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Invited Review

Control of the sheep blowfly in Australia and New Zealand – are we there yet?

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ABSTRACT

The last 50 years of research into infections in Australia and New Zealand caused by larvae of the sheep blowfly, *Lucilia cuprina*, have significantly advanced our understanding of this blowfly and its primary host, the sheep. However, apart from some highly effective drugs it could be argued that no new control methodologies have resulted. This review addresses the major areas of sheep blowfly research over this period describing the significant outcomes and analyses, and what is still required to produce new commercial control technologies. The use of drugs against this fly species has been very successful but resistance has developed to almost all current compounds. Integrated pest management is becoming basic to control, especially in the absence of mulesing, and has clearly benefited from computer-aided technologies. Biological control has more challenges but natural and perhaps transformed biopesticides offer possibilities for the future. Experimental vaccines have been developed but require further analysis of antigens and formulations to boost protection. Genetic technologies may provide potential for long-term control through more rapid indirect selection of sheep less prone to flystrike. Finally in the future, genetic analysis of the fly may allow suppression and perhaps eradication of blowfly populations or identification of new and more viable targets for drug and vaccine intervention. Clearly all these areas of research offer potential new controls but commercial development is perhaps inhibited by the success of current chemical insecticides and certainly requires a significant additional injection of resources.

1. Introduction

The sheep blowfly, *Lucilia cuprina*, was introduced on a number of occasions into Australian agriculture in the late 1800s and with the introduction of the Vermont Merino in the 1880s it became a major pest that has not been controlled to this day (Norris, 1990). The fly was added to the New Zealand fauna in the late 1970s or early 1980s from Australia (Gleeson et al., 2006). Chemical therapeutic and prophylactic drugs were and are the major control technologies and despite the repeated development of resistance to each class of chemicals (Levot, 2012) and the more recent issues around environmental and human contamination with residues, drugs are still the control of choice.

The link between blowfly and the Australian Society for Parasitology (ASP) can be argued to have begun with the scientific analysis of the fly problem from the early 1930s by Ian Mackerras (Mackerras, 1936) and his colleagues at the Council for Scientific and Industrial Research (CSIR), Australia. At this stage *L. cuprina* was only just being recognised as the major primary strike fly and flystrike was still spreading through the country, limiting and even halting sheep grazing in some areas (Waterhouse and Paramonov, 1950). Mackerras' pamphlet provides excellent reading nearly 80 years later, both in terms of the state of fly control technology in the 1930s and by comparison with the progress or lack of it in the intervening years. One area that might be said to have improved significantly would be chemical treatment where

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the use of boric acid and arsenic were the only treatments available, while today we have comparatively safe, efficacious and prophylactic treatments in the Insect Growth Regulators (IGRs) and a range of other compounds (Wall, 2012). Of course the rise of resistance in the fly population and the levels of residues in the environment and humans are legitimate concerns but current chemicals are a significant advance on the state of play at that time, when boric acid was being considered as a feed supplement to protect sheep.

Other controls mentioned by Mackerras include mulesing, which was only just being trialed (Beveridge, 1935) but which was gaining recognition as an effective preventative measure against breech strike. Of course, mulesing is still in use despite attempts to replace it with integrated control strategies and its continued use is hurting overseas wool markets through the intervention of animal welfare organisations (Sneddon and Rollin, 2009). These problems have spurred the introduction of non-mulesed wool marketing schemes (National Wool Declaration and Integrity Program. Australian Wool Exchange http://www.awex.com.au/media/1015/awx-041-nwd-ip-a4-final.pdf (accessed 1/8/2014)). Trapping of adult flies is still in use and while the baits have improved and the traps are more escape-proof, they are time consuming to ensure a significant effect on fly numbers when, as Mackerras points out, fly numbers are 'vastly greater than the numbers of sheep' (Mackerras, 1936) during periods of suitable weather. Biological control is mentioned as a possibility while selection of sheep for less skin wrinkle and better conformation was recognised as reducing flystrike incidence. Since that time, breeding has improved the overall susceptibility of sheep to flystrike with animals having plainer skin, white, dense fleeces and much improved body conformation (Hatcher et al., 2009). Finally Mackerras mentions the possibility of immunising against flystrike but maintains that the 'the experimental evidence is so far decidedly against it' (Mackerras, 1936)!

The following is not so much a comprehensive review of the last 50 years of blowfly research in Australia and New Zealand but instead tries to compare the state of knowledge of research into various potential control strategies at or about the time of the inception of the ASP through to the present, bearing in mind that the current state of funding for much of this research has stalled over the past 10 years, at least in Australia and New Zealand.

2. Insecticides and insecticide resistance

In 1964 the New South Wales Department of Agriculture, Australia, published a bulletin (Shanahan, 1964a) on the use of diazinon and other organophosphate chemicals (OPs) for the prevention and treatment of flystrike on sheep. Although organochlorine resistance had rendered dieldrin and aldrin ineffective against sheep blowfly, Shanahan's opinion, based on a laboratory selection study, was that *L. cuprina* was unlikely to develop resistance to diazinon (Shanahan, 1964a). Despite this optimism, he recommended that surveys be conducted so that new resistance could be recognised if it evolved. Adoption of this recommendation by the New South Wales Department of Agriculture, later with financial support from the Australian Wool Corporation, made resistance development in sheep blowfly one of the most thoroughly documented histories of its type. Also in 1964, Shanahan published a description of a new crook-shaped jetting wand that was said to provide significant advantages over the 'old T-shaped' jetting wand (Shanahan, 1964b). The front page featured a photograph of an operator jetting a sheep with diazinon while raking through the wet fleece with his bare hand – such was the technology of the time. Diazinon remained available for this purpose until 2007 when the Australian regulator banned its use via jetting and dipping on operator safety grounds. It is still registered as a flystrike dressing, so although application technology has improved considerably, other changes have come only slowly over the last 50 years.

The first resistance surveys of the mid-1960s detected resistance to OPs in adult flies within a year (Shanahan and Hart, 1966) and subsequently OP resistance was found to be widespread in New South Wales, Australia (Shanahan, 1966). By the early 1970s it was recognised that resistance in larvae was of practical relevance and an assay in which neonate larvae were exposed to strips of insecticide-treated chromatography paper soaked in sheep serum was developed (Roxburgh and Shanahan, 1973). Complementary biochemical studies (e.g. Hughes and Devonshire, 1982) identified the major resistance mechanism as an altered ali-esterase (E3null) and genetic studies (e.g. Arnold and Whitten, 1976; McKenzie and Whitten, 1982) described how resistance was inherited. These and other studies (e.g. Terras et al., 1983) demonstrated that secondary factors (e.g. microsomal oxidases) enhanced the base level resistance conferred by E3null and explained why resistance factors in larvae varied between two and 42-fold (Levot, 1995). OP resistance did not equate with total control failure but was expressed as a shortening of the flystrike protection period from 16 to approximately 4 weeks (Levot, 1995) and failure of OP dressings to kill third instar larvae (Levot et al., 1999). For nearly 15 years wool producers only had access to a suite of OPs. Under that sort of selection pressure resistance frequency approached fixation (>98%) in field populations and resistant flies overcame any fitness deficit that they might have had (McKenzie et al., 1982). With the susceptible phenotype almost extinct, OP-resistant flies effectively become a new 'wild-type' and it was against these blowflies that any new insecticides needed to be effective.

In 1979 a jetting formulation of the triazine, cyromazine, was registered by Ciba-Geigy, Australia (Hart et al., 1979). Triazines were known for herbicidal or chemosterilant activity but cyromazine was an insect growth regulator that exerted its insecticidal effect by inhibiting larval development (Hart et al., 1979). The mode of action of cyromazine has never been elucidated but it is non-toxic to mammals and unlike previous flystrike insecticides, did not target the nervous system. Compared with the OPs it is slow-working and so required a fundamental change to flystrike control. Nevertheless, in light of its superior performance, adoption was immediately very high with producers able to achieve at least 14 weeks flystrike protection with thorough application. Insecticides still had to be hand-jetted and product effectiveness often reflected the thoroughness of application. Hand-jetting was made easier when the Dutjet™ jetting wand (N.J. Phillips Pty. Ltd., Australia) became available in the mid-1980s, while numerous labour-saving automatic jetting races (AJRs) were also released. The effectiveness of these machines varied enormously and it was not until the landmark work of Roger Lund at Trangie, Australia (e.g. Lund et al., 1997) that the essential design features for an efficient and thorough AJR were identified.

Cyromazine had no toxic effect on adult flies and this, together with its slow action meant that the existing bioassays used to screen for OP resistance were unsuitable. Instead, larval growth assays in which larvae were fed homogenised liver containing cyromazine were developed. From these assays a conservative 'susceptible discriminating concentration' (1 mg of cyromazine kg-1) (Yen et al., 1996) was determined and used to screen for resistance.

The benzoylphenyl urea, diflubenzuron, was developed during the 1980s and became the second insect growth regulator larvicide registered against sheep blowfly. Diflubenzuron interfered with the synthesis of cuticular chitin, thereby weakening the exoskeleton, preventing successful moulting and inhibiting egg hatch