Foresight

Infectious Diseases: preparing for the future

OFFICE OF SCIENCE AND INNOVATION

T8.10: Predicting future areas suitable for vivax malaria in the United Kingdom

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Abstract:

Malaria was common in parts of southern and central England from 1500 to 1800. It declined sharply from the early 1800s before dying out by the mid-1900s because of better housing, the development of drugs, and land drainage that reduced the breeding grounds for mosquitoes. Less-crowded housing, closed windows and a reduced tendency for people to live close to their livestock all helped to reduce the malaria risk. But climate change will increase the risk of local transmission in the coming 30 years, and sea-level rise may add to the areas in which malaria mosquitoes can breed. The main risk is from the parasite vivax, rather than the more virulent falciparum parasite found in Africa, because it tolerates lower temperatures. Low numbers of biting mosquitoes, better housing and drugs mean that the disease is highly unlikely to become established in the UK, although sporadic outbreaks involving one or two people may well occur in the future. Health authorities in central and southern England need to be alert to the possibility of local malaria transmission, particularly in areas near saltmarsh. .

This review has been commissioned as part of the UK Government's Foresight project, Infectious Diseases: preparing for the future. The views expressed do not represent the policy of any Government or organisation.

Introduction

Malaria was common in marshland communities in central and southern England between 1500 and 1800, before finally disappearing in the early 1900s (Dobson 1997). Worst affected areas included the Fens, Thames Estuary, the Kent coast, the Somerset levels, the Severn Estuary and the Holderness of Yorkshire, all substantial areas of marshland.

The disease declined progressively from the 1820s onwards as living conditions in the marshes improved. Drainage of the marshlands reduced the number of mosquito breeding sites in water channels crossing the marshes. Housing improved, and the lighter, drier rooms were less suitable for resting mosquitoes. Fewer people slept in the same room. They also slept upstairs in rooms that had closed windows, making it more difficult for an adult female mosquito to locate a human blood meal. Cattle and horses, the preferred hosts, were no longer stabled in the same house as people, further reducing the chance of disease transmission. At the same time, quinine, an effective anti-malarial, became more affordable (Shute and Maryon 1974).

The last epidemic of malaria occurred in 1917 and 1918 (Newman 1919). There were 330 cases of locally transmitted vivax malaria when infected servicemen returning from Macedonia were billeted near saltmarshes on the Isle of Sheppey. The disease was eradicated by making malaria notifiable, with appropriate and prompt treatment of cases. All reported cases of indigenous malaria in the 1900s were vivax malaria, except for an unusual case of falciparum malaria in Liverpool. While vivax malaria is a debilitating infection, it is rarely a killer like falciparum malaria (Hutchinson and Lindsay in press – a). Thus, although historically mortality rates in the marshlands of southern England were several orders higher than inland areas, it is unlikely that the elevated mortality in the marshes was due to vivax malaria.

Mosquito vectors and malaria transmission

Recently it has been shown that *Anopheles plumbeus* can transmit *Plasmodium falciparum* parasites (Curtis 2003). This mosquito typically breeds in tree holes and has a widespread distribution that includes London and its suburbs, Cheshire and the mouth of the Firth of Forth (Snow et al. 1998). It is possible that falciparum malaria could be transmitted for a few months in the UK, but since this mosquito is found in very low numbers (Hutchinson and Lindsay, unpublished data) any outbreak is likely to be rare and limited.

There are six species of Anophelines in Britain capable of transmitting both temperate and tropical strains of vivax malaria: *An. atroparvus*, *An. algeriensis*, *An. claviger*, *An. daciae*, *An. messeae* and *An. plumbeus* (Linton et al. 2005; Shute and Maryon 1974). *An. atroparvus* only transmits European strains of falciparum malaria (Ramsdale and Coluzzi 1975), but is completely refractory to strains of the same parasite from the tropics (quoted in Ramsdale and Coluzzi 1975). This mosquito is therefore considered the most important potential vector of malaria in the UK since its distribution is coincident with the historical distribution of the disease. It also rests inside homes and will feed avidly on people.

Malaria and climate

Importantly, the malaria parasite *P. vivax* is better suited to the British climate than is *P. falciparum*. Vivax malaria requires lower temperatures (by 1–2^{o}C) than falciparum to develop as fast in mosquitoes, and thus replicates better in cooler conditions. Vivax parasites, unlike those of falciparum, also sequester in the liver of an infected person, to be later released to infect new generations of mosquitoes in the spring. As few parasites develop in mosquitoes below 15^{o}C, the period of potential transmission is between June and September.

Temperature and rainfall both affect the risk of malaria transmission (Lindsay and Birley 1996). Higher temperatures speed the development of mosquitoes and how frequently the female mosquito feeds, as well as the maturation of malaria parasites in the mosquito. Extremely high temperatures, though, may reduce adult mosquito survival. Rainwater, groundwater and diluted seawater provide mosquito breeding habitats, along with a moderately humid environment which is conducive to vector survival.

Impact of temperature changes

Here, we model the current risk of vivax malaria in the UK transmitted by *An. atroparvus* and the future risk for the periods to 2015 and 2030. Future risk is modelled using the UKCIP02 medium–high climate change scenario for the UK. This scenario uses the Hadley Centre global climate model (HadCM3) for a medium–high climate change scenario (SRES A2), which is used, via a further stage, to drive a regional version of the model that has a resolution of 50km over Europe. Results from this regional model over the UK form the UKCIP02 scenario. Maps of malaria suitability using present-day climate (Figure 1) and for the two future periods (Figures 2a and 2b) show the number of months that vivax malaria, if it were introduced, could persist each year in different parts of the country. Unfortunately, within this climate suitability zone, we are uncertain where we will find the vectors. The actual distribution of potential vectors in the UK is sketchy and is based on data collected over 100 years ago or by entomologists in an unsystematic fashion (Lang 1918; Nuttall et al. 1901; Rees and Snow 1990; Snow et al. 1998). The concern is that these distributions may be outdated and reflect the distribution of entomologists rather than the true distribution of vector species. As a proxy measure to identify sites likely to have *An. atroparvus*, we provide a landcover map of saltmarsh areas, likely sources of this mosquito, for the southern UK (Figure 3b) in relation to the climate suitability zone for 2030 (Figure 3a).

Our maps showing areas at high risk from malaria need to be treated with caution. Although they consider the effects of changing temperature on variables in the transmission process, they do not take into account changes in precipitation, humidity or the availability of mosquito breeding sites. These latter factors may not be so critical for the UK because the risk of malaria transmission is likely to be highest near extensive areas of wetland, which provide numerous breeding sites and are less affected by small changes in rainfall.

The 1961–1990 distribution of malaria risk (Figure 1a) corresponds extremely well with past records of ague cases (that will have included patients with malaria) in England during the 19th century (Figure 1b; Nuttall et al. 1901). In order to validate this approach, we compared temperatures from 1800–1829, when ague was relatively common, with those for 1961–1990, using the central England records for these periods (Manley 1974; Hadley Centre, UK). While the more recent period has warmer annual temperatures than the older period (1800–1829 = 9.10°C, 95% confidence intervals, CIs = 7.82–10.17°C; 1961–1990 = 9.47°C, 95% CIs = 8.54–10.55°C; $t = -2.443$, $p = 0.018$), the summer months, when conditions are most suitable for malaria transmission, were similar for both periods (1800–1829 = 14.71, 13.17–16.16; 1961–1990 = 14.89, 13.76–16.43; $t = -0.936$, non significant). Thus, we are confident that our temperature–malaria model is relatively robust and that the 1961–1990 summer temperatures are comparable with those experienced in the early part of the 19th century, when ague was endemic in the country. It should also be appreciated that winter temperatures are not likely to greatly affect the dynamics of transmission since *An. atroparvus* rests indoors during the winter and does not rest in sites that drop below 0°C (Hutchinson 2004), and the parasite remains sequestered in the liver over winter. Under the UKCIP02 medium–high scenario used here, the risk of transmission is predicted to increase in the south of England, spreading northwards towards the Scottish border. The areas at greatest risk include areas bordering the Wash, Thames Estuary, Romney marshes, the Southampton coastline and the Severn Estuary (Figure 3).

At present, temperatures in the south of the UK are able to support the transmission of vivax malaria for a few months each year. For most areas, this is just for two months, although the heat-island effect of London means this city could support transmission for three months. Although such transmission occurred in the historical past, it is a minor threat at present because living conditions have improved considerably since the 1800s. If the climate becomes warmer, conditions for transmission become more favourable and last for longer. Interestingly, by 2030, the areas where the climate is predicted to be suitable for malaria for three to four months are those that supported malaria in the past: the coastal and inland marshes of southern England.

It is likely that our present standards of living will mitigate this increasing threat to a large extent, but not necessarily wholly in high-risk areas. In regions of extensive marshland in south-east England, local inhabitants are plagued by large numbers of mosquitoes even today (Hutchinson and Lindsay in press – b).

Impact of habitat changes

An. atroparvus is largely restricted to saltmarshes and their margins, because it is tolerant of brackish water. There are 42,251ha of saltmarsh in Britain, with the largest areas, 8,525ha, along the Greater Thames Estuary in Essex and Kent (Davidson et al. 1991). Coastal wetlands are being reduced by drainage and other land ‘improvements’. Rises in sea level that breach sea defences and inundate lowlands that are at present prevented from adapting naturally to saltwater may result in less saltmarsh. Elsewhere, gradual saltwater intrusion into coastal lowlands may increase breeding sites for *An. atroparvus*. With summer droughts, other mosquito species may find more breeding sites in pools left in river beds and water butts. There will be greater exposure to mosquitoes as people stay outdoors in warmer summer evenings, or sleep with the windows open (Snow 1999).

It is possible that climate changes will allow new vector species to become established in Britain. This would be most serious if it involved better European vectors of vivax, such as *An. saccharovi*, *An. labranchiae*, *An. superpictus* and *An. sergentii* (Bruce-Chwatt and Zulueta 1980; Hackett 1949). Introduction of new pests into the country may have occurred in the past. *An. algeriensis* is a rare species in the UK, but is once more commonly found in parts of the Mediterranean (Marshall 1938; Snow 1990). However, it is impossible to say whether this species was actually introduced or is simply at the edge of its species range. Planes arriving at our international airports are known to bring in mosquitoes, but these are rare occurrences (Hutchinson et al. 2005).

Health authorities need to remain alert to the possibility of future European malaria outbreaks, as occurred in Italy after 40 years of being free of malaria (Simini 1997), and to the arrival in the UK of better European vectors of the disease. Any outbreaks in the UK, however, are likely to be on a small scale, and people at greatest risk (i.e. those who live near wetlands) are likely to take precautions against being bitten by mosquitoes. Prompt reaction to any outbreak will prevent malaria becoming endemic in the UK.

Modelling future risk

The analyses to produce the maps of vivax malaria risk in Figures 1, 2 and 3 are based on the concept of the basic reproduction rate (R_o), which represents the number of future cases of malaria derived from one infective case at the present time, before this case is cured, or the infected person dies. This analysis follows on from earlier work that adopted a similar approach (Lindsay and Thomas 2001). Where R_0 is ≥1, the disease can become established; when it is <1 it becomes extinct. One common expression for R_0 is shown below:

$$R_0 = \frac{ma^2bp^n}{-\ln(p)r}$$

where ma is the number of mosquito bites per person per day or night. Here, we assumed that this value equalled 1, since we thought that few people would tolerate more than one bite each night. This is the daily rate at which an individual mosquito will feed on a person:

$$a = \frac{h}{u} \text{ bites/person/day}$$

where h is the proportion of mosquito blood meals taken from people (rather than animals that are not infected with human malaria) and u is the period in days of the gonotrophic cycle _ the interval between laying each egg batch and, generally, each mosquito blood meal. The present model assumes a mean value of h of 0.42 for indoor-resting mosquitoes (Jetten and Takken 1994).

u is the length of the gonotrophic cycle, as described below:

$$u = \frac{f_1}{T - g_1} \text{ days}$$

Where f_1 is a thermal sum, measured in degree days, that represents the accumulation of temperature units over time to complete the cycle (36.5°C), g_1 is a threshold below which development ceases (9.9°C), and T is ambient temperature (Detinova 1962).

p is the daily survival probability of adult mosquitoes. The present model takes the median value of the mortality rate for *An. atroparvus* = 0.029/day (n = 24, range 0–0.294/day) (Jetten and Takken 1994).

n is the period of parasite development in adult mosquitoes, in days (the sporogonic cycle) as shown below:

$$n = \frac{f_2}{T - g_2} \text{ days}$$

Where f_2 is a thermal sum, measured in degree days, representing the accumulation of temperature units over time to complete the development (105 degree days), g_2 is a development threshold below which development ceases (14.5°C) and T is ambient temperature (Jetten and Takken 1994). Generally, as conditions warm, the rate of parasite development increases (Figure 4). There is uncertainty about the minimum threshold for parasite development, with figures ranging from 14.5°C to 16.0°C (Boyd 1949; Detinova 1962; Macdonald 1957).

b is the proportion of female mosquitoes developing parasites after taking an infective blood meal (0.19) (James 1931).

r is the rate at which humans with malaria recover from the infection. It is usually considered that the duration of each infection is therefore 1/r days. We assumed that an average infection would be patent for 60 days, giving a value for r of 0.0167/day (Boyd 1949).

In the model, these formulae were combined with the 1961–1990 UKCIP climate data at a 5km resolution for present-day climate, and with two future scenarios for 2015 and 2030. The latter two scenarios were calculated using the UKCIP02 medium–high scenario for climate change in the UK at a 5km resolution. The model outputs the number of months of the year when R_0 is >1.0, indicating potential disease spread. Under conditions when R_0 is <1.0 for a considerable proportion of the year, the disease probably cannot persist without continuous introduction from elsewhere, or possibly as quiescent stages within apparently recovered people.

The distribution of saltmarsh was derived from the Land Cover Map of Great Britain 1990 (Fuller et al. 1994), which classifies land use in the UK into 25 classes at a 25m resolution from satellite information. Here we classify 1km cells as containing saltmarsh if they contained more than 0.5% saltmarsh according to the Land Cover Map.

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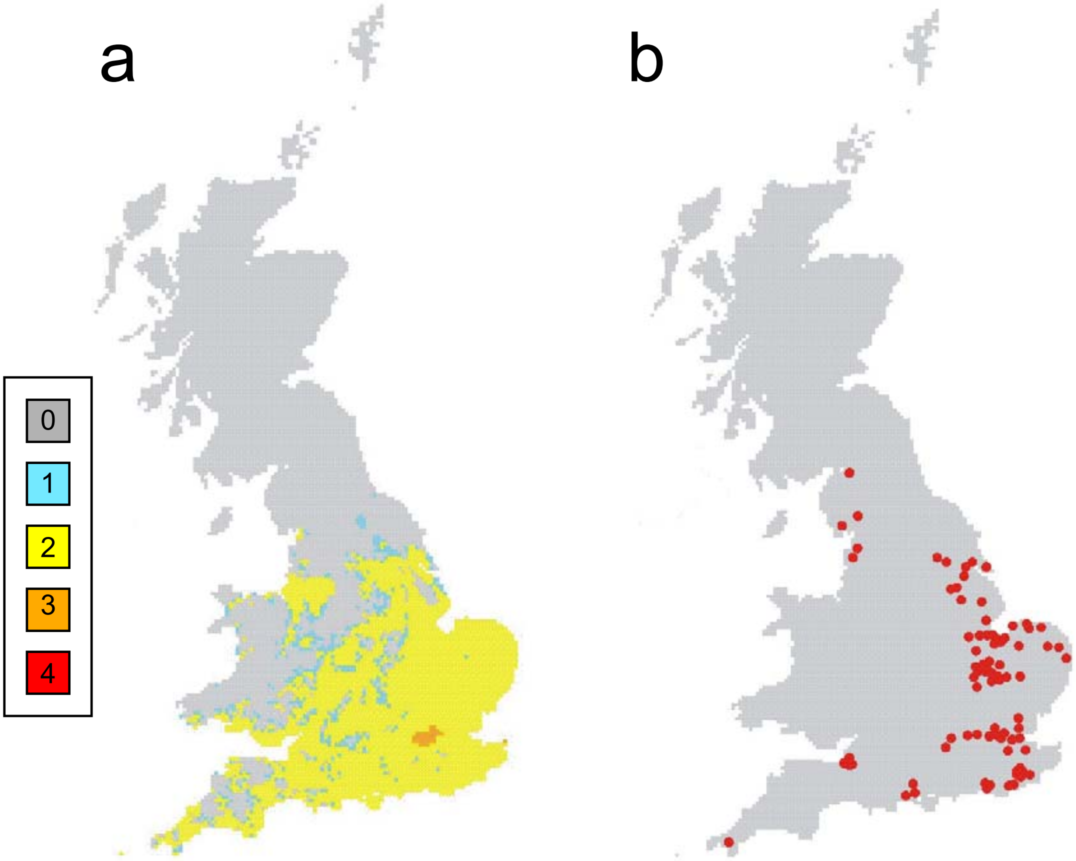

Figure 1: Malaria risk across Great Britain for 1961–1990. (**a**) Shading represents the number of months in which the climate could support vivax malaria if it were introduced; (**b**) Red circles show cases of ague (some of which will have been malaria cases) in the 19th century (Nuttall et al. 1901).

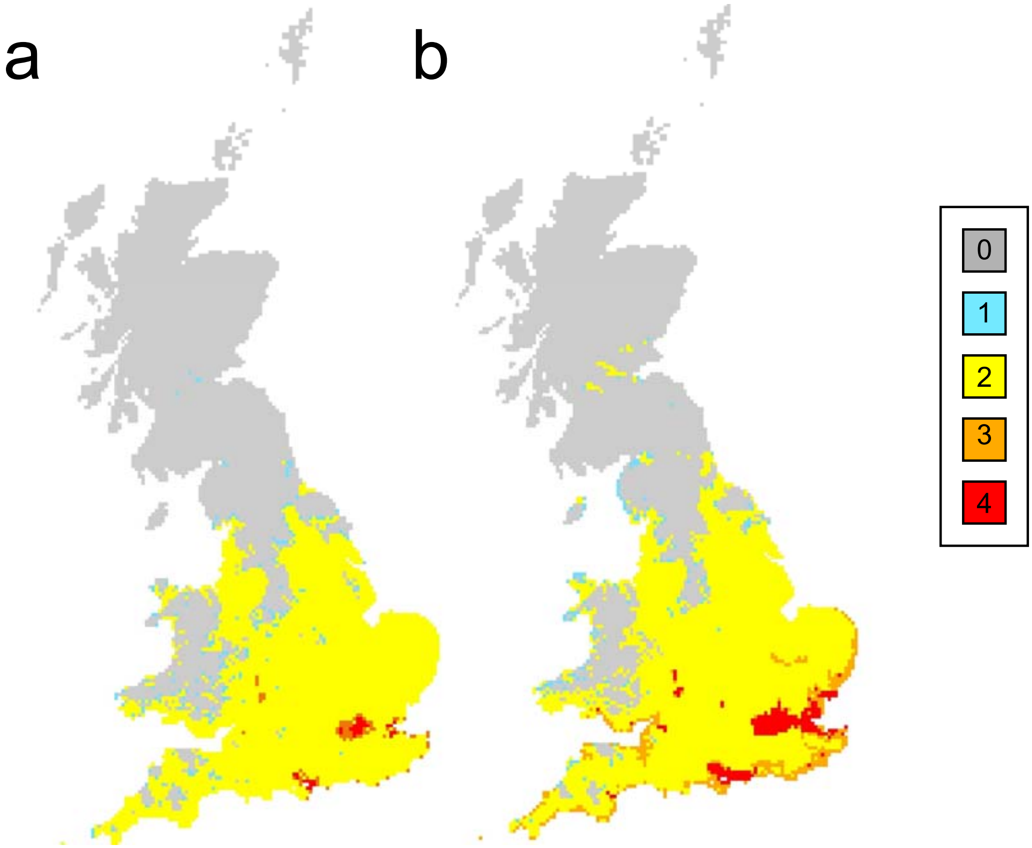

Figure 2: Malaria risk across Great Britain. Number of months in which the climate could support vivax malaria if it were introduced: (**a**) 2015; (**b**) 2030.

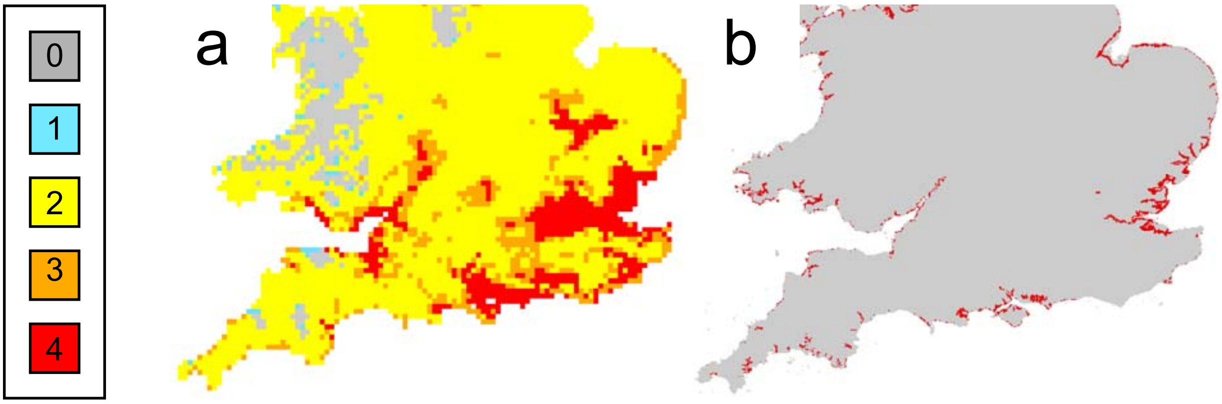

Figure 3: Climate suitability zone for vivax malaria in the southern UK: (**a**) 2030; (**b**) Areas of saltmarsh in 1990 that are the most suitable habitats for *Anopheles atroparvus*, the historical vector of vivax malaria. Shading represents the number of months where the climate could support vivax malaria if it were introduced.

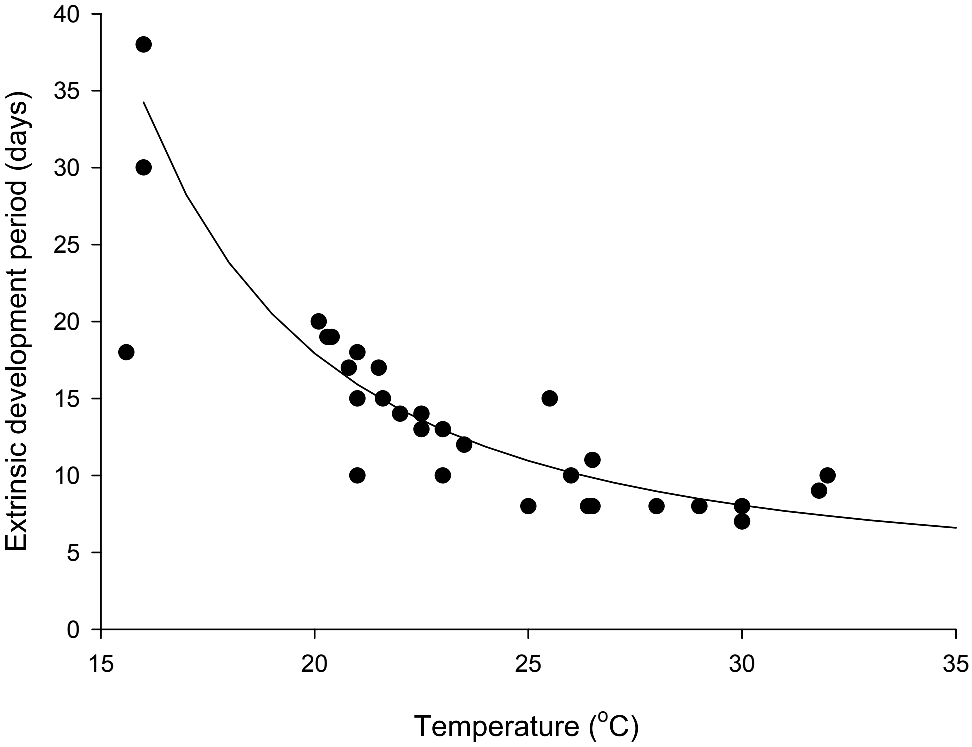

Figure 4: Development time of vivax malaria in mosquitoes kept at different temperatures. Data were taken from MacDonald (1952), including the record of 38 days at 16°C. The maximum likelihood parameters for these data (excluding the value of 18 days at 15.6°C) was described by the general equation, $y = \alpha (x - T^{*})^{-\beta} + D^{*}$; solved so that the period of development $y = 2{,}591\ (T^{o}C - 7.18)^{-2.04} + 3.66$, where T is ambient temperature.

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First published April 2006. Department of Trade and Industry. www.dti.gov.uk