

Text of Dr Giovanna Messei and Dr Julie Lane's presentations to the Cornwall Red Squirrel Project and to the Cornwall & Devon Forestry Stake Holders Group

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The work of the National Wildlife Management Centre in York, part of APHA, an executive agency of Defra. The main focus of our work is to provide solutions to prevent or mitigate the environmental and economic impact of wildlife.

We would like to offer a brief overview of our work on fertility control to manage human-wildlife conflict, talk about progress on oral contraceptives and present a study that we would like to conduct and that we believe has potential to revolutionize this field.

Non-lethal methods of managing human-wildlife conflicts. You may be aware of the environmental and economic impacts of wildlife that I have listed in this slide. To resolve such conflicts we can use either lethal control (poisoning, shooting, trapping and culling) or non-lethal methods. Among the latter, the use of fertility control and particularly of an approach known as immunocontraception is increasingly advocated to manage these conflicts. I also wish to emphasize that we do not consider contraception as the sole method to control populations of grey squirrel but we see this as one of the options in the tool box of methods to manage wildlife impact.

Reproduction control. To prevent reproduction, we must target one of the several steps that lead to sperm production, ovulation and conception. One key hormone in this process, sometimes referred to as the “master hormone” is the GnRH (Gonadotropin Release Hormone) that initiates the cascade of reproductive processes. Immunocontraceptives are vaccines that induce antibodies to proteins or hormones essential for reproduction. In particular, single-dose injectable vaccines are now available, targeting the GnRH, that render most animals infertile for several years, thus making practical applications credible. GnRH-based vaccines work by inducing antibodies that block the action of GnRH and, in turn, the production of sex hormones essential for reproduction.

Labour intensive capturing of animals. To be injected, animals must be captured first, which is labour intensive and thus expensive. Hence, the availability of oral immunocontraceptives would reduce significantly the cost and thus substantially broaden the scope of potential application of fertility control.

Single dose needed Work carried out by our group (funded by Defra) with our collaborators in the US showed that after a single injection of the vaccine most animals stop reproducing for several years.

What does an ideal contraceptive look like: An ideal oral contraceptive would have **no side effects** on welfare, physiology and behaviour, **long-term** effectiveness with single/few doses, be effective on/deliverable only to **target species**, have no effects on **food chain** (predators, risks to humans), be **inexpensive** to produce and administer and also be **deliverable to a large proportion of the population**

Effective? We have also modeled the population consequences of applying different levels of fertility control to grey squirrels. Our results suggest that a population (Y axis) is likely to be eradicated in a few years if > 70% of the animals are rendered infertile.

Grey Squirrel Dispenser. We know squirrel-specific hoppers have been developed that can deliver bait to squirrel only, thus preventing non-target species from being affected by any drug.

Any negative side effects affecting carrion animals? So far, the advantages of GnRH vaccine-based contraception are that there are no persistent residues in treated animals, no known negative side-effects, GonaCon and another GnRH-based contraceptive (Improvac) are already registered in a few countries.

A disadvantage and then a solution found. The disadvantages are that an oral formulation is not yet available to induce immune response and we do not know how long the effect of an oral formulation will last. The National Wildlife Management Centre and our US collaborators at the US Government's National Wildlife Research Center developed a small immunogenic molecule based on GnRH-based vaccine. **80% of rats** fed this molecule had antibodies that suggested infertility. However, when this molecule was incorporated in a bait fewer rats responded and had lower antibodies to the vaccine. Hence a novel formulation is required for the oral vaccine to produce an increased immune response.

- **Oral vaccination.** We have recently focused on oral contraceptives as the key way of realizing large-scale applications. Encapsulation technology is commonly employed in pharmaceutical preparations to achieve controlled drug release. Amongst novel technologies we identified the shells of spores and pollen grains as the most promising method to achieve our goal.
- **Delivery mechanism.** Through this expanding technology, patented by the UK company Sporomex Limited, shells are emptied of their internal genetic material to obtain the sporopollenin exine capsules (SpECs) outer layer. SpECs have many advantageous properties for microencapsulation as detailed in this slide. This technology has been proven to have high bio adhesive properties that help maintain the capsules within an organism, and has been used successfully to increase the delivery of fats, vitamins, enzymes, oils, hormones and other drugs such as ibuprofen.

Next steps to study:

- More excitingly, a recent study showed that a model vaccine, delivered in SpECs and fed to mice, increased the serum and faecal antibodies in treated animals. The antibody response persisted for up to 7 months and the authors suggested that this was achieved as the spores embed themselves into the mouse gut wall.
- **A plausible mechanism:** Crucially, this study offered a plausible mechanism for oral vaccination and demonstrated the potential to stimulate and to maintain the immune response for at least a few months.
- **Captive trials:** The study we propose will identify the species of spores or pollen to encapsulate the novel contraceptive delivered to a model species (lab rat) in captive trials.
- **Field pilot trials:** These trials will be repeated with grey squirrels at our Animal Unit in York and followed by field pilot trials to confirm the efficacy of the contraceptive

and to monitor the proportion of the population that will ingest the bait containing a placebo vaccine.

- **Large scale field trials:** Finally, we plan large-scale field trials to monitor the effects of contraception at population level.

Scalable technology to apply to other human-wildlife conflicts thus benefitting from economies of scale. We believe this approach is scalable to a wide variety of species and diverse contexts. These include non-native invasive species, feral animals, overabundant wildlife, and contexts where culling is illegal, unfeasible or undesirable, where fertility control can complement culling to control populations or their economic and environmental impact.

A prospective timeline:

Where are we now - Done: ○ We have a proven vaccine.

- ○ We have modelled it
- ○ We have an oral contraceptive available
- ○ We have a delivery method available
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In progress: ○ We have to confirm the effectiveness of the contraception, have had some great results with other species.

- ○ We have to sort out the test bait
- ○ Manage public expectations: contraception as complementary to other methods

To do: ○ Captive field trials

- ○ Registration of drugs

Outcomes 70% infertility to eradicate population in a few years

Summary: In summary, we believe SEC-based oral immunocontraception has potential to revolutionise the mitigation of human-wildlife conflicts and that the approach is scalable to other species and contexts. So far, we have proven the effectiveness of injectable GnRH-based contraception, modelled the impact of fertility control on population dynamics. We also have a candidate oral contraceptive and a delivery method available. We also have a proposal to confirm effectiveness of oral contraception and to test bait uptake by target proportions of grey squirrels and we are aware we must manage public expectations so that the public understands that we see contraception as complementary to other control methods. We need to conduct captive and field trials and to tackle the registration of drugs. To achieve this, funding, public support and stakeholder engagement will be crucial.

Dr. Julie Lane

National Wildlife Management Centre

Traps...tried and tested, but are they the answer?

Control methods for grey squirrels.

Warfarin, drey poking and shooting, cage trapping and dispatch and spring trapping. All traps need to be on the Spring Trap Approval Order.

How do traps get approved?

There is an initial trap testing application from industry to DEFRA. The traps are then tested by APHA at DEFRA's request. The APHA then makes a recommendation to DEFRA to add successful traps to the Spring Trap Approval Order. A few months later approval is given. The approximate cost is £5 to £10k

The process of testing traps. The manufacturer/supplier has to supply 10 traps. The traps have to pass the following condition: in 80% of 12 trials the animal must be rendered unconscious or dead within 5 minutes.

Traps on the STAO (the Spring Trap Approval Order) – Those traps concerned with grey squirrel control are: Magnums, Fenns (soon to be removed as not humane); Kania; DOCS; WCS; Procoll.

Pros and cons of using traps.

The pros: Simple to use, no legal training required, user safety, relatively humane, cheap, no secondary poisoning.

The cons: User safety (disease, live animals, injuries)

Unpleasant – body damage / blood; not public friendly; non-target risk; trap needs to be checked daily and re-set (labour intensive)

Goodnature A24 trap

Special attention was given to this new NZ manufactured trap.

Pros: Lightweight, easy to set up, baited and re-sets itself. The gas canister is expected to last 24 shots. Cons: The trap is quite visible but it is being manufactured in either black or green; carcasses are visible to public as the dead squirrel drops out of the trap onto the ground, non-target risk; has not passed the STAO tests.

If it passes does this mean, it's a good trap?

No – it means it is humane!

There are questions that need to be answered....

- What are the non-target risks?
- Does the bait/lure work in the field setting – and for how long?
- How many times can it fire before it resets?
- Does temperature affect it?
- Efficacy (how many trap nights per animal)

Are traps the answer?

Could be part of the answer....?

An integrated approach. There is a view that we need to develop an Integrated Pest Management approach

- Sustained control over longer periods
- Less staff intensive
- More publically acceptable