

What form does wild animal contraception take?

To begin with, no one is proposing that wild animals could be 'put on the pill'; that is, there is no prospect of getting wild animals to eat the kind of steroidal hormones used in human oral contraceptives. These are based on the ovarian hormones progesterone and oestrogen, or their derivatives. They need to be given every day in precise doses by mouth; they would affect the fertility of anything that ate them; they persist in the carcass and offal and would affect scavengers; they contaminate the environment when they are excreted and they have negative effects on males. In the case of deer, it would be impossible to dose females alone and these hormones interfere with puberty, antler growth and rutting behaviour in male deer. Progestagins are used by mouth to control fertility in domesticated mares and have been used in some zoo animals that receive individual daily feeds; some captive animals can be contracepted by long-acting injections of these hormones, but individual animals need to be caught, restrained and injected with a depot or an implant.

It is impossible to conceive how they could be used to contracept free-living deer in the open landscape, or even, for that matter, in a deer park. No properly informed conservationist or wildlife biologist is proposing that they can be used.

The form of contraception most widely promoted for wild animals is immuno-contraception (IC) by vaccination. The principle of vaccination is easy to understand, especially in protection against infection. Take a bit of the infectious agent, like an inactivated virus or dead bacterium, and inject it into the patient. This is the antigen. The recipient's immune system recognises the foreign material, the antigen, and makes antibodies to it, which persist in the animal or person. When that animal or person then encounters the living or active bacterium or virus, there are already antibodies in the system that fight the infectious agent and prevent disease.

IC uses the same principles. Take some substance from the complicated process of ovarian function, ovulation or conception, alter it slightly and inject it into the animal. The immune system will produce antibodies to this and these



will attack the genuine substance in the animal and block fertility.

There are two current candidates for IC antigens. The first is the zona pellucida (ZP), a matrix of protein jelly that surrounds the egg after ovulation. By taking pig zona pellucida (PZP) and manipulating it a bit, an antigen is manufactured that stimulates the production of antibodies to the genuine, healthy ZP of the vaccinated female. When she ovulates, these antibodies attack the ZP of her own eggs and prevent any sperm from successfully binding to the egg. She cycles, is mated, ovulates, but does not conceive.

The second candidate as an IC antigen is gonadotrophin releasing hormone (GnRH), which is a small peptide molecule produced by the hypothalamus of the brain. GnRH is one of the peptides that controls the pituitary gland, which in turns secretes hormones like luteinising and follicle stimulating hormones that control the ovaries. When an animal is injected with a synthetic GnRH analogue, antibodies are produced to the animal's own GnRH and fertility is blocked. In theory, this should suppress all cycling and the vaccinated female should not come into

There are commercial IC products of both PZP and GnRH that have been produced and widely used in one form or another since the mid 1990s. Both initially needed two injections with a short interval then regular

boosters, but long-acting forms of both types of IC vaccine have been developed.

Does immuno-contraception work?

Yes, it does. It works very well indeed. There are dozens of excellent, peer reviewed reports proving that IC can stop female animals from conceiving. With both PZP and GnRH vaccines, a single injection can render some female mammals infertile for several years. As examples, IC vaccines have been used to control fertility in elephants for more than 20 years across South Africa. In 2018 more than 800 elephant cows in over 25 game reserves and national parks were on a contraceptive programme using IC vaccines. Hundreds of feral horses in several isolated populations in the USA have been subject to IC vaccination for more than 20 years and populations have been reduced and stabilised over that period. These vaccines have also been used to control fertility in fallow deer, white-tailed deer, American elk, black-tailed and mule deer, muntjac, bison, various antelopes, tahr, wild boar, feral horses, kangaroos, koalas, lions, other big cats and many other mammals.

Results have been impressive, with conception rates of deer reduced from over 80% to 11 or 12% with a single injection. There is no doubt that IC vaccine injection is an effective method of reducing fertility in female deer. It works.



So why is immuno-contraception vaccination not used more widely in deer?

There is no doubt at all the IC vaccination works really well in individual female deer of many species. There are some glitches and species idiosyncrasies, for instance Reeves's muntjac seem to need more frequent dosing than other deer and in one study Sambar failed to respond at all to the vaccine, but the bulk of the literature confirms that IC is a good way of controlling fertility in individual female deer. But that does not mean that it is a good way of controlling fertility in free-living deer populations.

When the successful use of IC over the past 30 years is reviewed, it is clear that success of the various projects has depended upon several crucial factors. First, and most obviously, the contraceptive vaccine must be given by injection. This means either catching the deer to inject it, or getting so close that the deer can be darted with the vaccine. In most of the studies, deer have been caught up, rounded up or trapped for injection. In the handful of cases where darting has been used in deer, it has been possible to dart them at ranges of no greater than about 30 metres. Some of the darting has been with deer in enclosures, but even

when free-living 'wild' deer have been darted in urban control programmes, they have been white-tailed deer tempted in to feed stations or habituated to human activities. Urban white-tailed deer are notoriously relaxed and tolerant of human approach. Feral horses can be approached much more closely for darting than can wild deer. Most wild deer in the open rural landscape do not permit human approach to within 150 metres, let alone 30, and because of this, darting wild deer with IC in woodlands, forests, farmland or deer parks has been discounted by everyone who has considered it.

The second crucial factor for successful IC is vaccination rate. In order to slow down or halt population expansion in long-lived ungulates like deer, at least 50% of the females must be effectively contracepted. This means that more than half of the wild hinds or does in a landscape population must either be caught and injected or darted in order for there to be any effect on population growth, and the evidence clearly shows that contraception rates with darts are significantly lower than with injections by hand.

This raises the third crucial problem: identification. If you are catching deer and

injecting them, you can tag them or mark them to show that they have been dosed. If these animals are caught again, they can be released without double dosing. Apart from the fact that no licence would be granted to trap or catch hundreds of wild deer in the UK, if darting is proposed, even in deer park situations females cannot be identified to prevent repeat dosing. Individual feral mares in USA National Parks can easily be recognised, but fallow does in lowland English woods? Red hinds on the open hill in Scotland? Muntjac does in the Home Counties?

Fourthly, and just as crucially, the successful IC programmes for deer and horses in the USA, elephants and lions in Africa, kangaroos and koalas in Australia have all been in populations isolated and separated from other populations. The animals have been on islands or fenced reserves or in pockets of population where there was no immigration of new animals into the contracepted populations. Once 50% or more of the females were treated, they continued to be the core female cohort, with no supplementation of numbers from outside the study group. This is clearly not achievable on an open landscape scale,

where deer populations over many miles are contiguous or even continuous.

The IC fertility control of feral horses in the USA is often cited as a model for wild deer contraception. A few studies have reported on IC progress over 20 or more years, with herds like the horses on Assateaugue Island or Shackleton Banks, both isolated island populations. In these studies, all the mares could be included in the project because they were on an island, individuals could be identified and all could either be approached for darting or the herds were annually rounded up. IC has worked here, eventually, but when the Australian authorities have seriously considered whether IC can offer anything to control their feral horse populations they realised that in Australia most populations of wild horses are large, dispersed over varied and difficult-to-access terrain, are timid to approach and open to immigration and introductions. They therefore concluded that use of fertility control as the sole technique for halting population growth is simply not feasible in Australia, the country with the largest feral horse population in the world.

Precisely the same conclusions are made about wild deer; the vaccines work in individual deer, but there is an obstacle to their use on a wild population scale that is currently insurmountable: delivering them to the deer – getting enough vaccine into enough deer of the correct sex. It is currently impossible, and no progress has been made with delivery systems for wild deer in the past 10 years.

Are there any side effects of immunocontraception vaccines?

An unexpected side effect of the successful use of IC on feral horses has been that contracepted females, without the burden of carrying and suckling a foal every year, have lived longer and more healthily than their fertile, breeding counterparts. A whole new generation of healthy, active, geriatric mares was created by the IC programmes. This in turn has led to the effects of IC taking longer to appear than had been predicted. In a longlived species like horses and large deer with no or few predators, the intensive use of IC will slowly halt the growth of the population, but it will not start to fall until animals die off. This assumes that observers are content to let senile animals decline and die slowly of old age (if culling of geriatrics on humane grounds is introduced, the opposition to culling is harder to sustain).

In practice this has meant that with annual rounds-ups and annual vaccination of mares on one island, it took 13 years of IC to see the horse population decline by about 20%. In an IC vaccination experiment of an island white-tailed deer population, the numbers of deer increased by 11% annually for 5 years before

declining by about 16% per annum, so that it actually took 12 years to reduce the numbers. Individual does were marked to prevent double dosing. Population effects with IC are therefore only modest and take many years to achieve, which has led most authorities to agree that with current vaccines, IC has nothing to offer to the management of over-abundant wild deer.

There are also some worrying side effects. In contrast to predicted effects, GnRH vaccines do not prevent female deer showing evidence of oestrus. With both ZPZ and GnRH IC products, the rut is prolonged and females are repeatedly covered by males. In feral horses, another polygynous herding species, male-on male-aggression is increased by the use of IC in the females and, where conceptions do occur, the season for delivering foals is prolonged. Such effects may raise welfare issues in some quarters, especially if females are harried and mated repeatedly or if neonates are delivered at times when the dam has insufficient forage to support her lactation.

PZP vaccines have no effects on male deer, but GNRH vaccines do. They interfere with puberty, antler growth, male behaviour and fertility. They cannot be given to all deer in a population, but must only be given to the females.

There are unanswered questions about whether long term contraception is inherently likely to reduce welfare.

In species where breeding success is linked to social status, are contracepted females condemned to a perpetually low rank in the social group?

If positive welfare includes the freedom to express all normal behaviour, does denying an adult female the experience of breeding and nurturing young compromise her welfare?

Is the presence of some neonates, juveniles and subadults necessary for normal, stable social groups?

Will IC inadvertently select for those individuals whose immune system is least vigorous? In other words, if the animals with the better and more healthy immunological physiology respond best to IC vaccination and those with the poorer, less vigorous immune systems are not contracepted, what will be the long-term effect of allowing only the less vigorous to breed?

Such questions are actively under consideration but they are, at present, only questions, not established facts. But they do need answering.

Is there any hope of further progress with immunocontraception vaccines? Work has been underway for some years to try to develop oral IC vaccines. The problem is that both PZP and GnRH analogues are broken down during digestion before

they can stimulate circulating antibodies. One possible line of research is looking at inserting the IC antigens into pollen or plant spore capsules. Pollen and spores are natural and renewable. They are also commercially available and it is possible to remove the plant genetic material to produce what are called 'sporopollenin exine capsules' (SpECs), which withstand stomach conditions. They have already been used to deliver fragile medicines orally that would otherwise be broken down in the stomach. If IC vaccines could be wrapped up in SpECs, real progress may be possible in some species – grey squirrels are the current target species for this research in Europe.

In conclusion, the truth about IC is this: it works very well when it is injected into female deer, but there are currently no delivery systems that can be used to implement IC in free-living, wild deer.

In another 10 years, who knows?

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