Institution: London School of Hygiene & Tropical Medicine (LSHTM)

Unit of Assessment: UoA1 – Clinical Medicine

Title of case study: Eliminating blinding trachoma through single dose treatment

1. Summary of the impact

Trachoma, caused by ocular infection with *Chlamydia trachomatis*, is the leading infectious cause of blindness. Research by Professors David Mabey and Robin Bailey, LSHTM, has shown that a single oral dose of azithromycin is an effective, feasible mass treatment and could eliminate trachoma from affected communities. As a result, the manufacturer Pfizer agreed to donate azithromycin to trachoma control programmes for as long as necessary and WHO established an Alliance for the Global Elimination of Blinding Trachoma by 2020. Since 2008, 205m azithromycin doses have been donated, and WHO elimination targets have been achieved in nine countries.

2. Underpinning research

In 1995, WHO estimated there were 150m cases of active trachoma, 10m cases of potentially blinding trachomatous trichiasis (eyelashes rubbing against the front of the eye) and 6m people blind from trachoma. Trachoma was responsible for 15% of blindness worldwide. At that time, the recommended treatment for trachoma was tetracycline 1% ointment, delivered twice daily to both eyes for six weeks. Few if any affected individuals completed this treatment course.

In 1993, David Mabey (then Senior Lecturer) and Robin Bailey (then PhD student) of LSHTM published the results of a randomised controlled trial in The Gambia comparing standard treatment with six weeks of tetracycline ointment, given under close supervision, with a single oral dose of azithromycin. The two treatments were shown to be equivalent.[3.1] However, reinfection was common in both groups, as there were many untreated individuals in the study village.
They then set up a multi-centre study, in collaboration with Johns Hopkins University (JHU) and the University of California at San Francisco (UCSF), to compare oral azithromycin with six weeks of topical tetracycline given to entire communities. Mass treatment with oral azithromycin was shown to be as good as or better than mass treatment with tetracycline ointment given under supervision.[3.2]

In 1998 they obtained a Wellcome Trust programme grant for further studies on the use of azithromycin for trachoma control and recruited two outstanding doctors, both completing PhDs on the work. Anthony Solomon (then PhD student) eliminated ocular *Chlamydia trachomatis* infection from a trachoma endemic village in Tanzania with a single round of mass treatment, with no one infected in the village five years later,[3.3, 3.4] and showed that mass treatment did not lead to the emergence of macrolide resistance in *C trachomatis* or *Strep. pneumoniae* in this community. In The Gambia, Matthew Burton (then PhD student) found a similar effect from a single dose, but also identified the importance of cross-border population mobility in reintroducing infection following mass treatment.[3.5] They were subsequently able to eliminate ocular *C. trachomatis* infection from two regions in The Gambia.[3.6]

In 2002, they were awarded a grant by the International Trachoma Initiative (ITI) to evaluate and monitor trachoma control programmes in eight countries. They published a systematic review of the evidence underlying the WHO-endorsed SAFE strategy (Surgery, Antibiotics, Face washing, Environmental improvement) for trachoma control, and were commissioned by WHO to write a handbook for trachoma control programme managers, based on their research findings and experience, which was published in 2006 and has been distributed to every national programme manager.

In 2008, with Gates Foundation funding, they set up a partnership for the rapid elimination of trachoma, comparing the impact and cost effectiveness of different strategies for the administration of azithromycin. They showed that, in low prevalence communities, it is more cost-effective to use a test for *C. trachomatis* infection to decide when to stop mass drug administration than to follow WHO recommendations, which are based on clinical signs.

3. References to the research

3.1 Bailey, RL, Arullendran, P, Mabey, DCW and Whittle, HC (1993) Randomised controlled trial of single-dose azithromycin in treatment of trachoma, *Lancet*, 342(8869): 453–456, doi:10.1016/0140-6736(93)91591-9. Citation count: 134

3.2 Schachter, J, West, SK, Mabey, David, Dawson, CR, Bobo, L, Bailey, R, Vitale, S, Quinn, TC, Sheta, A, Sallam, S, Mkocha, H, Mabey, Denis and Faal, H (1999) Azithromycin in control of trachoma, *Lancet,* 354(9179): 630–635, doi:10.1016/S0140-6736(98)12387-5. Citation count: 148

3.3 Solomon, AW, Holland, MJ, Alexander, NDE, Massae, PA, Aguirre, A, Natividad-Sancho, A, Molina, S, Safari, S, Shao, JF, Courtright, P, Peeling, RW, West, SK, Bailey, RL, Foster, A and Mabey, DCW (2004) Mass treatment with single-dose azithromycin for trachoma, *New England Journal of Medicine*, 351(19): 1962–1971, doi:10.1056/NEJMoa040979. Citation count: 118

3.4 Solomon, AW, Harding-Esch, E, Alexander, NDE, Aguirre, A, Holland, MJ, Bailey, RL, Foster, A, Mabey, DCW, Massae, PA, Courtright, P and Shao, JF (2008) Two doses of azithromycin to eliminate trachoma in a Tanzanian community, *New England Journal of Medicine*, 358(17): 1870–1871, doi:10.1056/NEJMc0706263. Citation count: 25

3.5 Burton, MJ., Holland, MJ, Makalo, P, Aryee, EAN, Alexander, NDE, Sillah, A, Faal, H, West, SK, Foster, A, Johnson, GJ, Mabey, DCW and Bailey, RL (2005) Re-emergence of *Chlamydia trachomatis* infection after mass antibiotic treatment of a trachoma-endemic Gambian community: a longitudinal study, *Lancet,* 365(9467): 1321–1328, doi:10.1016/S0140-6736(05)61029-X. Citation count: 62

3.6 Harding-Esch, EM, Edwards, T, Sillah, A, Sarr, I, Roberts, CH, Snell, P, Aryee, E, Molina, S, Holland, MJ, Mabey, DCW and Bailey, RL (2009) Active trachoma and ocular *Chlamydia trachomatis* infection in two Gambian regions: on course for elimination by 2020? *PLoS Neglected Tropical Diseases,* 3(12): e573, doi:10.1371/journal.pntd.0000573. Citation count: 12

Key grants

3.1 Bailey, MRC Clinician Scientist fellowship, 1990–1993
3.2 Mabey, A trial of community based azithromycin treatment, Edna McConnell Clark Foundation, 1994-1995 £113,846
3.3–3.5 Mabey, Strategies for the Control of Blinding Trachoma, Wellcome Trust, 2000–2005, £744,872
3.6 Mabey and Bailey, Partnership for the Rapid Elimination of Trachoma, Bill & Melinda Gates Foundation, 10/10/2004–31/3/2013, £1,544,734

4. Details of the impact

The impact of this research has been life-changing for millions of people in communities affected by trachoma. As a result of the first two studies, in 1998 the researchers, along with collaborators at JHU and UCSF, and the Clark Foundation, persuaded Pfizer to donate azithromycin (then still under patent) to trachoma control programmes in 8 countries (subsequently increased to 21). In the same year the Clark Foundation and Pfizer jointly set up the ITI[5.1] to oversee the donation programme, and WHO set up the Global Alliance for the Elimination of Blinding Trachoma by 2020, supported by a resolution at the World Health Assembly. This was based on the SAFE strategy: Surgery for trichiasis, Antibiotics to treat *C. trachomatis* infection, and Face washing and Environmental improvement to reduce transmission of *C. trachomatis*. Mass treatment with azithromycin was recommended for the 'A' component. Since then more than 250m azithromycin doses have been donated to national trachoma control programmes in 21 countries. Year on year, there has been a very considerable scale-up of these programmes, working towards the elimination of blinding trachoma, which was triggered and is underpinned by the science carried out by the LSHTM team as well as by their information and advocacy.[5.2]

Danny Haddad, Director of the ITI (www.trachoma.org), said in 2012: 'The research into strategies to control trachoma performed by Professors Mabey and Bailey and their group has paved the way

for an azithromycin donation programme that has improved the health of millions of poor people around the world.' It has also profoundly influenced the trachoma programmes of NGOs.[5.3]

Since 2008, Morocco, Ghana, Libya, Mexico, Iran, Oman, Algeria, Vietnam and The Gambia report that they have met WHO targets for trachoma elimination.[5.4, 5.5, 5.6] According to WHO estimates, the number of cases of active trachoma in the world has been reduced from 150m in 1995 to 40m in 2012, and the number of people blind from trachoma from 6m to 1.2m[5.7] – highly significant reductions in which the LSHTM team's research findings played a crucial part. In January 2012, at a meeting in London attended by Bill Gates and the CEOs of 13 major pharmaceutical companies, the UK Minister for International Development pledged £50m towards programmes for the elimination of blinding trachoma by 2020. £10.6m of this has been awarded to Sightsavers International and LSHTM to complete the world map of trachoma.[5.8]

Every year since 1998 WHO has hosted a meeting of partners in the Global Alliance for the Elimination of Trachoma. This meeting is attended by national trachoma control programme managers from all countries supported by ITI, and by the major NGOs involved in the control of trachoma. It is preceded by a one-day scientific meeting at which the results of research in the previous year are reported. The LSHTM team has presented at this meeting every year, helping to ensure that their research is translated into policy and practice, nationally and internationally, at the earliest possible opportunity. Anthony Solomon (now Senior Lecturer, LSHTM) is a member of the Trachoma Expert Committee of the ITI, which is chaired by Allen Foster (Professor of Tropical Ophthalmology, LSHTM).

At LSHTM's study site in The Gambia in 2009, no infections were found among 6,000 children sampled in four districts who had received mass treatment with azithromycin.[3.6] Researchers are now working with the award-winning Gambian National Eye Care programme (NECP)[5.9] to set up a national surveillance network, to ensure that trachoma is not reintroduced into the country. Ansumana Sillah, Director of the NECP, said in 2012: 'The research led by Drs Bailey and Mabey on trachoma showed for the first time that a single dose of azithromycin can cure trachoma, and can even eliminate trachoma if it is given to the whole community. This led the ITI to donate azithromycin for mass treatment of affected communities in the Gambia, Senegal and other countries in West Africa, and has enabled us to come close to eliminating active trachoma in The Gambia.'

Mass treatment with azithromycin may have had additional benefits. LSHTM researchers showed that it reduced the incidence of clinical malaria and other illnesses in Gambian children.[3.6] Studies in Ethiopia published in 2009 and 2011 showed that all-cause mortality was significantly lower in children aged 1–5 years in communities which received azithromycin.[5.10]

5. Sources to corroborate the impact

5.1 Vice President, Clinical Research Head, Specialty Therapeutics, Pfizer Inc.

5.2 Solomon, AW, Zondervan, M, Buchan, J, Kuper, H, Mabey, DCW, Foster, A and Sinclair, J (2004) *Trachoma Initiative in Monitoring and Evaluation (TIME)*. London: LSHTM, CD ROM. DVD on our trachoma research programme in Tanzania made by Anthony Solomon with Rockhopper Productions as part of their 'Kill or Cure' series on neglected diseases.

5.3 Director of the Carter Center trachoma programme, Carter Center.

5.4 International Coalition for Trachoma Control (2011) *The End in Sight*: *2020 INSight, ICTC*, http://www.cbm.org/article/downloads/75741/2020_INSight__English_.pdf (accessed 10 September 2013).

5.5 Yayemain, D, King, JD, Debrah, O, Emerson, PM, Aboe, A, Ahorsu, F, Wanye, S, Ansah, MO, Gyapong, JO and Hagan, M (2009) Achieving trachoma control in Ghana after implementing the SAFE strategy, *Transactions of the Society of Tropical Medicine and Hygiene*, 103(10): 993–1000,

doi:10.1016/j.trstmh.2009.02.007.

5.6 WHO (2012) Global WHO Alliance for the Elimination of Blinding Trachoma by 2020: progress report on elimination of trachoma, *WHO Weekly Epidemiological Record*, 87(17): 161–168, http://www.who.int/wer/2012/wer8717.pdf (accessed 10 September 2013).

5.7 WHO (2013) Global Alliance for the Elimination of Blinding Trachoma by 2020: progress report on elimination of trachoma, 2012, *WHO Weekly Epidemiological Record*, 88(24): 242–251, http://www.who.int/wer/2013/wer8824.pdf (accessed 19 September 2013).

5.8 Sightsavers (2012) Press release at the International Trachoma Initiative, 19 December, http://trachoma.org/news-releases/2012/global-survey-identify-180-million-risk-blinding-disease-begins-ethiopia-today.

5.9 Ansumana Sillah, Director of the Gambia National Eye Care programme, http://thepoint.gm/africa/gambia/article/national-eye-care-program-receives-award.

5.10 Porco, TC, Gebre, T, Ayele, B, House, J, Keenan, J, Zhou, Z, Hong, KC, Stoller, N, Ray, KJ, Emerson, P, Gaynor, BD and Lietman, TM (2009) Effect of mass distribution of azithromycin for trachoma control on overall mortality in Ethiopian children: a randomized trial, *Journal of the American Medical Association*, 302(9): 962–968, doi: 10.1001/jama.2009.1266.