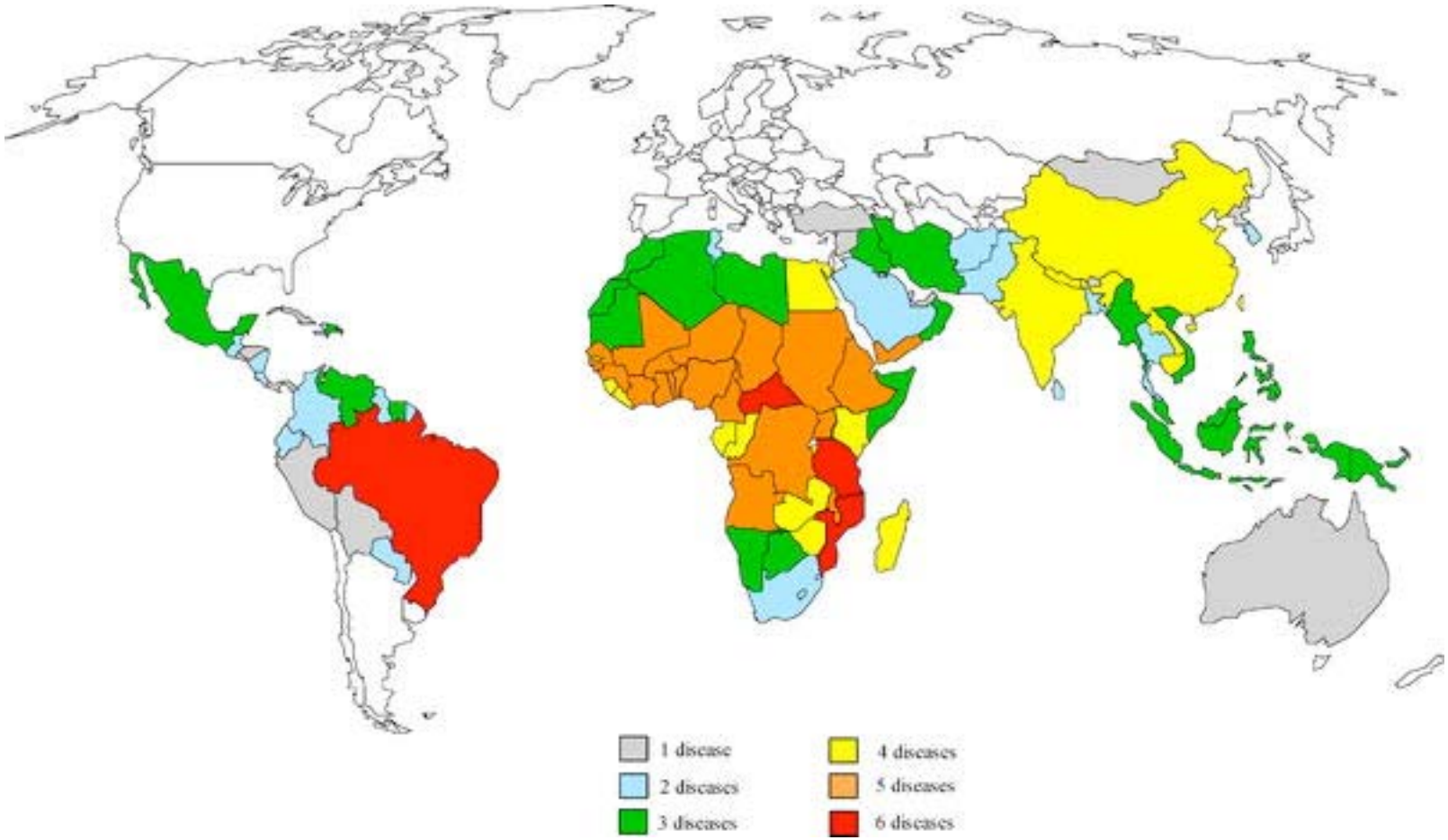
Massachusetts Institute of Technology

D-LAB HEALTH
SP 725

Jose Gomez-Marquez

Neglected Tropical Diseases

The Neglected Diseases Map



Source:
Molyneux DH, Hotez PJ, Fenwick A. "'Rapid-Impact Interventions': How a Policy of Integrated Control for Africa's Neglected Tropical Diseases Could Benefit the Poor." *PLoS Medicine* Vol. 2, No. 11, e336 doi:10.1371/journal.pmed.0020336.
Map courtesy of Molly Brady, Emory University. License: CC by.

The Neglected Diseases

1 Billion People Affected

500,000 Deaths Annually

Box 1. The Thirteen Neglected Tropical Diseases in Africa and Their Major Etiologic Agents

Protozoan Infections	
African trypanosomiasis	*Trypanosoma gambiense, T. rhodesiense*
Kala-azar (visceral leishmaniasis)	*Leishmania donovani*
Helminth Infections	
STH Infections	
Ascariasis	*Ascaris lumbricoides*
Trichuriasis	*Trichuris trichiura*
Hookworm infection	*Necator americanus*
Schistosomiasis	
Urinary schistosomiasis	*Schistosoma haematobium*
Hepatobiliary schistosomiasis	*Schistosoma mansoni*
Lymphatic filariasis	*Wuchereria bancrofti*
Onchocerciasis	*Onchocerca volvulus*
Dracunculiasis	*Dracunculus medinensis*
Bacterial Infections	
Trachoma	*Chlamydia trachomitis*
Leprosy	*Mycobacterium leprae*
Buruli ulcer	*Mycobacterium ulcerans*

(Modified from [3])

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The Neglected Diseases

Burden of Disease

Condition	Cases in Africa	Proportion of Global Burden in Africa	Source
Hookworm infection	198 million	27%–34%	[54]
Ascariasis	173 million	14%–22%	[54]
Schistosomiasis	166 million	89%	[55]
Trichuriasis	162 million	20%–26%	[54]
Trachoma	33 million	40%	[56]
Lymphatic filariasis	46 million	38%[a]	[57]
Onchocerciasis	18 million	99%	[21]
African trypanosomiasis	0.5 million	100%	[58]
Dracunculiasis	<0.1 million	~100%	[59]

[a]Estimates from proportion of African share of global burden of lymphatic filariasis.

DOI: 10.1371/journal.pmed.0020336.t001

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The Neglected Diseases

Treating the Patients

Disease	Target Population	Numbers to Be Treated in Target Population	Drug, Source, and Cost If Not Donated	Delivery Strategy	Distribution Costs[a] (Ex Drug)	Annual Cost Required
Lymphatic filariasis	Total eligible[b] population in endemic areas	300 million	Mectizan donated by Merck and albendazole by GlaxoSmithKline	MDA for five years	$0.10 per person treated = $30 million	$30 million + donated drug
Schistosomiasis	School-aged children plus other high risk groups	200 million	Praziquantel at $0.25 per treatment = $50 million	MDA in high risk areas plus school health programmes	$0.15 per person treated = $30 million	$30 million + $50 million = $80 million
Intestinal helminths	Pre-school-aged and school-aged children	400 million	Albendazole at $0.02 per treatment = $12 million	Health days and school health programmes	$0.10 per person treated = $40 million	$40 million + $12 million = $52 million
Onchocerciasis	Total eligible[b] population in hyper/mezzo endemic areas	80 million	Mectizan donated by Merck	MDA via community directed treatment	$0.10 per person treated = $8 million	$8 million + donated drug
Trachoma	Total population in endemic areas	168 million	Zithromax donated by Pfizer	MDA for five years	$0.20 per person treated = $34 million	$34 million + donated drug
Summary	The population of sub-Saharan Africa is an estimated 700 million	Up to 500 million individuals will receive treatment for one or more of these infections	$62 million + drug donations		$142 million	$142 million + $62 million for drugs + donated drugs
		500 million	$62 million		$142 million	= $204 million for five years

Source:
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Addressing the Challenges

- Find a dual-use solution, but don't let that hamper you in addressing the main problem
- Innovation requires bottom-up parameters and top-down medical guidelines

River Blindness

- Video

PBS/NOVA. “Preventing River Blindess: The River Eats Your Eyes.” http://www.pbs.org/wgbh/rxforsurvival/series/video/c_uch_dis_riverblind1_qt_h.html Accessed 20 October 2009.

Sleeping Sickness

- Fever, weakness
- African trypanosomiasis
  - Pentamidine
  - Suramin
- Second stage treatments
  - Melarsoprol
  - Eflornithine
    - It is only effective against T.b. gambiense.

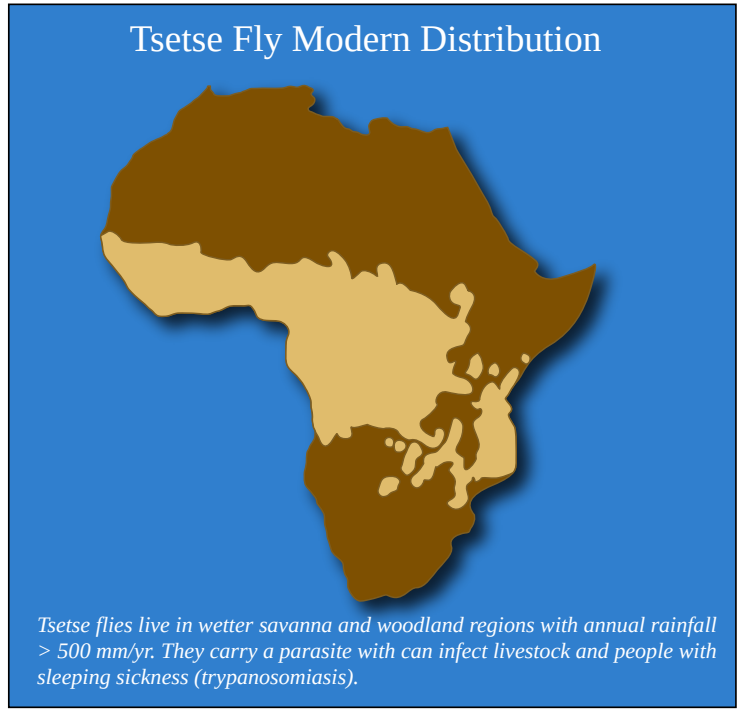


Image by MIT OpenCourseWare.

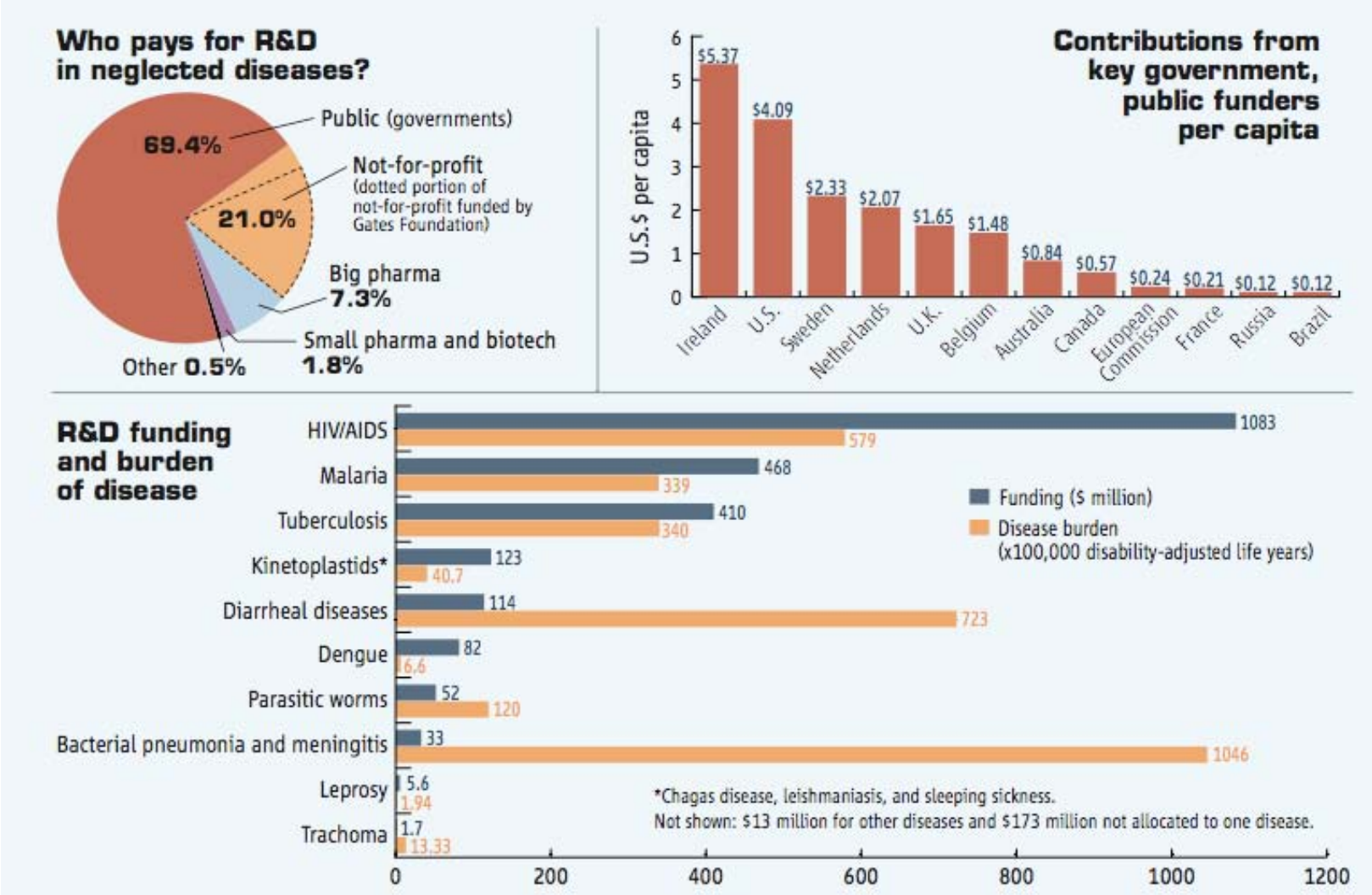
Eflornithine

Vaniqa!

Image removed due to copyright restrictions.
Screenshot of website for the drug Vaniqua®.

See Part I, “How a Beauty Regime Salvaged a Cure for Sleeping Sickness.” In Rosenberg, Tina. “The Scandal of ‘Poor People’s Diseases.’” *The New York Times*, March 29, 2006.
http://select.nytimes.com/2006/03/29/opinion/29talkingpoints.html?_r=1

Some Neglected Diseases Are More Neglected Than Others….



Moran M, Guzman J, Ropars AL, McDonald A, Jameson N, et al." Neglected Disease Research and Development: How Much Are We Really Spending?" PLoS Medicine Vol. 6, No. 2, e30 doi:10.1371/journal.pmed.1000030. Licensed CC – by.

PDPs Focused on Neglected Diseases

PDPs and TDR	Amount (US$)
International AIDS Vaccine Initiative	81,297,482
Medicines for Malaria Venture	75,982,931
European and Developing Countries Clinical Trials Partnership	50,803,467
International Partnership for Microbicides	46,311,916
Aeras Global TB Vaccine Foundation	40,121,983
Global Alliance for TB Drug Development	39,587,358
PATH Malaria Vaccine Initiative/PATH Meningitis Vaccine Project	38,024,679
TDR	32,675,307
Drugs for Neglected Diseases initiative	28,520,251
Institute for One World Health	27,377,321
Other PDPs	123,671,134
Total Funding to PDPs and TDR	584,373,827

TDR, Special Programme for Research and Training in Tropical Diseases.
doi:10.1371/journal.pmed.1000030.t005

Moran M, Guzman J, Ropars AL, McDonald A, Jameson N, et al." Neglected Disease Research and Development: How Much Are We Really Spending?" PLoS Medicine Vol. 6, No. 2, *e30 doi:10.1371/journal.pmed.1000030*. Licensed CC – by.

- OneWorld Health Programs

  - Visceral leishmaniasis: an old drug becomes a new treatment for an ancient disease
  - Diarrheal disease: an anti-secretory agent could prevent unecessary childhood deaths
  - Malaria: A unique partnership will apply synthetic biology to help solve a drug supply problem in many countries of the world.

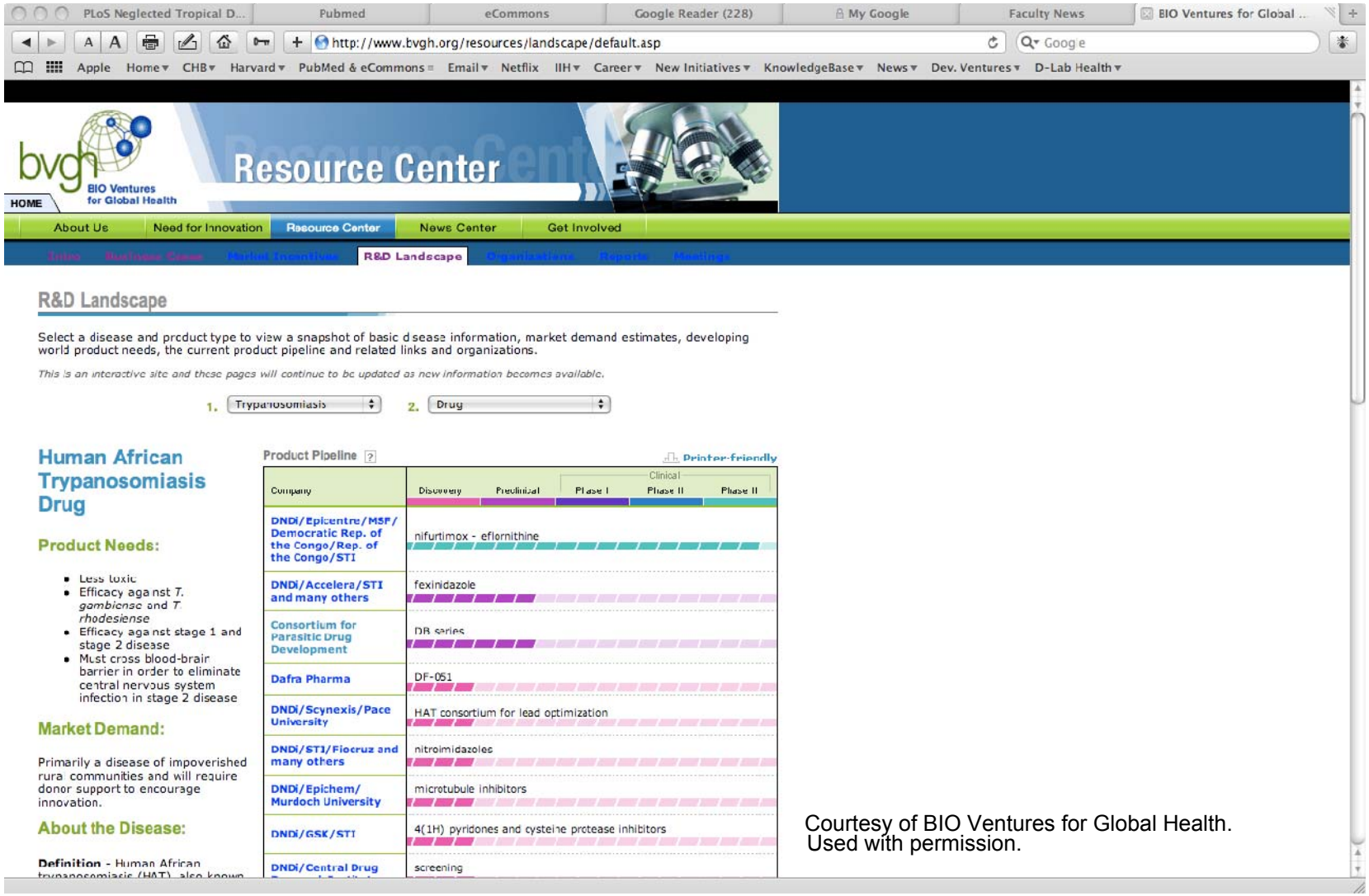
R&D Spending on Neglected Diseases

Disease	Amount (US$)	% of Total Funding
HIV/AIDS	1,083,018,193	42.30
Malaria	468,449,438	18.30
Tuberculosis	410,428,697	16.03
Kinetoplastids	125,122,839	4.89
Diarrhoeal diseases	113,889,118	4.45
Dengue	82,013,895	3.20
Helminths (worms and flukes)	51,591,838	2.02
Bacterial pneumonia and meningitis	32,517,311	1.27
Typhoid and paratyphoid fever	9,117,212	0.36
Leprosy	5,619,475	0.22
Buruli ulcer	2,412,950	0.09
Trachoma	1,679,711	0.07
Rheumatic fever	1,670,089	0.07
Cannot be allocated to one disease	120,918,862	4.72
Core funding of a multi-disease R&D organisation	110,921,673	4.33
General diagnostic platforms	4,791,152	0.19
Adjuvants and immunomodulators	2,685,148	0.10
Delivery technologies and devices	2,520,889	0.10
Other R&D	51,619,120	2.02
Grand Total	2,560,068,749	100.00

doi:10.1371/journal.pmed.1000030.t002

Moran M, Guzman J, Ropars AL, McDonald A, Jameson N, et al." Neglected Disease Research and Development: How Much Are We Really Spending?" PLoS Medicine Vol. 6, No. 2, e30 doi:10.1371/journal.pmed.1000030. Licensed CC – by.

Resource for Information on Neglected Diseases – bvgh.org



Courtesy of BIO Ventures for Global Health. Used with permission.

Enter the Devices

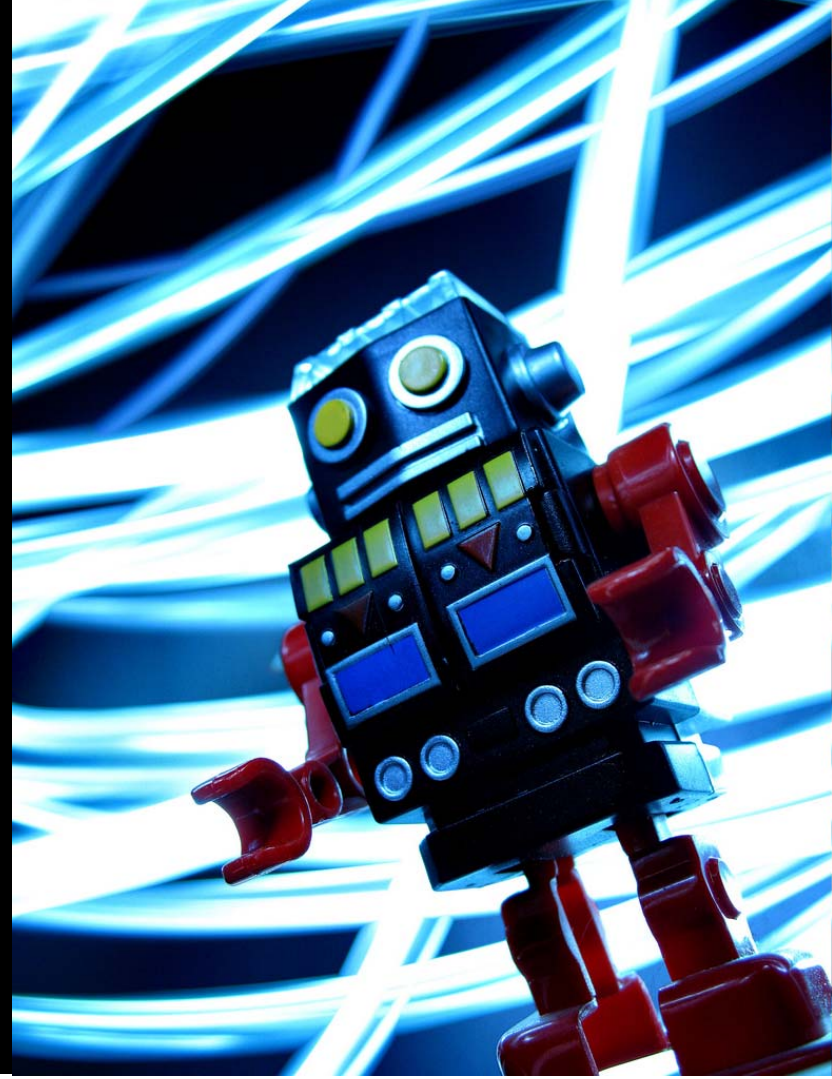


Photo courtesy of Don Solo on Flickr.

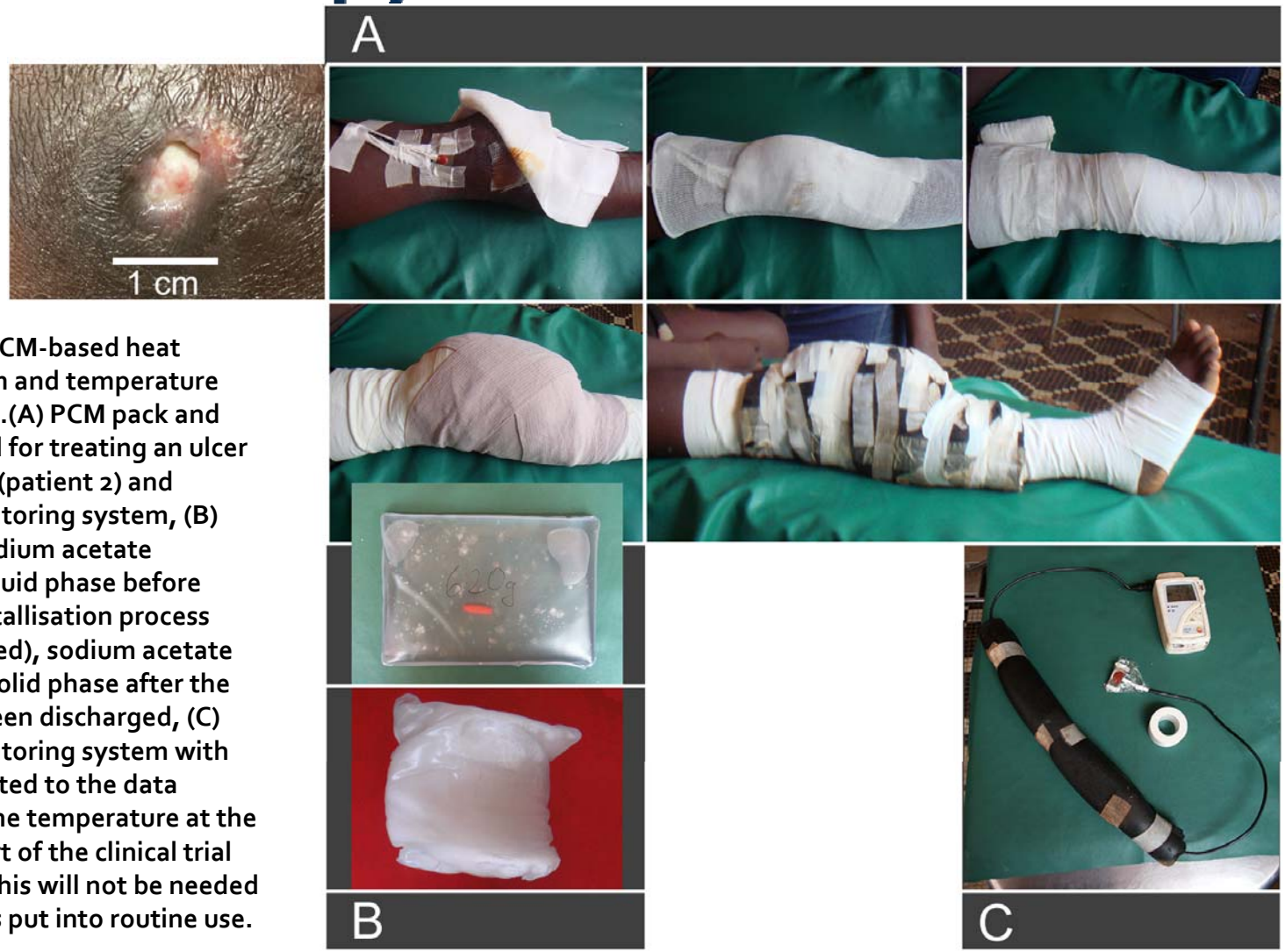
Phase Change Material for Thermotherapy of Buruli Ulcer

- **"Buruli ulcer** (BU) is a chronic necrotizing disease of skin and soft tissue caused by *Mycobacterium ulcerans*. The disease starts as a subcutaneous nodule, papule or plaque that eventually ulcerates and progresses over months to years."
- "BU has been reported in >30 countries, but the major burden lies on children living in remote areas of West Africa associated with swamps and stagnant water bodies."
- "Traditionally wide excision of the infected tissue alone was the standard treatment for BU. This is hampered by traumatic interventions, high cost and very high recurrence rates. Chemotherapy with streptomycin and rifampicin is currently re-evaluated as an adjunct treatment to surgery and as a therapy in its own right [5],[6],[7],[8]."

- "*M. ulcerans* differs from most other pathogenic mycobacteria in that it grows best at 30–33°C and not above 37°C. This characteristic feature of the pathogen was first used for therapeutic purposes in the early 1970s. Meyers et al. treated 8 patients from Zaire maintaining a temperature of approximately 40°C in the ulcerated area for a mean duration of 68 days [10]. There was no evidence of local recurrence during follow-up periods of up to 22 months. Based on this impressive success rate, **WHO guidelines listed the application of heat as a treatment option for BU**. However, the heat application devices employed so far were impractical in most endemic countries."

Junghanss T, Um Boock A, Vogel M, Schuette D, Weinlaeder H, et al. "Phase Change Material for Thermotherapy of Buruli Ulcer: A Prospective Observational Single Centre Proof-of-Principle Trial." PLoS Negl Trop Dis 3, no. 2 (2009): e380. doi:10.1371/journal.pntd.0000380. License CC-by.

Phase Change Material for Thermotherapy of Buruli Ulcer



Mounting of the PCM-based heat application system and temperature monitoring device.(A) PCM pack and bandage mounted for treating an ulcer on the lower limb (patient 2) and temperature monitoring system, (B) PCM pack with sodium acetate trihydrate in the fluid phase before initiating the crystallisation process with the starter (red), sodium acetate trihydrate in the solid phase after the stored heat has been discharged, (C) temperature monitoring system with the sensor connected to the data logger to record the temperature at the skin surface as part of the clinical trial documentation. This will not be needed when the device is put into routine use.

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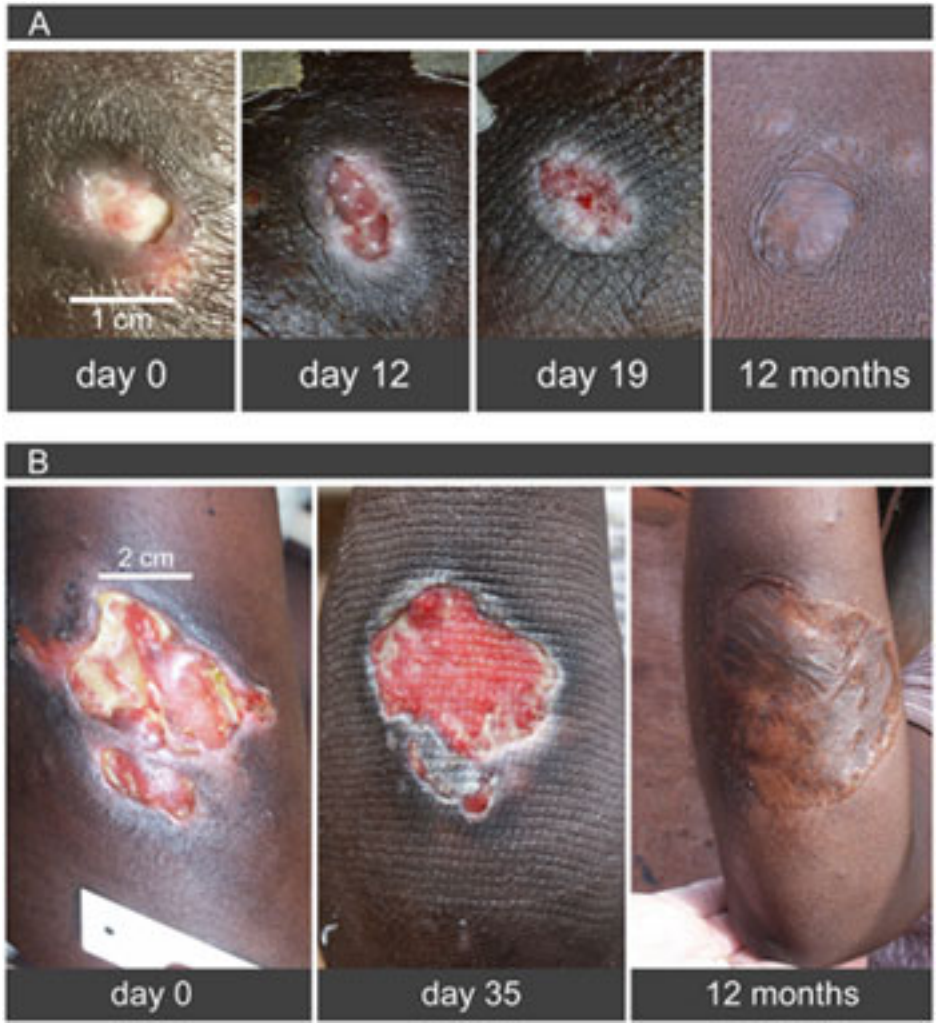

Healing of Buruli ulcers under PCM-based heat treatment and long term results.(A) Patient 2, (B) patient 5: Progress of healing during heat treatment. Note in particular early onset of epithelialisation. Far right follow-up 12 months after completion of heat treatment. Patient 5 (B) after skin grafting.

Junghanss T, Um Boock A, Vogel M, Schuette D, Weinlaeder H, et al. "Phase Change Material for Thermotherapy of Buruli Ulcer: A Prospective Observational Single Centre Proof-of-Principle Trial." PLoS Negl Trop Dis 3, no. 2 (2009): e380. doi:10.1371/journal.pntd.0000380. License CC-by.

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