

# Reconstructive Surgery for the Neglected Tropical Diseases: Global Gaps and Future Directions

Kala T. Pham, BS\*†  
Peter J. Hotez, MD, PhD‡  
Kristy L. Hamilton, MD§

**Background:** Several neglected tropical diseases (NTDs) are highly disfiguring, particularly those in resource-poor countries that lack access to basic surgery. There has been a push to integrate surgery into treatment programs for NTDs. In this article, we provide an overview of the major disfiguring NTDs and discuss the processes and barriers that impede access to reconstructive surgical treatments or their integration into health systems.

**Methods:** A review of the literature was conducted using the online database PubMed, from 2008 to 2021 with the specific diseases listed as NTDs either on the World Health Organization or the *PLoS Neglected Tropical Disease* websites. Reference lists of identified articles and reviews were also searched, as were databases from the World Health Organization's *Weekly Epidemiological Record*.

**Result:** Success in the surgical treatment and postoperative care of disfiguring NTDs would benefit from standardization and harmonization of surgical approaches and procedures. In some settings, reconstructive surgery should be used cautiously, emphasizing appropriate use of antibiotics, partnerships with global and local surgical teams, and local capacity building. Preventative hygiene approaches remain paramount in resource-poor areas.

**Conclusions:** Surgery is a promising treatment for NTDs that result in disfigurement and disability. The expansion of local capacity building, with medical trips and surgical training of local health workers, together with the development of universal surgical protocols remain essential cornerstones for NTD reconstructive surgery. Antibiotics and drug management should comprise key first steps before turning to surgery. (*Plast Reconstr Surg Glob Open* 2023; 11:e4987; doi: 10.1097/GOX.0000000000004987; Published online 17 May 2023.)

## INTRODUCTION

Neglected tropical diseases (NTDs) comprise at least 20 poverty-related and chronically debilitating parasitic, bacterial, and fungal infections that affect billions of people worldwide (Table 1).<sup>1,2</sup> Several NTDs are highly disfiguring, particularly those in resource-poor countries that lack access to basic surgery. A Lancet Commission on Global Surgery has highlighted this aspect of global

health disparities, prompting an initial call to bundle or integrate simple surgeries into mass treatment programs for NTDs and other conditions.<sup>3,4</sup>

Disfigurement and disability are elements common to many of the NTDs, often leading to social stigma, and have been noted to be especially harmful to girls and women living in poverty.<sup>5,6</sup> Many of these include conditions with chronic skin changes such as onchocerciasis, scabies and yaws.<sup>7</sup> Additional NTDs that are even more disfiguring and stigmatizing also present opportunities for low-cost higher throughput reconstructive surgery. Mycetoma, lymphatic filariasis (LF), leprosy, and noma are four widely prevalent NTDs where reconstructive surgery has and can play an instrumental role in the treatment process. In this article, we discuss the processes and barriers in place for reconstructive surgery to be an effective tool for treating highly disfiguring NTDs.

Here, we briefly review current knowledge on the prevalence, distribution, and disease burden resulting from NTDs, focusing on the disfiguring NTDs that recommend surgery for treatment or chronic management. We extend an earlier 2017 *PLoS Neglected Tropical*

From the \*Departments of Biology and Biochemistry, University of Houston, Houston, Tex.; †Houston Premedical Academy, University of Houston and Baylor College of Medicine, Houston, Tex.; ‡Departments of Pediatrics and Molecular Virology and Microbiology, National School of Tropical Medicine, Baylor College of Medicine, Houston, Tex.; and §Private Practice, Houston, Tex. Received for publication September 30, 2022; accepted March 15, 2023.

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DOI: 10.1097/GOX.0000000000004987

Disclosure statements are at the end of this article, following the correspondence information.

**Table 1. The NTDs Recognized by the WHO**

| Neglected Tropical Diseases                       |   |
|---|---|
| <i>Buruli ulcer</i>                               | <i>Mycetoma</i>                                   |
| Chagas disease                                    | <i>Chromoblastomycosis and other deep mycoses</i> |
| Dengue and chikungunya                            | <i>Onchocerciasis (river blindness)</i>           |
| Dracunculiasis (Guinea-worm disease)              | Rabies  |
| Echinococcosis                                    | <i>Scabies and other ectoparasitoses</i>          |
| Foodborne trematodiasis                           | Schistosomiasis                                   |
| Human African trypanosomiasis (sleeping sickness) | Soil-transmitted helminthiasis                    |
| <i>Leishmaniasis</i>                              | Snakebite envenoming                              |
| <i>Leprosy (the Hansen disease)</i>               | Taeniasis/cysticercosis                           |
| <i>Lymphatic filariasis</i>                       | Trachoma  |
|   | <i>Yaws and other endemic treponematoses</i>      |

Italicized entries include the NTDs commonly associated with chronic deformities, skin changes, or disfigurement, which often result in social stigma.

Diseases report specific for LF and trachoma surgery as a component of mass drug administration efforts.<sup>4</sup> The review of the literature was conducted using the online database PubMed from 2008 to 2021 with the specific diseases listed as neglected tropical diseases either on the WHO or PLoS Neglected Tropical Disease websites (<http://www.plosntds.org/static/scope.action>).<sup>8</sup> Reference lists of identified articles and reviews were also searched by hand, as were databases from the WHO (<http://www.who.int>), including the WHO’s *Weekly Epidemiological Record*.

### MYCETOMA

Mycetoma is a chronic granulomatous inflammatory disease caused by fungi or bacteria that infect subcutaneous tissue, yielding painless, soft tissue lesions with seropurulent discharge (Fig. 1). The disease represents one of the newest conditions to be recognized as an NTD by the WHO.<sup>9</sup> The disease is common in the Sahel region of Africa and extends across to a “mycetoma belt” in the

### Takeaways

**Question:** What is the recommended surgical treatment or chronic management for neglected tropical diseases resulting in disfigurement and disability?

**Findings:** For successful surgical treatment and postoperative care of neglected tropical diseases, standardization of surgical procedures is needed. Currently, reconstructive surgery should be used cautiously, and focus must be placed on antibiotic administration and partnerships with global and local surgical teams.

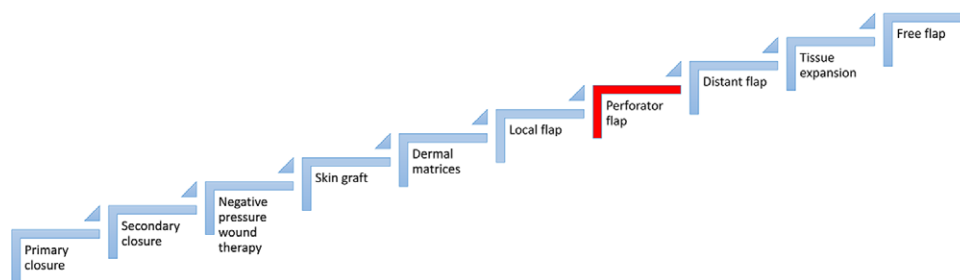
**Meaning:** Surgery is a promising treatment for neglected tropical diseases that result in disfigurement and disability; however, the expansion of medical trips and surgical training of local health workers alongside development of universal surgical protocols is required to utilize reconstructive surgery beneficially.

tropics and subtropics.<sup>10</sup> Over 82% of cases are of the lower extremities.<sup>11</sup> The disease results in these granulomatous open wounds that are often complicated by superimposed bacterial infections, which can require debridement and drug administration to control and prevent ongoing infection or progression to sepsis.<sup>9,12,13</sup> Depending on if the mycetoma is caused by actinomycetoma (bacteria) or eumycetoma (fungus), patients will either use cotrimoxazole or itraconazole, respectively, after surgical debulking.<sup>14</sup> However, these treatments are costly and require patients’ adherence for an extensive period of time. To address this, the first clinical trial for mycetoma treatment started in Sudan in 2017 to develop fosravuconazole for eumycetoma.<sup>15</sup> The goal for this new treatment is for it to be more accessible to rural populations.<sup>15</sup> Drug management may be required for up to 12 months after surgery, which is costly, and surveillance is required for 2 years to ensure a definitive cure.<sup>12</sup>

Many of the surgical methods used are focused on improving immediate outcomes. Initial surgical management involves establishing local control with the addition



**Fig. 1.** Clinical presentation of mycetoma. (From the Centers for Disease Control and Prevention Public Health Image Library. <https://phil.cdc.gov/Details.aspx?pid=19089> and <https://phil.cdc.gov/Details.aspx?pid=14740>. These images are in the public domain and thus free of any copyright restrictions.)



**Fig. 2.** Reconstructive surgery ladder.

of systemic antimicrobial therapies.<sup>11,16</sup> Soft tissue lesions require local excision and closure, while being sure to avoid puncturing the capsule of the granuloma, seeding additional sites of infection.<sup>12</sup> Multiple debridements may be required for the most severe lesions, or even amputation when preserving life over limb.<sup>17</sup> A study from Gezira Mycetoma Center in Sudan found that the most common operation for mycetoma was surgical excision (87.8%), while amputation (12.2%) was conducted much less frequently.<sup>18</sup> The most common amputations were below-knee amputation and toe amputation.<sup>18</sup> The three guiding factors to determine which operation to perform are lesion size, bone involvement, and ability to close primary excision. Wide surgical excision is preferred when the lesion is small, there is little bone involvement, and primary excision is closed.<sup>18</sup> When the lesion is large and there is bone involvement, amputation is the more likely course.<sup>18</sup> Even with aggressive surgical control, the recurrence rate may be as high as 50%.<sup>12</sup>

Once local control has been established, reconstructive surgery may be required to close larger legions.<sup>11</sup> In the setting of limited resources in low- and middle-income countries, the simplest techniques along the reconstructive ladder such as split-thickness skin grafts, local tissue rearrangement with random pattern flaps, and local pedicled flaps (musculocutaneous or muscle flaps), are preferred (Fig. 2).<sup>19</sup> Perforator flaps should be avoided when operating in centers with limited resources and surgical education, given their higher failure rate and the likelihood of postoperative complications compared with muscle flaps.<sup>20</sup> Similarly, free tissue transfer can be a risky and costly procedure to perform in a low-resource setting. Improvements in reconstructive surgery are critical to avoiding amputation of affected limbs. Amputation is still considered a social stigma in many of the countries most affected by mycetoma, including Sudan, Senegal, and Yemen.<sup>16</sup> Postoperative care requires monitoring of peripheral circulation, regular dressing of wounds, and physiotherapy.<sup>21</sup> Overall, there is limited research and application of surgical techniques for mycetoma both in number and case volume.<sup>11</sup> More study is needed on reconstructive techniques to improve the recovery and disfigurement of mycetoma. Surgeons are prioritizing the preservation and restoration of affected limbs to promote the continued function of these limbs, but there is a need for published guidelines and standardized operative treatment

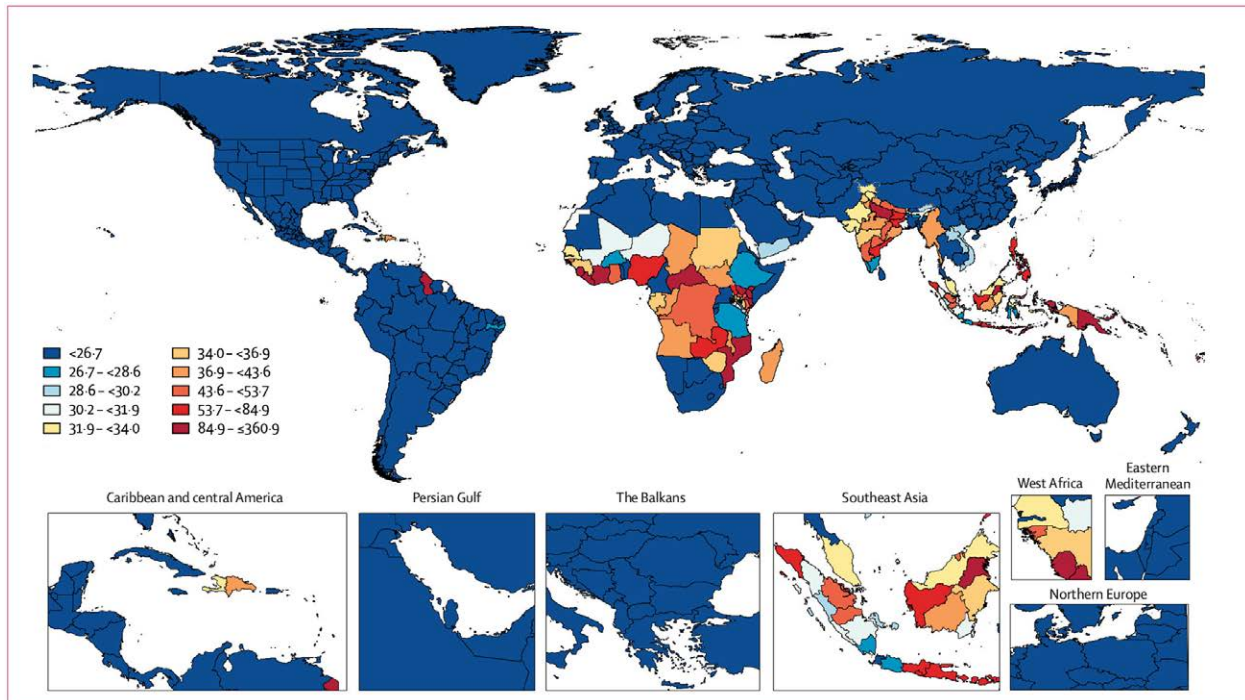
protocols for mycetoma.<sup>11,16</sup> Until then, antimicrobial therapy should be used as the first course of treatment (Fig. 2).<sup>19</sup>

### LYMPHATIC FILARIASIS

LF is a parasitic disease caused by adult filarial worms that live in the human lymph system and causes lymphedema, hydrocele, and elephantiasis (Fig. 3).<sup>22,23</sup> An estimated 72 million globally are infected with filarial



**Fig. 3.** Clinical presentation of lymphatic filariasis. (From the Centers for Disease Control and Prevention Public Health Image Library. <https://phil.cdc.gov/Details.aspx?pid=22458>. This image is in the public domain and thus free of any copyright restrictions.).



**Fig. 4.** Global distribution and age-standardized disability adjusted life years (DALY) rates (per 100,000) of LF in 2019. (From the Institute of Health Metrics and Evaluation. [https://www.healthdata.org/results/gbd\\_summaries/2019/lymphatic-filariasis-level-3-cause](https://www.healthdata.org/results/gbd_summaries/2019/lymphatic-filariasis-level-3-cause)).

worms. Lymphedema is the buildup of fluid when the lymph system is blocked due to the presence of dead and dying adult filarial worms and causes large swelling in the affected areas.<sup>24</sup> Lymphedema and hydrocele resulting from LF are considered among the leading causes of disabilities in the world, affecting over 30 million individuals worldwide, especially in Central and West Africa and Southeast Asia (Fig. 3).<sup>22,23,25</sup> There is a devastating social stigma associated with the disfigurement from LF.<sup>26</sup> Many with the disease drop out of school or work and confine themselves to their homes, due to the loss of function in affected limbs and stigma (Fig. 4).<sup>26</sup>

Prevention of LF consists of triple therapy delivered in programs of annual or semiannual mass drug administration or preventive treatments with ivermectin, diethylcarbamazine, and albendazole.<sup>27</sup> This approach targets the microfilarial larval stages of the parasite, which may not cause improvements in patient clinical outcomes, but can lower worm burdens to interrupt transmission if the entire community receives these medicines simultaneously. For some patients, direct treatment of LF with diethylcarbamazine or another drug may be beneficial, as is treatment of hydrocele complications.<sup>28</sup> However, many individuals with chronic LF can progress to lymphedema and its complications. Therefore, beyond surgical repair of hydrocele, early management of lymphedema includes decompressive massage, physical therapy, compression garments, and weight management.<sup>29,30</sup> Early surgical intervention has demonstrated efficacy in improving limb diameter and symptomatic relief by bypassing the blocked lymphatic channels—either with vascularized lymph node transfers, lympho-venous bypasses, or a combination of

the two.<sup>25,31</sup> Both of these interventions involve advanced microsurgical capabilities including super-microsurgery and advanced imaging that can map the lymphatic systems in real-time—and thus, although effective, they are limited to surgical specialty centers, even in the West, making access a concern in low- and middle-income countries.<sup>25</sup> In these cases, surgical treatment can lead to worse outcomes for the patient, including disfiguring healing and even amputation.<sup>25</sup> The reasons for the worsening outcomes may also be due to the dermal tissues and supportive tissues often targeted in the surgical procedures, which heal with much more difficulty than regular tissue.<sup>25</sup> However, given that a single intervention can improve quality of life, it is reasonable to consider “mission-style” trips by plastic microsurgeons to treat these patients in resource-poor settings. Postoperative monitoring must be implemented if this style of surgical intervention is attempted as infection is possible after surgical treatment, which can compromise the treatment.<sup>25</sup>

Additionally, for this chronic disease, surgical treatment can be focused on symptomatic relief rather than an attempt at a cure. This is performed in the form of debulking procedures such as liposuction of affected limbs or even radial excision and skin grafting—known as the Charles procedure. Liposuction can successfully reduce volume long term by removing adipose tissue, but patients must undergo compression therapy postoperatively to prevent recurrence.<sup>29</sup> The Charles procedure effectively reduces volume by completing the removal of subcutaneous tissue, but this can also be very disfiguring and require blood transfusions and extensive wound healing.<sup>29</sup> Given the greater simplicity of these procedures, they may present



**Fig. 5.** Clinical presentation of leprosy. (From the Centers for Disease Control and Prevention Public Health Image Library. <https://phil.cdc.gov/Details.aspx?pid=15355> and <https://phil.cdc.gov/Details.aspx?pid=15455>. These images are in the public domain and thus free of any copyright restrictions.)

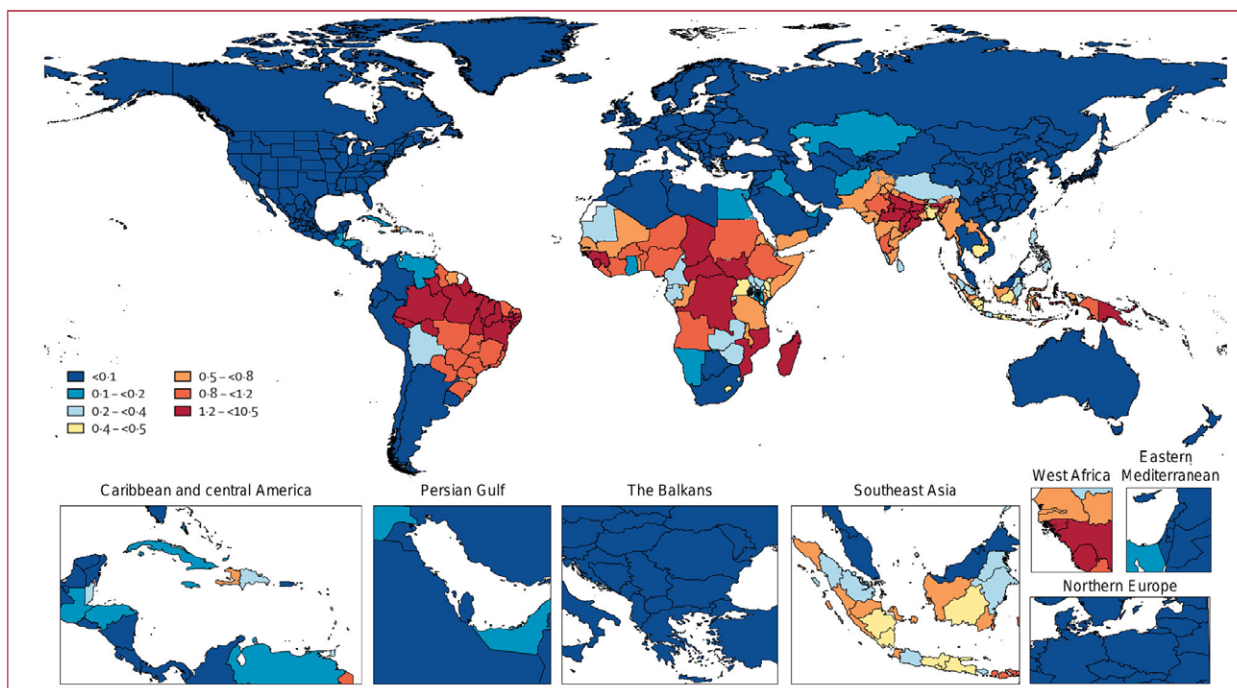
a better option for patients in low-and middle-income countries to reduce disability.<sup>32,33</sup> The Charles procedure does pose a real risk of substantial infection if not managed appropriately, given the large surgical surface area.

For reconstructive surgery to play a successful role in LF recovery, better medical support and adequate post-surgical care are needed to avoid failed recovery from surgery and limb amputation. Thus, as of now, reconstructive surgery remains a profound challenge in countries and regions without strong medical systems or where access to appropriate surgical care cannot be assured. In LF-endemic areas, preventive treatments using triple drug therapy remains a priority.

## LEPROSY

Leprosy is caused by the *Mycobacterium leprae* bacteria that attacks the nerves, skin, and eyes (Fig. 5).<sup>34</sup> Early diagnosis and treatment are highly effective, but if left untreated, nerve damage can cripple hands and feet and lead to blindness.<sup>34</sup> Other physical disabilities of leprosy include paraesthesias, muscle paralysis, ulcers, and amputations.<sup>35</sup> Leprosy affects about 500,000 people annually and is mainly found in South Asia, Central Africa, Brazil, and elsewhere in Latin America (Fig. 3).<sup>36</sup>

Leprosy often causes a permanent disability, with 3 million people currently living with a leprosy-associated deformity (Fig. 6). Although multi-drug therapy



**Fig. 6.** Global distribution and age-standardized DALY rates (per 100,000) resulting from leprosy in 2019. (From the Institute of Health Metrics and Evaluation. [https://www.healthdata.org/results/gbd\\_summaries/2019/leprosy-level-3-cause](https://www.healthdata.org/results/gbd_summaries/2019/leprosy-level-3-cause)).

composed of dapsone with rifampicin, and sometimes clofazimine, stops the progression of the disease, many patients are left with disabilities that affect their daily life.<sup>37</sup> Patients with deformities are often not referred to surgery because of lack of access to specialty centers in the affected areas.

Reconstructive plastic surgery in the management of leprosy focuses on the treatment of primary neuropathies (namely the ulnar nerve), digital ulcers leading to osteomyelitis requiring amputation, and facial skin excess improved with excision and local tissue rearrangement. Surgical treatment reduces deformities and helps patients recover movement and improve strength and mobility in affected areas.<sup>35</sup> Common surgeries performed for leprosy include ulnar nerve release to avoid the later expressions of this disease such as ulnar claw hand and joint contractures. Late-stage ulnar nerve palsies may require flexor digitorum superficialis opponensplasty, soft tissue release, and wound management with local flaps or split-thickness skin grafting.<sup>35</sup> Postoperatively, physiotherapy is needed to regain function and mobilization in limbs targeted for surgery.<sup>36,38</sup> Reconstructive surgery also effectively drains nerve abscesses and relieves compression of nerves in leprosy, which can restore affected limb function, including motor and sensory functions.<sup>35</sup> Reconstructive surgery in a camp setting could be an effective low-cost approach to providing surgical treatment for patients with leprosy. This approach has been used for conditions such as cleft lip palate.<sup>39</sup> A leprosy surgical camp was piloted in India with high success for patients, but more study is needed to evaluate if a camp setting is reasonable.<sup>36</sup> Notably, the introduction of the reconstructive surgery camp for leprosy in Gujarat, India increased reconstructive surgery for leprosy in other parts of India.<sup>36</sup>

Reconstructive surgery is an important part of recovery from leprosy and there is great potential for reconstructive surgery to decrease disabilities caused by leprosy-associated nerve damage.<sup>40</sup> All in all, more study on plastic surgery is needed to establish a standardized method of surgical treatment to reduce disabilities and deformities caused by leprosy, thus improving patients' function and reducing stigma.<sup>35</sup>

## NOMA

Noma is a necrotizing orofacial gangrene that starts in the gums but can advance to destroy the hard tissues and skin of the face, ultimately causing death in a high percentage of its victims (Fig. 7).<sup>41,42</sup> Survivors of noma acquire significant facial deformities during the disease progression, leading to stigma and neglect. Malnourished children are most affected by noma, with an estimated 35,000 incidence and 210,000 prevalence.<sup>41</sup> Reconstructive facial surgical treatment for noma aims to improve functionality and reduce facial disfigurement of the face.<sup>41,42</sup> Most surgeries release trismus and transfer tissue flaps to replace lost tissue.<sup>41</sup> After surgery, proper physiotherapy and follow-up is essential to reduce the risk of complication and loss of oral



**Fig. 7.** Clinical presentation of noma. (From the Centers for Disease Control and Prevention Public Health Image Library. <https://phil.cdc.gov/Details.aspx?pid=20297>. This image is in the public domain and thus free of any copyright restrictions.)

competency.<sup>43</sup> Due to the complexity of the surgery, it is mostly done in strong medical systems such as those in Europe or by nongovernmental organizations. Surgical treatment significantly improves social situations by reducing stigma and giving patients a better chance at education and normal life. However, because noma is found mostly in sub-Saharan Africa, where the majority of countries have weak healthcare systems, surgery is often not easily feasible.<sup>42</sup> Improvements in nutrition, immunization, and hygiene in these areas would help reduce the prevalence of this condition. Noma in these cases is treated with antibiotics, such as ampicillin-cloxacillin and metronidazole, but patients are often left with facial deformities that may cause life-long difficulties in speaking, breathing, and eating.<sup>42,44</sup> Therefore, reconstructive surgery must be made possible in areas most affected by noma.

## CONCLUDING COMMENTS

These NTDs cause disfigurement and disability that impact tens of millions of individuals globally. To address the backlog of needed surgery and improve methods of treatment, surgical procedures need to be standardized, and surgical systems need to be strengthened. Surgery is often only available in tertiary medical systems, but many NTDs occur in low-income rural areas without adequate access to specialty interventions. This further highlights

the importance of delivering reconstructive surgery for those affected in resource-poor areas. Because some countries affected by these NTDs often lack the resources and medical professionals to perform reconstructive surgery in remote rural areas and those with poor access, the prevention of these NTDs through antibiotics and other measures should still remain a therapeutic goal. Prevention measures including an attention to hygiene and drug administration should be the priority where these NTDs occur to limit the incidence and severity of the disease. This focus would limit the need for high risk surgery in resource-constrained areas. While building surgical capacity, efforts to scale up partnerships with local health systems remain essential to ensuring successful surgical outcomes. Strengthening surgical health systems will also decrease the possibility of a superimposed bacterial infection after surgery, which is likely without proper postoperative management and may exacerbate the disease or decrease quality of life.

As of now, medical management of mycetoma, LF, leprosy, and noma centers around antibiotic administration, which can be effective in low-income countries, even in those with weaker health systems. Treatment with antibiotics is used either to replace surgical intervention, or it is also used prior to surgery or postoperatively to minimize infection in many of the afflicted regions. However, reconstructive surgery is still necessary because many times antibiotics may not be delivered early enough or surgery is needed in conjunction with antibiotics, thus resulting in disfigurement and disability for patients currently. In some instances, health systems may consider accommodating mission-styled trips where plastic surgeons can perform surgery for these NTDs and provide proper immediate postoperative care.<sup>45</sup> However, a better and more sustainable option is for plastic or reconstructive surgeons to train local physicians and health workers in the affected regions, emphasizing effective surgical strategies and postoperative management, including physiotherapy and proper wound healing. Through this method of care, both supplies and medical training will be brought over during each visit that can then be sustained for the future. By forming links with local healthcare systems, complications can be managed and monitored after surgery to ensure successful outcomes. As an interim strategy, we support the continuation and further implementation of mission-styled trips to create mutually beneficial partnerships that provide healthcare throughout surgery and postoperative healing. However, the aspirational and capacity building goals of the Lancet Commission on Global Surgery remain paramount and relevant to a global commitment for universal health care access<sup>3</sup>

It is vital to note that the research currently available on surgical treatment of NTDs is limited and more clinical and long-term studies are necessary. We urge for research that studies which surgical treatments would be most effective and how these surgical treatments can be made accessible to the afflicted countries. Providing access to basic surgery can decrease the disfigurement and disability of NTDs, aiding in the reduction of stigma

and improving both survival and quality of life for patients.

**Kristy L. Hamilton**

Baylor College of Medicine  
Houston, TX  
E-mail: klhamilt@bcm.edu

## DISCLOSURE

*The authors have no financial interest to declare in relation to the content of this article.*

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