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Editorial

Investment in drugs for neglected diseases: a portrait of the last five years

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The last two Editorials of the Journal of the Brazilian Society of Tropical Medicine (JBSTM), namely *Parasite, vectors and reservoirs as determinants of tegumentary leishmaniasis* and *Dengue in Brazil* were highlighted because of their content and the quality of their work, dealing with important issues for Brazil and for some developing regions/countries.

Neglected tropical diseases have afflicted humanity since ancient time and have acquired notoriety as disabling and deforming diseases[1]. Their serious impact on health and productivity in the past led to considerable knowledge about the diseases, and effective control tools were developed for many. Moreover, opportunities for transmission were drastically reduced, as living conditions improved. Therefore, in populations that enjoy good access to health services and a reasonable standard of living these diseases are now rarely seen[2].

Although diverse, neglected tropical diseases share features that allow them to persist in conditions of poverty. Approximately 1 billion people (one sixth of the world's population) suffer from one or more neglected tropical diseases[1]. Conflict situations or natural disasters aggravate conditions that are favorable to the spread of these diseases.

The three neglected tropical diseases (NTDs) highlighted in the articles of JBSTM above and seventeen more are currently been focus by the World Health Organization (WHO) and lack effective or adequate treatments[1]. The NTDs, classified by the type of infection, are: Protozoan infections (Chagas disease, leishmaniasis and human African trypanosomiasis); Bacterial infections (Buruli ulcer, cholera, endemic treponematoses - yaws, endemic syphilis-, leprosy - Hansen disease-, and trachoma); Helminth infections (cysticercosis, dracunculiasis, echinococcosis, fascioliasis, lymphatic filariasis, soil-transmitted helminthiasis, onchocerciasis, schistosomiasis, taeniasis), Viral infections (dengue and rabies)[3].

Despite this need, the drugs used to treat these diseases are old and have many toxic effects[4]. Therefore, there is urgency for new drugs, more effective and safer. However, a fundamental problem with neglected diseases is how to induce pharmaceutical companies to invest resources for developing effective treatments. The issue arises because most of these diseases affect poor components of the world population, which implies that although the potential demand for such drugs is large its market value is low because those affected cannot pay for medications[5].

An analysis of FDA drug approvals in the past five years shows that, of the 119 drugs approved for human use from 2007 to 2011, including biopharmaceuticals, only five belong to the class of antimicrobials (which include antibiotics, antimycobacterial, antiprotozoal and antifungal)[6-10].

In 2007 it were approved ratapamulin (Altabax®, GlaxoSmithKline), a bacterial protein-synthesis inhibitor indicated for impetigo, and doripenem (Doribax®, Johnson & Johnson), a synthetic broad-spectrum carbapenem antibiotic used in urinary tract infections[6]. 2008 was a year of drought, none antimicrobial drug was approved for use[7]. Unlike this, 2009 was a year of progress, in which the combination artemether-lumefantrine (Coartem®, Novartis) was approved for the treatment of malaria, and two antibiotics were also approved, besifloxacin (Besivance®, Bausch and Lomb), a fluoroquinolone antimicrobial agent indicated for the treatment of bacterial conjunctivitis, and the lipoglycopeptide antibacterial agent telavancin (Vibativ®, Theravance), indicated for complicated skin and skin-structure infections[8]. In 2010 it was approved the broad-spectrum cephalosporin antibiotic caftaroline (Teflaro®, Cerexa), indicated to treat skin and skin-structure infections, and community acquired pneumonia[9]. Also, in 2010 it were approved two vaccines, one indicated for meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, Y and W-135 (Menveo®, Novartis) and another one for disease caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F (Prevnar 13®, Pfizer)[9]. In 2011 came the RNA polymerase inhibitor Fidaxomicin (Dificid®, Optimer) indicated for *Clostridium difficile*-associated diarrhea[10].

In relation to antiviral drugs the past five years had four drugs approved for the treatment of HIV-1 and two for the treatment of HCV. In 2007 came the maraviroc (Selzentry®, Pfizer), a CCR5 co-receptor antagonist of HIV-1, and raltegravir (Isentress®, Merck), an HIV-1 integrase strand transfer inhibitor[6]. In 2008 came to market etravirine (Intelence®, Tibotec), an HIV-1 non-nucleoside reverse transcriptase inhibitor[7]. 2009 and 2010 were drought years in the antiviral area[8,9]. In 2011 it were approved boceprevir (Victrelis®, Merck & Co.), a genotype 1 HCV NS3/4A protease inhibitor, rilpivirine (Edurant®, Tibotec), an HIV-1 non-nucleoside reverse transcriptase inhibitor, and telaprevir (Incivek®, Vertex), a genotype 1 HCV NS3/4A protease inhibitor[10].

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The analysis of these data shows that over the past five years, except for malaria, there was no approved drug for the treatment of neglected diseases, which continue with little investment[5]. Even with the approval of some antibiotics, the investment in this area is still low if one compare the total number of approved drugs (119) in that period. The pharmaceutical industry has still invested little in that area. The focus of pharmaceutical companies has been anticancer, with seventeen FDA drug approvals between 2007-2011, and CNS-acting drugs, with fifteen approvals in this period[6-10].

For 2013, FDA antecipates five medicines[10]. Two obesity drugs, lorcaserin and a combination of phentermine and topiramate; on the cancer front, they highlight pertuzumab; in the biotech space, the top picks for 2012 approvals are BG-12, an immunomodulator for the treatment of multiple sclerosis, and MDV3100, an oral androgen inhibitor to treat prostate cancer.

Despite these data, there is hope for the future. Partnering models comprising academic institutes, large and small pharma industry members are emerging with defined goals, for example, to identify and validate new targets or therapeutic approaches. Foundations and government bodies, such as Bill and Melinda Gates Foundation, Drugs for Neglected Diseases, and other consortia and funds are available to promote basic research and bridge the translational gap. Bill and Melinda Gates Foundation has a consortium in collaboration with thirteen large pharmaceutical, with $785 million fund to eradicate ten long-neglected tropical diseases by 2020. The primary objective of DNDi is to deliver thirteen new treatments by 2018 for leishmaniasis, sleeping sickness, Chagas disease, malaria, paediatric HIV, and specific helminth infections. Expanding upon R&D networks built on South-South and North-South collaborations, DNDi aims to bring medical innovation to neglected patients by developing field-adapted treatments. The academic collaboration on novel treatments encompass the breadth that includes neglected diseases.

CONFLICT OF INTEREST

The author declare that there is no conflict of interest.

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