645215

237. Sousa MG, Reid DM, Schweighoffer E, Tybulewicz V, Ruland J, Langhorne J et al. Restoration of pattern recognition receptor costimulation to treat chromoblastomycosis, a chronic fungal infection of the skin. Cell Host Microbe. 2011 May 19; 9(5):436–43. https://doi.org/10.1016/j.chom.2011.04.005 PMID: 21575914

238. Gomes RR, Vicente VA, Azevedo CM, Salgado CG, da Silva MB, Queiroz-Telles F et al. Molecular Epidemiology of Agents of Human Chromoblastomycosis in Brazil with the Description of Two Novel Species. PLoS Negl Trop Dis. 2016; 10(11):e0005102 https://doi.org/10.1371/journal.pntd.0005102

239. Rasamoelina T, Maubon D, Andrianarison M, Ranaivo I, Sendrasoa F, Rakotozandraindy N et al. Endemic Chromoblastomycosis Caused Predominantly by Fonsecaea nubica in Madagascar. Emerg Infect Dis. 2020; 26(6):1201–1201. https://doi.org/10.3201/eid2606.191498 PMID: 32441639

240. Esterre P, Inzan CK, Ramarcel ER, Andriantsimahavandy A, Ratsiohara na M, Pecarrere JL et al. Treatment of chromoblastomycosis with terbinafine: preliminary results of an open pilot study. Br J Dermatol. 1996 Jun; 134 Suppl 4 6:33–6. https://doi.org/10.1111/j.1365-2133.1996.tb15658.x PMID: 8763467

241. Marques SG, Bomfim MRQ, Azevedo CMPS, Martins CVB, Marques ACG, Gonçalves AG et al. Mixed secondary bacterial infection is associated with severe lesions of chromoblastomycosis in a neglected population from Brazil. Diagn Microbiol Infect Dis. 2019 Oct; 95(2):201–207. https://doi.org/10.1016/j.diagmicrobio.2019.05.018 PMID: 31262546

242. Azevedo CM, Marques SG, Santos DW, Silva RR, Silva NF, Santos DA et al. Squamous cell carcinoma derived from chronic chromoblastomycosis in Brazil. Clin Infect Dis. 2015 May 15; 60(10):1500–4. https://doi.org/10.1093/cid/civ104 Epub 2015 Feb 13. PMID: 25681378

243. Mazo Fávero Gimenes V, Da Glória de Souza M, Ferreira KS, Marques SG, Gonçalves AG, Vagner de Castro Lima Santos D et al. Cytokines and lymphocyte proliferation in patients with different clinical forms of chromoblastomycosis. Microbes Infect. 2005 Apr; 7(4):708–13. https://doi.org/10.1016/j.micinf.2005.01.006 PMID: 15848277

244. Azevedo CD, Bruña-Romero O, Marques SG, Nascimento FR, Pinto MC, Silva LA et al. Association of IgG immunoglobulin and subclasses level with the severity of chromoblastomycosis due to Fonsecaea pedrosii and therapeutic response to itraconazole. Eur J Clin Microbiol Infect Dis. 2014 Oct; 33 (10):1781–7. https://doi.org/10.1007/s10096-014-2138-3 PMID: 24832023

245. Santos DW, Camargo LF, Gonçalves SS, Ogawa MM, Tomimori J, Enokihara MM et al. Melanized fungal infections in kidney transplant recipients: contributions to optimize clinical management. Clin Microbiol Infect. 2017 May; 23(5):333.e9–333.e14. https://doi.org/10.1016/j.cmi.2016.12.024 PMID: 28062320
246. Ogawa MM, Peternelli MP, Enokihara MM, Nishikaku AS, Gonçalves SS, Tomimori J. Spectral Mani-
festation of Melanized Fungal Infections in Kidney Transplant Recipients: Report of Six Cases. Myco-
pathologia. 2016 Jun; 181(5–6):379–85. https://doi.org/10.1007/s11046-016-0005-8 PMID: 27025729

247. Negroni R, Tobón A, Bustamante B, Shikanai-Yasuda MA, Patino H, Restrepo A. Posaconazole treat-
ment of refractory eumycetoma and chromoblastomycosis. Rev Inst Med Trop Sao Paulo. 2005 Nov-
Dec; 47(6):339–46. https://doi.org/10.1590/s0036-46652005000600006 PMID: 16553324

248. Lima AM, Sacht GL, Paula LZ, Aseka GK, Goetz HS, Gheller MF et al. Response of chromoblastomy-
cosis to voriconazole. An Bras Dermatol. 2016 Sep-Oct; 91(5):679–681. https://doi.org/10.1590/
abd1806-4841.20165142 PMID: 27828652

249. de Sousa Mda G, Belda W Jr, Spina R, Lota PR, Valente NS, Brown GD et al. Topical application of
imiquimod as a treatment for chromoblastomycosis. Clin Infect Dis. 2014 Jun; 58(12):1734–7. https://
doi.org/10.1093/cid/ciu168 Epub 2014 Mar 14. PMID: 24633683; PMCID: PMC4036686.

250. Belda W Jr, Criado PR, Passero LFD. Successful treatment of chromoblastomycosis caused by Fon-
secaea pedrosoi using imiquimod. J Dermatol. 2020 Apr; 47(4):409–412. https://doi.org/10.1111/
1346-8138.15225 Epub 2020 Jan 21. PMID: 31960479.

251. Azevedo Cde M, Marques SG, Resende MA, Gonçalves AG, Santos DV, da Silva RR et al. The use of
glucan as immunostimulant in the treatment of a severe case of chromoblastomycosis. Mycoses.
2008 Jul; 51(4):341–4. https://doi.org/10.1111/j.1439-0507.2007.01485.x Epub 2008 Apr 28. PMID:
18444974.