

preparation for life at high altitude. Appropriately, however, an increase in placental surface area relative to the body weight of the foetus occurs at high altitude¹⁴. It is presumably only after birth that high altitude neonates are exposed to a greater hypoxic stimuli than at sea level. The adult pattern of responses and adaptations to hypoxia begins to develop shortly after birth. In teenage life a variety of effective gas transport adaptations develop, such as the increased area for gas exchange provided by large lungs, and ventilatory hypoxic drive assumes a less important role.

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Elimination of aziridine residues from chemosterilised mosquitoes

CRITICISM¹⁻⁴ of the use of the alkylating agent thiotepa (triethylene thiophosphoramidate) to sterilise mosquitoes, as part of an eradication programme in India, focused on its toxicity and the possibility that it or its breakdown products would harm other animal components of the food chain. For example, a Canadian team found reduced fertility in spiders fed on mosquitoes sterilised with thiotepa⁵. Some means was needed to ensure that no aziridine residues—breakdown products of thiotepa—remain in the insects after release into the environment. We have now achieved this, essentially by dipping the chemosterilised insects into acid and then alkaline solutions.

Complete breakdown of 3.1% thiotepa solution has been reported to occur in 90 min at pH 4, but aziridine activity persists for 24 h. This is due to the production of ethyleneimine which is stable in acid medium and tends to accumulate. Ethyleneimine is cytotoxic and mutagenic and may in some cases be carcinogenic⁶ and therefore potentially

hazardous. It breaks down to non-aziridine compounds at pH 9 (ref. 7).

The decomposition of thiotepa in acid medium was monitored by bioassay. A 0.6% solution was prepared in 0.01 N H₂SO₄, pH 1.8-2.0, and pH 3 was maintained by addition of small increments of N H₂SO₄ for 90 min. A hundred mosquito pupae (*Culex pipiens fatigans*) were placed in this solution for 3 h, washed twice in tap water and held in cages at 28-29 °C and 75% relative humidity until emergence. An equal number of virgin females was introduced into the cages and egg rafts were collected for routine bioassay. Fifty rafts, scored for percentage hatch, gave 92.7% fertility, whereas the controls dipped in water and in 0.6% thiotepa (pH 8) showed 94.9% and 0.01% fertility, respectively. Breakdown of thiotepa was complete in acid solution and the main decomposition product, ethyleneimine, proved inactive as a sterilant for *C. p. fatigans*. Therefore dipping sterilised pupae in acid solution (0.0025 N H₂SO₄, pH 2.6-2.8) for 90 min would ensure complete decomposition of thiotepa to ethyleneimine. Although no appreciable accumulation of ethyleneimine is likely, traces present as the intermediate decomposition product in sterile males may contaminate the environment. Ethyleneimine is hydrolysed to deuteriophosphoric acid and D₂NCH₂-CH₂OD, and this conversion can be accelerated by dipping acidified pupae in alkaline solution, pH 9 (ref. 7), thus making the mosquitoes free of any traces of aziridine compounds.

We tested the biological fitness of sterile male *C. p. fatigans* produced when pupae were dipped in 0.6% thiotepa, pH 8, for 3 h, washed twice in tap water, dipped in 0.0025 N H₂SO₄ for 90 min, washed in tap water, dipped in alkaline solution, pH 9.1-9.4, for 90 min, washed and transferred to tap water for emergence. No pupae died after this treatment. To assess survival, 100 sterile and 100 normal males were held in cages (ten replicates) and offered water-soaked raisins daily. The number of mosquitoes found dead in each cage was recorded at 24-h intervals. Weekly (%) mortality of sterile males averaged 1.9, 12.7 and 17.4 (cumulative total 32.2 in 3 weeks) and controls averaged 3.6, 13.2 and 20.3 (cumulative total 37.1 in 3 weeks). Thus the treatment had no effect on the longevity of the mosquitoes.

Sterile males were also tested for mating competitiveness. In ten laboratory cages, 100 sterile and 100 normal, 1-2-d-old males and 100 virgin, 2-d-old females were fed on raisins and allowed to mate for 4 d. They were offered pigeons for a blood meal. A total of 622 egg rafts was collected, of which 327 were sterile. As sterility averaged 52.57%, sterile males proved competitive.

Thus residues of thiotepa, and other aziridine compounds can be eliminated from sterile mosquitoes by dipping them in acid and alkaline solutions. Residue-free emergent adults survive well for at least 3 weeks. As sterile males compete favourably with normal males in the insemination of females, mass release of these sterile males for population control would not be hazardous to the food chain and would not contaminate the environment directly or indirectly.

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