The effects of military service on spermatogenesis

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Synopsis

- Australian Defence Force personnel are, in general, young, healthy individuals, and it is normal for them to have concerns about the effects of military service on their fertility.
- There is general agreement that fertility in the male population has decreased over the past 50 years, with average sperm concentrations in Western countries falling dramatically. Any data from defence force populations must thus be interpreted with caution.
- Military duties expose personnel to a number of activities that may pose theoretical risks to spermatogenesis. Such activities include aviation, use of and proximity to microwave radars, and diving.
- Data relating military service to reproductive effects are limited, and should be treated with great caution. However, the limited current evidence does not suggest that service personnel, in general, should be worried.

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THE AUSTRALIAN DEFENCE FORCE, like military forces around the world, represents a large population of virile men. Although women are joining the ADF in increasing numbers, most serving members are males aged between 18 and 40 years. The physical standards required for armed service select for individuals who ought to be at the peak of their reproductive prowess. It should therefore be no surprise that concerns about reproductive health are often expressed by service members.

Service in any defence force can potentially expose personnel to a number of serious reproductive risks. For example, during heavy fighting in the Middle East in 1941, 4.1% of soldiers were rendered unfit for battle by sexually transmitted disease, compared with battle casualties of only 3.5%. Fortunately, the modern soldier or sailor is usually well informed about such reproductive risks.

Another risk is that modern theatres of conflict will expose Australian soldiers to chemical, biological or nuclear weapons. The extent of this risk to reproductive health is impossible to quantify, but, in my experience, the issues that concern serving personnel are much closer to their daily experience.

A commonly held belief is that involvement in certain military activities leads to a sex bias in offspring: for example, that the spouses of divers more commonly bear female children. Clear evidence of sex bias in the offspring of serving members of a defence force would be of concern. Offspring sex bias may be an indicator of exposure to reproductive hazard.[1-3] For example, it has recently been recognised that the assisted reproductive technique of *intracytoplasmic sperm injection* (ICSI) may be associated with a preponderance of female offspring.[4] An argument can be made that detection of a sex bias in offspring avoids the so-called “volunteer” bias.[5] Volunteers may tend to be drawn from a group of men who have higher scores on psychological tests of sensation seeking, which is further correlated with testosterone levels.[6,7]

Medical Officers in the ADF are often confronted with comments about the effect of various military activities on the formation and function of sperm. It is difficult to address these comments accurately and to provide useful information to personnel. This article briefly reviews the mechanisms of normal spermatogenesis in humans, and the available evidence examining reproductive outcomes in men exposed to military service.

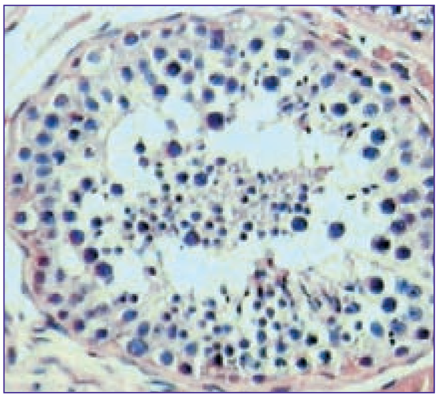
Normal spermatogenesis

In the normal male, each testis is composed of more than 750 seminiferous tubules. The tubules are U-shaped, each end converging at the *rete testis* and emptying into the *epididymus*. Individual tubules, dissected out and uncoiled, may reach up to 50 cm in length. If the testicular covering, the *tunica*, is opened and the contents are examined (to obtain sperm for in-vitro fertilisation, for example), the tubules resemble a pile of cooked spaghetti.

There are two distinct populations of cells within the seminiferous tubules: Sertoli cells, and spermatogonia (and their offspring, spermatozoa). Spermatogonia are descendents of the primitive germ cells that migrated to the gonadal ridge during the early part of fetal life. They divide to produce spermatocytes, which in turn undergo the reduction division — meiosis — giving rise to spermatids. The spermatids, each with 23 chromosomes, give rise to the spermatozoa that will eventually be ejaculated. The Sertoli cells act in a supporting role, and tight junctions between these cells form part of the “blood–testis” barrier that makes the interior of the seminiferous tubule an immunologically privileged site.

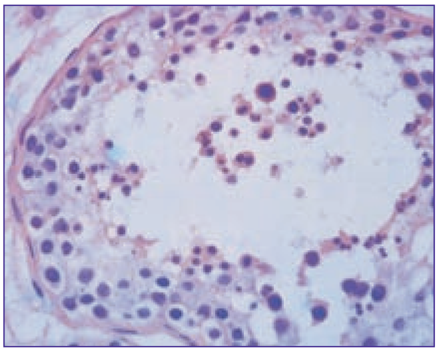
Hormonal support of spermatogenesis parallels that of ovulation in the female. Luteinising hormone (LH) from the anterior pituitary acts on receptors in the Leydig cells of the testis to stimulate synthesis and release of testosterone. This testosterone acts locally in the testis by diffusing into the seminiferous tubules, while serum testosterone provides negative feedback to the anterior pituitary. Increasing serum levels of testosterone reduce secretion of LH. Follicle stimulating hormone (FSH) acts on receptors in the Sertoli cells to directly stimulate spermatogenesis in the presence of testosterone. Spermatogenesis is associated with secretion of inhibin B by the Sertoli cell. Inhibin B completes a negative feedback loop and reduces further secretion of FSH by the anterior pituitary. There are thus two separate feedback loops: LH–testosterone and FSH–inhibin B.

Whereas the full complement of oocytes is present in the ovary from 20 weeks of fetal development, sperm are continually manufactured from a stable population of germ cells. Maintenance of DNA integrity in the sperm is vital for the successful transmission of genetic information to potential offspring. The nuclear chromatin in mammalian sperm is a nearly inert crystalline conformation, and this protects sperm DNA from environmental insults before fertilisation.[8] DNA is thus most vulnerable during meiotic reduction division.



***1a:** Cross-section of human seminiferous tubules, showing normal spermatogenesis (haematoxylin and eosin stain; original magnification* x *200).*

***1b:** Cross-section of human seminiferous tubules showing spermatogenic arrest (haematoxylin and eosin stain; original magnification* x *200).*



The vulnerability of human sperm

There is evidence from around the world that human sperm quality has been falling since before the Second World War.[9] Meta-analysis of pooled data has revealed a remarkable decline in population mean sperm concentration from 113 million/mL in 1938 to 66 million/mL in 1990. Although considerable argument ensued,[10-12] there is now virtually no doubt that males in Western society are becoming less fertile.[13] Furthermore, there have been increases in the incidence of penile abnormalities such as hypospadias,[14] testicular maldescent[15] and testicular cancer.[16] With such alarming negative changes in the fertility status of Western males, historical data from military populations need to be interpreted with great caution.

It has recently been recognised that small deletions of genetic material from the Y-chromosome, particularly from the DAZ and RBM regions (so-called Y-microdeletions), are associated with severe oligospermia and complete azoospermia.[17] When reductions in sperm concentration are encountered, there are a number of potential aetiologies: obstruction of the excurrent ducts and the outflow tract; arrest in the process of maturation of the spermatozoa (Figure 1); or an overall reduction in spermatogenesis (Figure 2). Spermatogenesis is particularly vulnerable to thermal stress. Indeed, the reason that the testes are suspended outside of the abdominal cavity is to cool them, and a counter-current mechanism is in operation where heat from the blood in the spermatic artery is cooled by contact with the venous network (the pampiniform plexus) surrounding it. Even a mild fever can totally arrest spermatogenesis in an otherwise normal man.

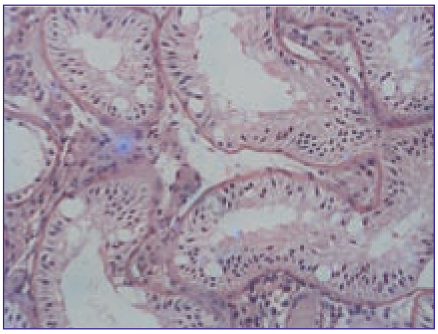
Aviation and fertility

There is no evidence that the incidence of infertility is greater in an Air Force population than the general population.[18] Two specific subsets of Air Force personnel have been evaluated — aircraft maintenance workers and pilots. In one study, a cohort of 50 aircraft maintenance workers were compared with a control group of eight unexposed men.[19] Breath sampling was undertaken for jet fuel components such as benzene, toluene, xylenes and naphthas, and full morphometric analysis of semen was performed. The highest mean breath levels of the components were found in sheet metal workers, but were still within acceptable standards. The semen parameters of the cohort remained within the normal range throughout the 30 weeks of the study.

Large studies of fertility in pilots are limited. Responses to questionnaires distributed to pilots of the German Federal Armed Forces suggest that there is no gender bias in the offspring of transport pilots. During the first 1000 flying hours of their careers, there was an over-representation of male offspring to jet pilots, which reversed after 1000 logged flying hours.[20] However, there is a severe limitation to studies of this nature imposed by the numbers of offspring required to provide suitable statistical power. Calculations suggest that about 2000 offspring of these men are needed to obtain valid answers. Jequier has reported oligospermia in a fast jet pilot that reverted to normal once flying duties were ceased.[21] It was hypothesised that G-forces induced a varicocoele-like situation, and possibly even testicular ischaemia, although this could not be proven. Attempts at a wider study were abandoned due to the small numbers, both of pilots and their offspring, available for investigation (Anne Jequier, personal communication).

Diving and fertility

Few areas of military activity seem to generate as much myth and legend as diving. It is a common belief that male divers' offspring tend to be female, and the mechanism for this is often quoted as a hyperbaric effect on testicular perfusion. In an unpublished study, Edmonds conducted a retrospective review of Royal Australian Navy divers' offspring. Of 240 offspring, 122 were conceived before diving activities, the remaining 118 after the divers received their diving qualifications. Edmonds further divided these groups into air divers and oxygen divers, and generated 2×2 contingency tables that were analysed by χ^2 test. There was no significant difference between the groups and no support for the hypothesis that divers have a propensity to female offspring (Edmonds, quoted by Commander Robyn Walker, personal communication).



2: Cross-section of human seminiferous tubule, showing total absence of spermatogenesis in Sertoli-only syndrome (haematoxylin and eosin stain; original magnification x 200).

There is now clear evidence that diving in extreme conditions has an adverse effect on spermatogenesis.[22] The demonstration dive "Aurora" imposed severe hyperbaric conditions on divers, involving a 33-day diving program in which participants were exposed to a maximum pressure of 4.6 megaPascals (MPa) for seven days. Studies of the divers' semen parameters were made before exposure, and at various points out to 263 days post-Aurora. Three months after the dives, there were profound reductions in sperm concentration, motility, and even normal morphology of the sperm.[22]

Military radars and fertility

Microwave radar equipment is operated by all branches of the ADF, and has been in use by the RAAF since the Second World War. Radiofrequency radiation extends from 300 kHz to 300 GHz; the spectrum from 3 GHz to 300 GHz is the microwave range.[23] Concerns about the potential effects of exposure of military personnel to microwave radiation are not new. There have been suggestions that such exposure of RAAF personnel in World War II was associated with a preponderance of twin offspring, both in women exposed to microwaves and from exposed men with unexposed females.[24]

Important investigations of the effect of microwave exposure were conducted in animal studies in the 1980s. Mice were exposed to 2.45 GHz microwaves for 30 min/day for six days a week over two consecutive weeks, at power densities of 1.0, 100 or 400 Wm^{-2}, and compared with a group of sham-exposed mice.[25] When the mice were killed, there was no significant difference in the frequency of spermatozoa chromosome aberrations between the groups. Studies of rats exposed to eight hours of continuous 1.3 GHz microwave radiation at 9 mW/g specific absorbed dose rate were similarly reassuring, with no evidence of disruption of testicular function demonstrated.[26] Even when mice were exposed to 100 Wm^{-2} at 2.45 GHz for a total of 120 hours over a two-month period, no significant increases in mutagenesis of male germ cells were found.[27] Similarly reassuring results have been obtained from numerous similar animal studies.[28-30]

Evidence in humans has obviously been more difficult to obtain, and studies are often severely flawed. Flaherty surveyed former RAAF personnel who had operated microwave radar during the Second World War.[24] He noted a preponderance of twin offspring in these individuals (1:40, compared with a general population rate of 1:85), but the methodology was not rigorous and reanalysis cast serious doubt on these findings.[31] Retrospective studies of the health of US naval personnel exposed to microwave radar emissions during the Korean War detected no differences between the health of 20 000 personnel with "maximum potential for microwave exposure" and 208 000 personnel with "minimum potential for exposure".[32]

Early reports from a collaborative study between the US Army Biomedical Research and Development Laboratory (USABRDL) and the National Institute for Occupational Safety and Health (NIOSH) were alarming. A group of radar operators ($n = 20$) were compared with howitzer crews ($n = 30$) and an unexposed control group ($n = 31$).[33] Although there were no differences in the endocrine variable between the groups, the radar operators in the study had a lower sperm concentration ($P = 0.009$) and total number of ejaculated sperm ($P = 0.027$) than the control group. This finding caused considerable concern, and was the stimulus to a larger study by the same group. While that expanded study was underway, a Danish group published data from a group of 19 military personnel who used mobile ground-to-air missile units that employed microwave radar systems.[34] There was an overall reduction in sperm concentration in the study group ($n = 19$) when compared with an unexposed control group ($n = 489$): 40 M/mL (95% confidence interval, 26–63 M/mL) compared with 62 M/mL (95% confidence interval, 29–112 M/mL). This difference was not significant after adjustment for the period of abstinence ($P = 0.07$). As well, the exposure dose was highly variable among the exposed personnel, with a maximum mean exposure of only 0.01 mW/cm^2.

The expanded USABRDL/NIOSH study results were reassuring as well. A larger radar-exposed group ($n = 33$) was compared with a control group of 103 soldiers, and measurements of testosterone, FSH and LH were made in addition to semen parameters. No statistical differences ($P < 0.05$) in any parameter were noted between the groups.[35]

On the limited data available from animal models and human surveys, it seems reasonable to suggest that occupational exposure of military personnel to microwaves is unlikely to be associated with either an impairment of semen quality or propensity to twin progeny. The main criticism of published studies is that sex bias in offspring has not been studied in this group,[36] although this has been hotly disputed.[37]

Military service in general

Fertility in Western societies is decreasing: many women are delaying childbearing until later in life, when natural fecundity is reduced. Similarly, mean sperm concentrations are reduced.

Bearing this important trend in mind, contemporary studies of military populations, although limited in number, do not suggest that infertility is more common in this group.[18] When a subpopulation of the Centers for Disease Control Vietnam Experience Study cohort ($n = 571$) was analysed, Vietnam veterans were found to have lower mean sperm concentrations and a lower mean proportion of morphologically normal sperm. In spite of these differences, Vietnam and non-Vietnam veterans had fathered similar numbers of children.[38] The mechanism for such a difference is not clear. A study of exposure to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (dioxin) — the contaminant of Agent Orange — was conducted in veterans of the unit responsible for aerial spraying of the herbicide. Measurements were made of testosterone, FSH, LH, as well as testicular abnormalities and semen parameters, and the study group was compared with a control group of veterans who had served in South East Asia with no involvement with herbicides. There was no significant relationship between dioxin levels and any outcome variables.[39]

Conclusions

One of the basic human drives is reproduction, and this is an understandable concern of young, healthy service personnel.

There are large gaps in our knowledge of the effects of military service on spermatogenesis. A paucity of data is not the only problem encountered when trying to accurately address the risks military service may pose to spermatogenesis. When large groups of fit individuals are studied, certain biases can occur. For example, when fit and healthy populations are specifically recruited (which is exactly what happens with military recruiting processes), the "healthy worker effect" can occur.[40,41] Among healthy workers, all kinds of adverse health outcomes are less common than in the general population, and this healthiness can mask the negative effect of exposure to health risks.

Unfortunately, there have been so few systematic studies with appropriate design that the effects of military service on spermatogenesis, or on fertility in general, are still not clear. As with many environmental influences, extreme levels of hyperbaric pressure, G-force and exposure to radiation may have detectable biological effects on the semen. However, the basic questions asked by servicemen cannot satisfactorily be answered at the present time.

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