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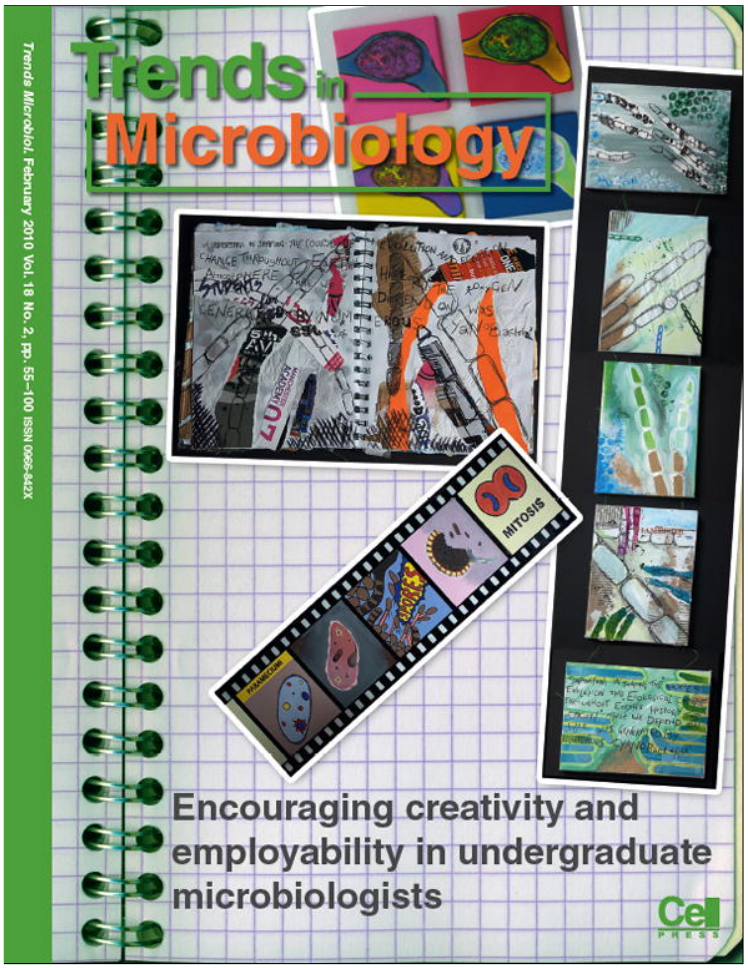


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Opinion

# Public health and bovine tuberculosis: what's all the fuss about?

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**Bovine tuberculosis (bTB) in UK cattle is increasing rapidly. Consequently, the UK Government is spending escalating sums of money in attempts at disease control. We propose that bTB control in cattle is irrelevant as a public health policy. In the UK, cattle-to-human transmission is negligible. Aerosol transmission, the only probable route of human acquisition, occurs at inconsequential levels when milk is pasteurised, even when bTB is highly endemic in cattle. Furthermore, there is little evidence for a positive cost benefit in terms of animal health of bTB control. Such evidence is required; otherwise, there is little justification for the large sums of public money spent on bTB control in the UK.**

## Control and re-emergence of tuberculosis in British cattle

Historically, tuberculosis caused by *Mycobacterium bovis* (bovine tuberculosis, bTB) was a major public health issue in the UK. bTB in humans was widespread in the UK before the introduction of pasteurisation of milk in the 1960s: in the 1930s, 40% of dairy cows were infected and 0.5% had tuberculous mastitis [1]. During this period, approximately 2500 people died annually from bTB. Therefore, measures were introduced to eliminate bTB from the UK. As a result, by the 1970s, bTB was eliminated from most of Britain, with persistent infection limited to the southwest [1]. Subsequently, bTB has re-emerged: in 2007, there were 4172 new herd breakdowns in England and Wales [2]. The resurgence of bTB has resulted in public expenditure now approaching £100 million annually (see http://www.defra.gov.uk/animalh/tb/stats/expenditure.htm). More and more extreme measures are being proposed to stop the spread of the disease such as widespread badger culling programmes, despite scientific studies casting doubt on the efficacy of such practices [3].

We argue that, apart from milk pasteurisation, these measures no longer make economic sense and hence are now resulting in gross misallocation of public resources. We are therefore of the opinion that there is no public health rationale for the multimillion bTB control programme in the UK provided that milk continues to be pasteurised. The logical conclusion arising from this is that without a public health perspective, bTB is essentially an endemic animal disease and hence any control programme should be economically effective in terms of improvements in animal health and welfare and industry profitability or viability.

## Transmission of bTB to humans rarely occurs in the UK

Before milk pasteurisation, *M. bovis* was isolated from 8% of churn samples and almost all 3000-gallon tankers [4] suggesting widespread exposure to bTB. Since milk pasteurisation was generally introduced in the UK in the early 1960s, bTB in humans has declined dramatically. Between 1993 and 2003, 315 human cases of bTB were confirmed [5]. Among the affected people, only 14 had been born in the UK after 1960, whereas most of them had been born either before 1960 (265 cases) or outside of the UK (36 cases). Molecular epidemiological studies of bTB have been unconvincing in terms of the present threat of *M. bovis* to human health. A genetic analysis of all 50 *M. bovis* isolates of human cases of bTB between 1997 and 2000 produced 25 individual spoligotypes (see Glossary) [6]. Of these, 15 spoligotypes had not been recorded in UK cattle, suggesting that they had not been transmitted from the animals, and were possibly the result of reactivation of old lesions in individuals that were infected 50 years previously with the spoligotype then circulating in British cattle. Indeed, 72% of subjects from which *M. bovis* was isolated were over 50 years old. The only proven case of recent transmission from cattle to humans in the UK was a cluster of two cases on a Gloucestershire dairy farm [7]. A further case in Cornwall has been described recently which might also have been transmitted from British cattle [8].

### Glossary

**Cost–benefit analysis**: the financial return of a control programme. A programme where the financial benefit of intervention is less than the costs of such an intervention has a negative cost benefit.
**Cost-effectiveness**: the cost of an intervention programme in terms of the improvement in public health. Highly cost-effective programmes will result in gains of many QALYs, or reduction in many DALYs lost, at modest cost.
**DALY**: Disability Adjusted Life Year. This is the measure of human population health preferred by the World Health Organisation. One DALY is approximately the loss of 1 year of healthy life. Although there are significant differences in the way QALYs and DALYs are calculated, very generally if a disease results in one DALY then there will be the loss of one healthy year of life or one QALY.
**QALY**: Quality Adjusted Life Year. This is a measurement of population health used in health economics. One QALY is approximately 1 year of healthy life.
**Spoligotype**: a form of polymorphism in the repeat units of DNA. Spoligotyping of isolates of *Mycobacterium* is used to study the molecular epidemiology of tuberculosis.
**Test and cull policy**: the method of bTB control in cattle. Cattle are tested with the intradermal tuberculin test, and animals testing positive are culled whilst the remainder of the herd is put on restrictions until the whole herd tests negative.

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The patient was a veterinary nurse and had the same spoligotype that was isolated in local cattle. Remarkably, local farmers, with a much higher contact rate with cattle, were not infected and, therefore, other means of transmission (such as from badgers via the household dog) are possible. Finally, there is a recent cluster of six cases reported in Birmingham [9]. All of these patients, linked to each other by contact, were young, indigenous to the UK and had a spoligotype that is common in UK cattle. One of them, possibly the primary case, had a history of unpasteurised milk consumption and contact with cattle both in the UK and overseas. It appears that transmission between these six people was likely to have been by aerosol. Human-to-human transmission of bTB is an exceptional event in the absence of immunosuppression [4]. However, four of the six patients were probably immunocompromised, and transmission likely occurred through repeated contacts in confined environments.

## bTB is a food borne disease in humans

Declining numbers of human cases despite massive increases in affected cattle is consistent with the hypothesis that bTB is a food borne disease transmitted by milk. Indeed, a recent familiar outbreak of bTB in Ireland was as a result of the consumption of unpasteurised milk [10]. Nevertheless, belief is widespread that transmission from cattle to humans by aerosol is also important. For example, Smith and Clifton-Hadley [11] concluded that bTB control in cattle must continue to prevent cattle developing advanced lesions resulting in increased aerosol transmission to humans. However, evidence presented in Box 1 suggests that there was little bTB transmission by aerosol from cattle to humans in the UK before bTB control. Contemporaneous evidence can also be examined from countries that have no programmes for control of bTB (Table 1). With the exception of a study from Nigeria, pulmonary tuberculosis (TB) cases have very low isolation rates for *M. bovis*. For some of these, however, the isolation rate might be artificially low owing to the inclusion of glycerol in the culture media, which can inhibit the growth of *M. bovis* but not that of *Mycobacterium tuberculosis*. However, other studies specifically looking for *M. bovis* failed to find any (e.g. a study from Burundi [12]). A further example is from South Africa where the prevalence of bTB exceeds 70% in African buffaloes in the southern part of the Kruger National Park. Sputum samples from 206 employees at the national park were examined, including 34 believed to be at particular high risk (workers who had direct, unprotected contact with tuberculous lesions or excretions). *M. bovis* was not isolated, although two cases of *M. tuberculosis* infection were diagnosed [13].

One of the very few studies that appears, at first inspection, to provide more convincing evidence for significant airborne transmission is from Burkina Faso [14]. Out of 39 individuals of high occupational risk of exposure to *M. bovis*, 37 had pulmonary TB. This group also had higher pulmonary TB rates than groups not exposed to cattle. In 199 cattle owned by these individuals, 13 had lung lesions that were confirmed to contain *M. bovis*. Unfortunately, the human cases were based on hospital records and the causal organism (i.e. *M. bovis*, *M. tuberculosis* or other) was not recorded. A more recent study from the same country [15] failed to find *M. bovis* in 120 samples of sputum that were positive for *Mycobacterium* spp., although it should be noted that most of the cases were from urban areas (where direct contact with cattle is less likely). A recent study from Mexico might also provide some evidence of aerosol transmission [16]. The researchers could isolate or culture *Mycobacterium* spp. from 94 out of 255 samples from patients symptomatic for TB. *M. bovis* was detected in five sputum samples and eight urine or gastric juice samples. It seems that 16% of Mexican dairy cows carry *M. bovis* [17]. In China, human bTB is a very low proportion of TB cases in patients that come from districts where milk is pasteurised, with a much higher proportion being reported in pastoral areas where raw milk is extensively consumed [18], thus supporting the hypothesis that human bTB in humans is primarily a food borne disease.

Finally, it should also be noted that isolation of *M. bovis* from sputum of individuals with TB falls far short of proving that aerosol was the means of acquisition. The

**Table 1. Presence of *M. bovis* in pulmonary TB, as reported in African studies[a]**

| Country | Samples with *Mycobacterium* spp. | Samples with *M. bovis* | Ref. |
|---|---|---|---|
| Cameroon | 455 | 1 | [54] |
| Ivory Coast | 346 | 0 | [55] |
| Ghana | 64 | 2 | [56] |
| Nigeria | 357 | 3 | [57] |
| Sierra Leone | 97 | 0 | [58] |
| Burundi | 170 | 0 | [12] |
| Burkina Faso | 120 | 0 | [15] |
| Nigeria | 65 | 10 | [59] |

[a]bTB control in cattle is generally neglected in Africa. Of 55 African countries, bTB control is undertaken inadequately, if at all, in 48 countries [53].

**Box 1. Aerosol transmission of bTB from cattle to human**

Pulmonary TB caused by *M. bovis* (bovine TB, bTB) was seldom diagnosed in the UK in the early 20th century [4]. Between 1908 and 1937, a total of 194 human cases of bTB were described in Great Britain (i.e. 6–7 cases per year) [44]. Of these 194, 38 had contact with cattle, and it was hypothesised that the remainder might have been infected through drinking milk. An analysis of 13 studies corresponding to 938 cases of pulmonary TB showed that, of these, 932 were caused by *M. tuberculosis*, three by *M. bovis* and another three were mixed infections [45]. Griffith and Smith [46] investigated 103 cases of pulmonary TB in NE Scotland and reported that 13 cases were bTB; the mode of infection was probably alimentary for five of them.

An extensive report of 2101 cases of pulmonary TB from the Cheshire sanatorium [47] represented the period 1934–1943. Of these, just 48 cases (2.28%) were bTB and only 10 were strongly suggestive of airborne transmission from cattle. Three cases were of familial airborne transmission, 16 were alimentary acquired, and in the remaining 19 cases the mode of transmission was not elucidated. The study confirmed that pulmonary bTB is an occupational health risk: *M. bovis* was detected in 16.4% of diseased individuals with cattle contact, whereas only 1.6% of patients without cattle contact were positive for bTB. However, the study also indicated that the absolute numbers of bTB transmission are small even when the disease is highly endemic in the cattle.

Likewise, at a time in the USA when bTB in cattle reached its peak, mycobacteria were isolated from 1220 human infections [48]. Of 680 cases of pulmonary TB, only two were caused by *M. bovis*. The bacterium was also isolated in 99 other cases that consisted of extrapulmonary TB, usually in children.

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evidence presented in Box 1 demonstrates that for many cases of pulmonary bTB the primary lesion is elsewhere.

### The economics of bTB

bTB control is big business. In 2007, there were 4172 new herd breakdowns in England and Wales [2]. The official figures probably underestimate the true numbers of cattle affected by bTB owing to, for example, the lack of sensitivity of surveillance at abattoirs [19]. Nevertheless, the direct costs can be estimated as £13,981 per breakdown [20]—overall in excess of £58 million. A detailed breakdown of expenditure [20] shows that expenditure is due to programme implementation. No animal health costs (such as loss of productivity in diseased animals) are reported. Unfortunately, there are few studies which examine such costs to animal health.

Although bTB control can provide some benefits to the cattle industry, what is lacking are good cost-effective studies in terms of animal health, welfare and productivity. Given the evidence regarding the low public health risk of this disease, such studies are required to justify the expenditure on control. One of the few cost–benefit analyses considering only effects on animal health and production is from Spain and it was demonstrated that bTB control is not economically efficient [21].

Another important consideration, if bTB were to be discontinued, is the economic effect of the blocking of live cattle exports [22]. However, the cost of the bTB programme is in excess of the value of such live exports from the UK [23]. In addition, only a minority of the UK cattle population (1.4%) is exported each year (approximately 140,000 out of 10 million animals) [24]. Thus, 98.6% of the industry would be unaffected by any export ban imposed.

More [25] presents an extensive review regarding various policies and public/private cost sharing for animal disease control. The degree of public sector financing would depend upon whether the disease is zoonotic, the degree of contagiousness, whether it is endemic or epidemic and the economic losses associated with the disease. Although bTB is zoonotic, we have argued that effective milk pasteurisation removes the threat of transmission to humans. Therefore, the degree of public investment in additional control measures should largely be guided by other concerns. Consequently, it is vital that cost-effectiveness studies are undertaken in terms of animal health. To justify bTB control, there should be firm estimates of any positive economic effects of the programme resulting from increased animal productivity, health and welfare, and they should exceed the implementation costs.

Comparisons have been made with the Foot and Mouth Disease (FMD) Control Programme as a justification for resource allocation for bTB control [22]. Indeed, it has been demonstrated that the economic effects of FMD went far beyond that of the animal disease but had bystander effects on many parts of the community [26]. However, both the direct and the indirect effects of FMD (such as mass cull of animals with burning on open pyres and complete closure of the local community during the control programme control) should be considered for comparison. FMD is not a fatal disease in livestock but results in substantive production losses following recovery. Because it is not fatal, many low-income countries do not prioritise FMD control [27]. The negative bystander effects of FMD control as seen in Cumbria (NW England) would not have occurred, but for the mass slaughter of animals and the severe movement restrictions in the countryside that the FMD control policy entailed. In addition, because of the widespread problems caused by the FMD control policy, alternatives such as the use of vaccines are being considered [28]. By the same argument, alternatives for bTB control should be considered, including the necessity of control.

### Misallocation of resources

Currently the UK invests large amounts of public resource to prevent bTB, which is essentially an animal disease. In the absence of data demonstrating economic benefits to animal health, such investment is, in our opinion, a clear example of misallocation of resources. If there are economic benefits to agriculture, then the industry rather than the tax payer should bear most of the costs because of the principles of cost sharing such as those reviewed by More [25]. From a public health perspective, routine vaccination against TB using BCG (Bacillus Calmette-Guérin, an attenuated strain of *M. bovis*) for UK schoolchildren was stopped owing to its poor cost-effectiveness [29]. Our calculations suggest that the cost for controlling bTB as a public health policy exceeds any positive effect in public health substantially (Box 2).

The reasons given by the UK government for bTB control include: (i) "to reduce the economic impact of bTB and maintain public health protection and animal health and welfare", and (ii) "to ensure minimal risks to public health from exposure to bTB through continuing cattle surveillance and control, slaughterhouse inspections and heat treatment of milk, occupational health controls and monitoring for human cases of bTB" [30]. Yet, this *public health benefit* is negligible provided that milk continues to be pasteurised. Indeed, operating the bTB control programme has health and safety risks. An incidence of 1.9 injuries to veterinarians per 10,000 cattle tested has been reported in the USA [31]. Of these, 10% were serious injuries that required immediate treatment, and one spinal cord injury was reported.

These public resources could be better spent on areas of disease prevention that would have an important impact on public health (or the tax burden on the UK population could be reduced). Prevention of human disease is an important role of the UK's National Health Service (NHS) that, in our opinion, is not adequately funded. HIV/AIDS, for instance, is an important long-term threat to the health of the UK population, yet at £38 million current expenditure for its prevention represents a real reduction compared with 10 years ago [32]. The cost-effectiveness of treatments used by the UK healthcare system is informed by the National Institute of Clinical Excellence (NICE) [33], which appears to be heavily influenced by economic decision-making. Interventions must be both effective and cost-effective. We argue that bTB control is neither (Box 2).

### A new way forward

The results of the randomised trial of badger culling (RTBC) in the UK suggested that badger culling is an ineffective use of public money. Indeed, the evidence

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**Box 2. Health economics of bTB control**

Estimates of the public health costs in England and Wales can be made should bTB control be abandoned. Pessimistic scenarios assume that the prevalence in cattle would return to levels seen in the early part of the 20th century with associated aerosol transmission to humans. Milk would continue to be pasteurised. In 1944, Cutbil and Lynn [47] suggested an annual incidence of pulmonary bTB in adults of approximately 1.6 and 0.2 per 100,000 in rural and urban populations, respectively. In children, bTB nearly always was extra-pulmonary [44]. The rural population of England and Wales is 10.5 million (2001 census) and no exposure of urban populations to cattle is supposed. Assuming that the 1944 incidence in rural populations would return, the upper limit of 168 cases of bTB per year would occur. Historical evidence suggests at least half and probably two-thirds of pulmonary bTB was primarily alimentary infections. Hence, we estimate approximately 56 cases per year arising by aerosol transmission. The 10 cases reported by Cutbil and Lynn [47] that were probably as a result of airborne transmission from cattle were in occupational risk groups (six farmers, three farm labourers, one tanner). In 1950, the agricultural associated population in the UK was 2.8 million, with a reduction to 910,000 by 2010 expected (see http://faostat.fao.org/site/552/default.aspx#ancor). Therefore, the population at risk in the UK is now one-third of that in 1950 and, hence, a prorate decrease in the numbers of bTB cases would be expected. This yields an expected maximum number of cases of approximately 19 per year.

In Texas, a case of TB was calculated to cost 1.4 QALYs (see Glossary) [49]. In the UK, each case of human bTB is likely to cost similar numbers of QALYs or DALYs. Thus, the £100 million per year spent on bTB control is preventing approximately 26.6 DALYs, or gaining 26.6 QALYs—that is £3.8 million per QALY saved or DALY averted. Few treatments are authorised by the UK National Institute of Clinical Excellence (NICE) for uses that exceed a cost per QALY gained of £20–£30,000 [33]. Thus, the possible cost per QALY gained of bTB control exceeds this benchmark by several orders of magnitude. In contrast, treating cases as they arise would be much less costly. In Germany, a case of pulmonary TB in an adult costs approximately £16,700 (May 2009 exchange rate) [50]. Assuming similar treatment costs on the NHS, the treatment cost of 19 cases would be £317,300, which is 0.3% of the cost of the bTB programme.

It should be noted that, during the 1940s and 1950s, adults might have possessed certain protection against pulmonary TB because of previous exposure to *M. bovis* in milk as children [51]. This would not be generally the case today, as drinking unpasteurised milk is rare in the UK. Therefore, the abandonment of the bTB control programme might result in a greater number of human bTB cases than that estimated above. If this were to be correct, then the use of BCG vaccination in humans at risk of infection could help to reduce the number of bTB cases [52].

suggested that culling not only wastes resources but it might worsen the problem [34] and is unlikely to be economically effective [20]. However, it is also possible that badger culling might have some positive effects, as there have been criticisms of the interpretations of the RTBC both in terms of statistics and study design (see Ref. [35]). In addition, there is some evidence that there might be a modest positive long-term effect once badger culling ceases [36]. Initially the Government's chief scientific officer discounted the results of the RTBC and recommended culling of badgers—although the Government subsequently decided that a badger cull was not appropriate [37]. However, the whole issue is mired in controversy and politics, in which the scientific message is in danger of being lost. Nevertheless, the Welsh assembly is proposing to undertake a badger cull [38] and the British Conservative party has indicated they would initiate a badger cull if they win the next general election [39,40].

Our simple calculation (Box 2) suggests that the current bTB elimination programme is extremely inefficient in terms of public health protection. We have already argued that an economic evaluation of the costs in animal health to the livestock industry that strips out the costs of the test and cull policy is also required. If there is a negative cost benefit in terms of animal health, then the UK Government should seek derogation from EU laws that compel member states to draw up plans for the elimination of bTB on their territories (e.g. Council Directive 77/391/EEC). This would enable the UK to abandon attempts at eliminating the disease from the UK cattle herd and develop alternative measures for animal health protection. In any case, if the tax payer should "only be expected to pay for genuine public good", as suggested by the UK governments Department for Environment, Food and Rural Affairs (DEFRA) [30], then costs should be borne by the livestock industry.

What would happen if the bTB control programme was abandoned in the UK? The disease would certainly increase further in the national herd (which is occurring, nevertheless, in the presence of the programme). Mathematical modelling might be able to predict the probable final level of endemic stability in the cattle population. However, farmers exporting animals or supplying raw milk for human consumption could have a self-funded programme. For others, bTB would be like most other endemic cattle diseases, probably causing some productivity losses, but farmers themselves could decide on the economic consequences of such losses and hence any intervention. Disease security on individual farms could be implemented through cooperation of farmers with their veterinarians. Possible use of the BCG vaccine could be introduced for cattle as an interim measure whilst better vaccines are being developed. Although BCG provides far from complete protection to cattle, evidence suggests that if given in the correct doses it can be used to reduce transmission, particularly if given before calves have been exposed to bTB [41]. As the test and cull policy would no longer operate, use of BCG vaccine would not interfere with this testing policy.

## Concluding remarks

More and more extreme measures for the control of bTB are largely supported by the farming industry and the veterinary profession [42]. Ironically, in the first half of the last century, farmers, consumers and legislators repeatedly resisted attempts to make testing of cattle and, more importantly, pasteurisation of milk compulsory in Britain, despite overwhelming evidence (particularly from the USA [43]) of its positive impact on public health.

In light of the evidence we have presented here, we would propose that the continuing bTB programme in the UK is economically unacceptable as a public health intervention. Furthermore, data is lacking with regard to the positive economic effects to animal health, given that the main costs are implementation expenditure. Thus, the most effective way of reducing the economic impact of bTB is to stop the bTB control programme in its present form. A shift away from prevention in cattle, whilst continuing with the regulation of milk and meat, should provide adequate public health protection at relatively

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modest costs. More and colleagues [35], when arguing in defence of badger culling, concluded: "It is important that interested policymakers and the general public are aware of varying perspectives surrounding this topic." We believe it is also vital that policy makers and the general public are aware of the alternative perspectives regarding the need for bTB control, particularly from the public health perspective.

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## Celebrating Darwin: evolution of hosts, microbes and parasites

During 2009, *Trends in Microbiology* and *Trends in Parasitology* jointly had a series on evolution to commemorate the 200th anniversary of Charles Darwin's birthday (12th February, 1809). The series focused on aspects of evolution and natural selection related to microbes and parasites. These are some of the articles that were published:

- **Darwinian interventions: evolutionary ecology thinking in the treatment of pathogens**
  Paul David Williams. *Trends in Parasitology*, January 2010.
- **The search for the fungal tree of life**
  David McLaughlin *et al. Trends in Microbiology*, November 2009.
- **Infrequent marine-freshwater transitions in the microbial world**
  Ramiro Logares *et al. Trends in Microbiology*, September 2009.
- **Genetic and genomic analysis of host-pathogen interactions in malaria**
  Philippe Gros *et al. Trends in Parasitology*, September 2009.
- **What did Darwin say about microbes, and how did microbiology respond?**
  Maureen A. O'Malley. *Trends in Microbiology*, August 2009.
- **Evolution of the Apicomplexa: where are we now?**
  David A. Morrison. *Trends in Parasitology*, August 2009.
- **Why do bacteria engage in homologous recombination?**
  Michiel Vos. *Trends in Microbiology*, June 2009.
- **Parasite adaptations to within-host competition.**
  Nicole Mideo. *Trends in Parasitology*, June 2009.
- **Looking for Darwin's footprints in the microbial world.**
  Eric J. Alm *et al. Trends in Microbiology*, May 2009.
- **Environment alters host-parasite genetic specificity: implications for coevolution?**
  Kayla King and Justyna Wolinska. *Trends in Parasitology*, May 2009.
- **Type III secretion systems in symbiotic adaptation of pathogenic and non-pathogenic bacteria.**
  Brian K. Coombes. *Trends in Microbiology*, March 2009.
- **Bacterial flagellar diversity and evolution: seek simplicity and distrust it?**
  Mark J. Pallen *et al. Trends in Microbiology*, January 2009.

**For a full list of articles, go to www.cell.com/trends/microbiology/Darwin**