Non-ionizing fields in sight

-a possible influence on male fertility?

Ole Jacob Møllerløkken

Dissertation for the degree philosophiae doctor (PhD)

at the University of Bergen

2013

Dissertation date: 18.03.2013

NON-IONIZING FIELDS IN SIGHT

- a possible influence on male fertility?

Photo: C. Bjørkeli, Royal Norwegian Navy

Contents

Abbreviations

ANSI	American National Standards Institute
B	Magnetic
BMI	Body mass index
CI	Confidence interval
E	Electric
ELF	Extremely low frequency
EMF	Electromagnetic field
E2	Estradiol
ESIS	European Studies of Infertility and Subfecundity
FPB	Fast Patrol Boat
FSH	Follicle stimulating hormone
gnRH	Gonadotropin releasing hormone
GPS	Global position services
HSE Navy	Health, safety and environment in the Navy
IARC	International Agency for Research on Cancer
ICNIRP	International Commission on Non-Ionizing Radiation Protection
ILO	International Labour Office
KNM	"Kongelig Norsk Marine" (the Royal Norwegian Navy)
LF	Low frequency
LH	Luteinizing hormone
MBRN	Medical Birth Registry of Norway
MRI	Magnetic resonance imaging
MTB	Missile-torpedo boat
NIOH	National Institute of Occupational Health
OR	Odds ratio
PR	Prevalence ratio

PRL	Prolactin
RADHAZ	Radiation Hazard, a project in the Royal Norwegian Navy working on protection from electromagnetic fields.
RF	Radio frequency
RNoN	Royal Norwegian Navy
SAR	Specific absorption rate
SFK	“Sjøforsvarets forsyningskommando” (the Norwegian Navy Material Command)
SHBG	Sex-hormone binding globulin
STANAG	Standardization agreement, an abbreviation used by the North Atlantic Treaty Organization
TSH	Thyreotropin
UV	Ultraviolet
W	Watt
WHO	World Health Organization
WLAN	Wireless local area networks
γ	Gamma

Scientific environment

The work in this thesis has been carried out in the Research group for Occupational and Environmental Medicine, at the Department of Public Health and Primary Health Care, Faculty of Medicine and Dentistry at the University of Bergen.

Several scientific environments have collaborated in the work of this thesis:

Lund University, Sweden: Faculty of Medicine, Department of Laboratory Medicine, Occupational- and Environmental Medicine; Lars Rylander.

Umeå University, Sweden: Radiation Sciences; Kjell Hansson Mild.

University of Bergen, Norway: Faculty of Medicine and Dentistry, Department of Clinical Medicine; Line Bjørge. Department of Surgical Sciences, Section for Radiology; Lars Ersland. Faculty of Psychology; Emanuel Neto and Kenneth Hugdahl.

Sør-Trøndelag University College (HiST), Trondheim, Norway: Faculty of Technology; Gunnhild Oftedal.

Norwegian Radiation Protection Authority: Merete Hannevik.

Uni Health, Bergen, Norway: Occupational and Environmental Medicine; Nils Magerøy and Valborg Baste.

Haukeland University Hospital, Bergen, Norway: Department of Occupational Medicine; Nils Magerøy and Bente Moen. Department of Clinical Engineering; Lars Ersland. Bergen fMRI group; Kenneth Hugdahl, Emanuel Neto and Lars Ersland. Hormone Laboratory; Anne Sellevold. Laboratory for clinical biochemistry; Bjørg Almås.

The Cancer Registry of Norway; Leif Åge Strand.

Oslo University Hospital, Aker, Oslo, Norway: Hormone Laboratory; Peter A. Torjesen and Nina Norstrand.

Acknowledgement

Throughout my work as a PhD candidate, and prior to that as a medical student, I have met numerous inspiring people all of whom have made it possible and a pleasure for me to continue doing research and to achieve as much as I have so far. Thanks to all of you for inspiring ideas and unforgettable moments.

First and foremost I must thank my supervisor, Bente (E. Moen). Whenever I have told someone that Bente E. Moen is my supervisor, the response has always been “Then you are in good hands”. And indeed I have been in good hands, and hope to continue our professional relationship in the future. You are truly inspiring in all that you do.

To Nils (Magerøy), my second supervisor. Thank you for being who you are and for inspiring me as I did my research. Your guidance has been of great value and much appreciated.

My project has been given invaluable help from a group of scientists especially interested in this topic. I thank you all sincerely. Valborg (Baste) for all the good advice and help during the research. Kjell (Hansson Mild) for being such a resource in the technical aspects of non-ionizing electromagnetic fields and for helping us understand this technology. Gunhild (Oftedal) and Line (Bjørge) for help in planning study designs and writing articles. Lars (Rylander) for helping with the planning of the study.

A number of people have also helped in the practical work involved with this thesis, both the field work and the article writing. Special thanks go to Trond (Riise) for valuable help in developing paper number I and for being a kindred spirit who continues to inspire me to keep on doing research. Kristin (Bondevik) and Emanuel (Neto) for fantastic help in the field work of paper IV. Lars (Ersland), Peter (A. Torjesen), Kenneth (Hugdahl), Anne (Sellevold), Nina (Norstrand) and Gørill (Skaale Johannesen) for planning, carrying out and finalizing the study reported in paper IV.

The Royal Norwegian Navy deserves special thanks because the majority of the studies in this thesis are carried out in their working environment. I would especially like to thank Jan (Sommerfelt-Pettersen), Captain (Navy), Chief Medical Inspector. Thank you for always being positive and for seeing the opportunities in doing research, for all the good stories especially pertaining to historic maritime medicine. Vilhelm (Koefoed), Surgeon Commander Senior Grade. Thank you for your continuously positive attitude and inspiration as both a researcher and a medical doctor, and for finding important studies revealing the correlation between work efficiency and screen size on computers. Steinar (Nestaas) and Jan Helge (Halleraker) for help in the expert group on electromagnetic fields in paper II. Ørjan (Pettersen), the crews of the missile torpedo boat "KNM Terne" and the submarine "KNM Utvær" for valuable help in the field work of paper III.

To the Research Group for Occupational and Environmental Medicine: Thank you for daily inspiration and for creating an environment in which it is easy to thrive. I have been attached to this group for several years, so there are many people to thank, all equally important and all having in their own ways made it interesting and enjoyable to go to work. Kjersti (Alsaker), Jan Vilhelm (Bakke), Lena (Bartz), Magne (Bråtveit), Kristin (Buhaug), Javier (Campos), Tim (Carter), Elisabeth (Flo), Kristian (Gould), Jens-Tore (Granslo), Hilde (Gundersen), Kaja (Irgens Hansen), Vegard (Mjelde Hansen), Camilla (Hauge), Inger (Haukenes), Bjørg-Eli (Hollund), Dordi (Høvik), Akwalina (Kayumba), Jorunn (Kirkeleit), Gunnhild (Koldal), Berit (Larsen), Simon (Mamuya), Arne Jacob (Misund), Tone (Morken), Julius (Mwaiselage), Gaby (Ortis), Maura (Pugliatti), Bjarte (Knappen Roed), Gloria (Sakwari), Kjersti (Steinsvåg), Leif Åge (Strand), Erlend (Sunde), Gro (Tjalvin), Alexander (Tungu), Kari (Stave Vågenes), Siri (Waage) and Zeyede (Zeleke). THANK YOU – each and every one of you!!!

To the Institute for Public Health and Primary Health Care: A warm thank-you to the institute leader, Rolv Terje (Lie), and the chief of administration, Alette (Gilhus).

To the Faculty of Medicine and Dentistry, especially the "forskarlina", – the research education programme for medical students that gave me the opportunity to do research during my medical studies. Thanks to the former leader, Steinar (Hunskaar), former student contact, Eldbjørg (Sanden Søvik) and my former "colleagues" in this programme: Knut (Forberg), Daniel (Hammenfors), Lars (Prestegarden) and Martin (Ystad).

Last, but not least, I want to thank my family and friends. I have a large family including parents, four siblings with partners, in-law parents, three in-law siblings with partners and a total of 15, soon to be 16, nephews and nieces. I love you all; thank you for being a tremendous support and inspiration to me, for all the good laughs and unforgettable occasions. To my parents, Gunhild and Ole Andreas: You have always been an inspiration to me and still are. You are truly amazing.

To my three boys, Ole Christopher, Halvor Andreas and Johannes. Thank you for filling each day with love.

To my wife Bjørg. Words fail to say what you mean to me.

> "You are my North, my South, my East and West,
> My working week and my Sunday rest,
> My noon, my midnight, my talk and my song"
>
> ….freely after W.H. Auden
>
> I love you – of that I am certain.

Abstract

Background. Our society is increasingly using equipment that produces and emits non-ionizing electromagnetic fields (EMF), and little is known regarding exposure to such fields and the possible impact on male reproductive health. The **main objective** of this thesis is to gain more knowledge regarding the possible influence of non-ionizing EMFs on male reproduction.

Material and methods. The Royal Norwegian Navy (RNoN) had specific concerns regarding non-ionizing EMFs and reproductive health, as there were worries related to work on-board a specific vessel, namely the "Kongelig Norsk Marine (KNM) Kvikk". Papers I and II were the result of cross-sectional studies conducted among all employees in the RNoN in 2002 by means of questionnaires. Paper I used self-reported exposures, and the questionnaire included variables regarding work history, physical health characteristics, education, diseases and reproductive health. In paper II the same questionnaire was used, and an expert panel categorized 18 work categories among the military men in the RNoN in terms of exposure or non-exposure to non-ionizing EMFs. Paper III was a dosimeter study on electric (E) fields on-board two vessels in the RNoN, a missile-torpedo boat (MTB) and a submarine. Personnel on-board wore the instrument in their breast pocket during their shifts and answered questions regarding location on-board and work tasks performed. In addition, the vessel's activity and use of non-ionizing EMF-emitting equipment was noted. Paper IV was a prospective randomized balanced cross-over study of magnetic resonance imaging (MRI) and influence on hormones relevant for male reproduction. Twenty-four male medical students who met a number of inclusion criteria were investigated by means of serum-blood samples immediately before and after a real and sham MRI investigation.

Results. Response rate in the cross-sectional studies (Paper I and II) was 58 per cent (n=2265) among all personnel (military and civilian personnel) and 63 per cent (n=1487) among the military men. The prevalence ratio (PR) of having a child with congenital anomaly was 4.0 (confidence interval (CI) 1.9 - 8.6) among the personnel

who had served on-board the "KNM Kvikk". Among the same personnel, the PR of having a stillborn child or a child that died within one week of birth was 4.1 (CI 1.7 - 9.9). In paper II, three work categories were classified as exposed to non-ionizing EMFs: "tele/communication", "radar/sonar" and "electronics". Logistic regression adjusted for age, whether the subject had ever smoked, military education and physical exercise at work displayed an increased odds ratio (OR) of 1.72 (CI 1.04 - 2.85) among "tele/communication" workers and OR of 2.28 (CI 1.27 - 4.09) among "radar/sonar" workers for self-reported infertility compared to unexposed workers. "Electronics" did not display an increased OR for self-reported infertility compared to the unexposed workers. In paper III, a total of 56 measurements were conducted on E-fields on-board two vessels in the RNoN. The E-field values measured were very low, averaging 0 – 10 per cent of the guidelines given by the International Commission on Non-Ionizing Radiation Protection (ICNIRP). In paper IV, there was no change seen in hormone levels either immediately after exposure or within the next 11 days when persons exposed to real and sham MRI were compared.

Conclusion. Paper I displayed an increased PR for having children with congenital anomalies, stillbirths or perinatal deaths after having served on-board a specific MTB vessel in the RNoN. Paper II showed an increased OR for self-reported experience of infertility among personnel serving in work categories categorized as being exposed to non-ionizing EMFs. Paper III investigated and described very low exposure for E-fields measured on-board two RNoN vessels. Paper IV did not find evidence for a significant impact on hormones relevant for male reproduction after exposure in MRI. This thesis could not establish non-ionizing EMFs as a cause for the findings in paper I and II. Furthermore, the studies could not explain the findings using other factors. The difference in exposure levels and duration may be of importance, as well as confounding factors that have not been investigated in this thesis.

Papers

The thesis is based on the following papers:

I. Magerøy N, Møllerløkken O J, Riise T, Koefoed V, Moen B E. *«A higher risk of congenital anomalies in the offspring of personnel who served aboard a Norwegian missile torpedo boat»*. Occupational and Environmental Medicine 2006; 63: 92–97.

II. Møllerløkken O J, Moen B E. *«Is fertility reduced among men exposed to radiofrequency fields in the Norwegian Navy?»*. Bioelectromagnetics 2008; 29: 345–352.

III. Møllerløkken O J, Moen B E. *«Electrical fields onboard two minor navy vessels»*. Medicina Maritima 2007; 7: 60–70.

IV. Møllerløkken O J, Moen B E, Baste V, Magerøy N, Oftedal G, Neto E, Ersland L, Bjørge L, Torjesen P A, Hansson Mild K. *«No effects of MRI scan on male reproduction hormones»*. Reproductive Toxicology 2012; 34: 133–139.

1. INTRODUCTION

1.1 Background

A safe working environment is a fundamental condition that has to be ensured for workers. Without safety at work, the health of the worker can be at risk. However, it can be difficult to ensure a safe working environment.

In the late 1980s and 1990s, the Royal Norwegian Navy (RNoN) became aware of a problem related to its working environment. Concern regarding the safety on-board a missile torpedo boat (MTB) – the “Kongelig Norsk Marine (KNM) Kvikk” – arose after a meeting between two fathers at an orthopaedic clinic in Bergen, Norway. Both had served on-board this vessel and both were accompanying their sons to a control medical examination for club foot. They began discussing their service in the Navy and their sons’ anomalies, and they learned that even more children with parents who had served on this vessel had congenital anomalies. To investigate this topic further, the RNoN ordered specific surveys regarding this vessel[1-3] to find the reason for these anomalies. The parents suspected that the special working environment of the vessel might be the cause. The “KNM Kvikk” operated as a leading vessel of the MTB command, and had specific tasks in electronic warfare. The vessel was therefore equipped with high powered high frequency jamming sending equipment operating at as high as 750 Watt (W) output power. Also the operating pattern of the “KNM Kvikk” was different from the other MTB vessels in the RNoN[1, 3] in that it would lie more still, for instance, than the other vessels when carrying out electronic warfare. This might have entailed different degrees of exposure compared to that of other personnel in the Navy.

The high frequency jamming sending equipment on-board the “KNM Kvikk” had an antenna mounted at the rear of the vessel. This was one of the main reasons for the concerns regarding the working environment on-board this vessel, because the equipment could potentially entail high exposure to non-ionizing electromagnetic fields (EMF). The concerns and studies regarding the “KNM Kvikk” were highly publicized in the media. It was difficult to study the topic and to draw conclusions, partly due to the nature of the problem as a cluster case, and partly due to lack of information from relevant archives in the Navy. This lack of information in the personnel archives made epidemiologic studies impossible at the time. Another limitation was the fact that the original “KNM Kvikk” was destroyed. Measurements of the non-ionizing EMF arising from the various emitting equipment on-board the actual “KNM Kvikk” were never performed. Later reports presenting exposure to non-ionizing EMFs on “KNM Kvikk” were extrapolated measurements done on a sister ship which was equipped identically to “KNM Kvikk”, but as mentioned in the reports, this may have been a source of errors due to differences between the two vessels[1]. An effort was made, however, to investigate the topic, and the work presented in the reports from the RNoN[1], the Medical Birth Registry of Norway (MBRN)[2] and from the National Institute of Occupational Health in Norway (NIOH)[3] was thorough and comprehensive. The reports discussed the possibility that the congenital anomalies might have been caused by a factor on this vessel[1-3], but no such factor was found.

Before and after these studies pertaining to “KNM Kvikk”, several other adverse factors in the working environment in the RNoN were discussed, both internally in the Navy and publicly in the media. Due to this, the command leadership of the RNoN decided, in 2001, to conduct a broad investigation into the working environment in the RNoN. The University of Bergen was commissioned to conduct a project called “Health, Safety and Environment in the Navy” (HSE Navy)[4]. The project included both work-place visits, literature studies and a large questionnaire study involving all employees at that time. The questionnaire study had many objectives the researchers wanted to investigate. One of these objectives was to study possible non-ionizing EMF exposure and eventual influence on reproduction. This became an important part of the further investigation. Non-ionizing EMFs were the main suspected source found on the “KNM Kvikk” at the time for the anomalies, and there was still a concern among the employees regarding exposure to these fields. To further investigate a possible effect of non-ionizing EMFs, the questionnaire study could give possibilities for both investigating self-reported graded exposures and expert graded exposures through classification of personnel based on work categories. Self-reported information on work history, health and reproductive health could also be assessed in the questionnaire. However, the questionnaire study and the HSE Navy project alone were inadequate to fully investigate the topic, especially in terms of exposure assessment and causality between non-ionizing EMF and reproduction; hence, more studies were needed. It was important to determine whether the workers in the RNoN were excessively exposed to non-ionizing EMFs when working on-board the vessels at normal activity at the time of the investigation. To fully establish a possible link between non-ionizing EMF and reproduction it was also important to investigate effects from a known source of non-ionizing EMFs on the reproductive health of men.

1.2 Electromagnetic fields

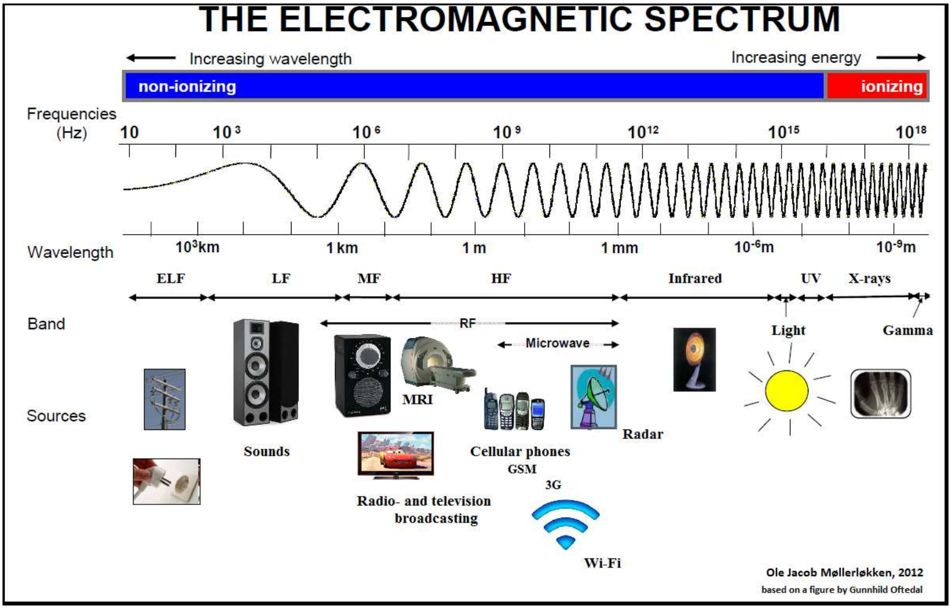

Figure 1: The electromagnetic spectrum.

E (extremely), L (low), F (frequency), R (radio), H (high), UV (ultraviolet), MRI (magnetic resonance imaging), GSM (global system for mobile), 3G (3rd generation).

Electromagnetic fields consist of electromagnetic waves of different frequencies and wavelengths[5]. To create these electromagnetic waves, one needs a source with accelerating electric charges and changing currents[6]. This produces the electromagnetic waves which radiate away from the source carrying energy. In a vacuum, the waves propagate indefinitely. Electromagnetic fields behave differently depending on the distance to the source. In the far field region, the waves propagate through the medium/space in a fixed relation to each other, and calculations, for instance, of the magnetic (B) field can be done by measuring the electric (E) field. The region close to the emitting antenna is called the near field, and in this region the fields are more complex, entailing a need to separately assess both the B- and E-field. The energy of the field depends on the frequency and the amplitude, i.e. of the field strengths[7]. In a medium, some of the energy will be absorbed. The proportion of energy that is absorbed depends on the E and B properties of the medium and of the frequency of the field. The EMFs with the highest energy are called ionizing EMFs (X-rays and gamma (γ) rays). In these high frequency fields, each photon contains enough energy to ionize molecules[5, 8].

In this thesis, the focus will be on the non-ionizing EMFs, especially radio frequency (RF) fields, but the studies in the thesis also include some exposure to extremely low frequency (ELF) fields.

1.2.1 Non-ionizing electromagnetic fields

Non-ionizing EMFs have lower frequencies and longer wavelengths compared to ionizing EMFs (Figure 1), and the photons in non-ionizing EMFs do not themselves contain enough energy to ionize molecules.

Radio frequency electromagnetic fields

RF EMF is in the frequency range of 100 kHz (1 kHz = 1000 Hz) to 300 GHz (1 GHz = 10^9 Hz) and is used, for example, in wireless communication technology (cell phones, wireless local area networks (WLAN), global position services (GPS), radar, radio- and television signals and medical devices like magnetic resonance imaging (MRI). The uses of RF EMFs have contributed to the advantages of our technological world, for example through the use of cellular phones to give health professionals early alerts of accidents and cardiac infarctions, thereby leading to an increase in survivals after these incidents[9]. Three main disadvantageous effects have been established and causally linked to RF EMFs:

Thermal effect

The amount of energy absorbed during one second per kilogram tissue is determined by the specific absorption rate (SAR, W/kg). This absorbed energy, if intense enough, will cause thermal heating of the tissue. Such thermal heating can if it is high enough cause tissue damage, and the most susceptible organs are the central nervous system, the testicles and the eyes[10, 11].

Nerve-excitation

Intense low frequency (LF) fields cause differences in the electric potential of cell membranes and give rise to electric currents thereby causing disadvantageous effects such as muscle contraction[10, 11].

Other effects

Strong fields in the RF EMF area may also cause rearrangement of cells and molecules which form chains along the direction of the field present; this rearrangement is known as the "pearl-chain formation". In addition, large microwave pulses, when absorbed by the soft tissue in the head, may launch a thermo elastic wave of acoustic pressure that travels by bone conduction to the inner ear causing an auditory phenomenon[10, 11]. Recently the International Agency for Research on Cancer (IARC) and the World Health Organization (WHO) classified RF EMF as a class 2B carcinogenic[12] based mainly on findings from studies on brain cancer and the use of cellular phones. The mechanisms behind these findings are unknown.

Extremely low frequency non-ionizing electromagnetic fields

ELF fields are used for E power supply and surround all E installations and are present in MRI. Studies have identified potential nerve excitation from such fields. There are also studies linking ELF fields to an increased risk of childhood leukemia and leading to the categorization of ELF B-fields as a class 2B carcinogenic[13]; however, a biophysical mechanism for a carcinogenic effect has not been established.

The International Commission on Non-Ionizing Radiation Protection

The International Commission on Non-Ionizing Radiation Protection (ICNIRP) is an independent scientific organization aiming to provide guidelines and advice on the health hazards of non-ionizing EMFs through reviewing the current scientific evidence concerning exposure to non-ionizing EMFs and consequences for health. It has formal relations with the WHO and the International Labour Office (ILO), but is non-governmental. Harmful health effects can be caused by exposure to strong EMFs[14]. Exposure to strong RF EMFs suggest that adverse biological effects can be caused by a temperature rise in tissue which exceeds 1 °C above the normal temperature of the tissue. Calculations adjusting for the normal human temperature regulation systems have established limit values for exposure which will not give a temperature rise in tissues. This limit occurs for RF EMF after whole body exposure which produces a SAR value of 4.0 W/kg (middle value over 30 minutes). Based on this, the exposure limit for occupational exposure is lowered by a factor of 10, which gives a SAR value of 0.4 W/kg to account for eventual non-thermal effects. For the public, the limit is lowered again by a factor of 5 to a SAR value of 0.08 W/kg whole body exposures to further account for eventual non-thermal effects and longer exposure durations[10]. Limit values is also made for LF fields to prevent nerve excitation and for static B-fields to avoid among others vertigo, nausea and influence on blood flow[14].

No mechanism for low exposure to RF EMF and health effects has been consistently demonstrated. Low exposure levels which do not cause heating are highly debated as there is no agreement on any health effects at such levels.

1.2.1.1 Occupational exposure on shore

Humans are often in contact with non-ionizing EMFs during work. Occupational studies of non-ionizing EMFs have concentrated mainly on ELF EMF exposure among welders and on exposure to RF EMFs among for example physiotherapists, cell phone users and military occupations. There are differences in terms of the levels of exposure to the RF EMFs in different occupations. Studies with measurements of exposure to RF EMFs in occupations do exist, many of which are summarized in an article by Mantiply et al. from 1997[15]. Occupations mentioned here are communication- and navigation personnel, plastic welders, medical workers such as surgeons and physiotherapists. However, in many other studies of workers and health effects from such fields, non-ionizing EMF measurements are frequently lacking. Many studies rely on a job-exposure matrix, expert categorization or self-reporting for exposure categorization. This is mentioned as a weakness in the guidelines given by the ICNIRP in 2009[10].

In Norway the working environment is constantly changing with regard to exposure to non-ionizing EMFs. The traditional occupation of plastic welder has been largely made obsolete by automation, and the level of exposure among workers is therefore much less today compared to earlier[16, 17]. However, plastic welders working close to the machines are still highly exposed. Heavy users of cellular phones in the workplace have also been focused on in research[18, 19], but technological developments have reduced exposure from these sources and the level of exposure is low at present[20]. Surgeons using diathermy have also been found to be exposed to levels exceeding the suggested international reference levels[21].

1.2.1.2 Occupational exposure on vessels

All personnel on-board vessels are exposed to non-ionizing EMFs[22, 23]. ELF EMFs are emitted through the E systems. Workers involved in navigation and communication, machinists and other personnel on-board are exposed to RF EMFs due to the equipment being used, and on smaller vessels, all workers are exposed because of proximity on-board between the sources and the crews. Few studies have measured and published exposure to EMFs on vessels. One study has investigated the exposure of radio officers on Danish merchant vessels to RF EMFs by taking measurements of both E- and B-fields[24]. It relates the findings to the American National Standards Institutes (ANSI) guidelines of 1982, stating that a distance of at least 0.5 m between the antenna feed and the personnel is recommended to ensure levels below the ANSI safety levels. Another study has calculated the induced E-field experienced shipboard when standing on a metal deck near a vertical antenna[22]. A person standing close to such an antenna will be exposed to an axial E- and a transverse B-field. The article uses a complex, but also simplified, calculation of the induced current in the body, but does not have any actual measurements.

In the RNoN the workers are exposed to RF EMFs from communication and navigation systems and tactical weapons. Systematic measurements of RF EMFs have been taken by the RNoN on their vessels since 1995. This is part of a Navy project called Radiation Hazard (RADHAZ). During the initial years, the project measured E-fields on-board the Navy vessels to indicate safe working distances in accordance with standardization agreement (STANAG) 2345. Later both E- and B-fields have been measured in accordance with the ICNIRP guidelines[10, 25-27]. Recently the information present in RADHAZ has been used for modelling exposure on RNoN fast patrol boats (FPB) [28, 29]. These vessels were generally equipped with high frequency antennas and Link 11, which operates at frequency bands 2.1 – 8 MHz and at output powers 10 – 250 W[30]. In addition to this, they were equipped with navigational- and weapon radars; both had 25 kW as peak output power, but operated at different frequencies, the navigational radar at 9.4 GHz and the weapon radar at 9.1 GHz. The E-field levels seen on this type of vessel in the model used were generally 2.0 – 109 V/m. The only place on-board that exceeded the ICNIRP guidelines was the captain's cabin.

Measurements were also performed on "KNM Kvikk"'s sister vessel[1]. The levels measured varied with exposure setting and measurement phase, but several areas exceeded the exposure limit. One example was measurement at the head of the bunk in the captain's cabin which was found to be 70 – 700 V/m depending on frequency. What has been lacking however, and might have led to concerns among the workers, are measurements of the actual exposure experienced by the workers during sailing.

1.3 Reproductive health

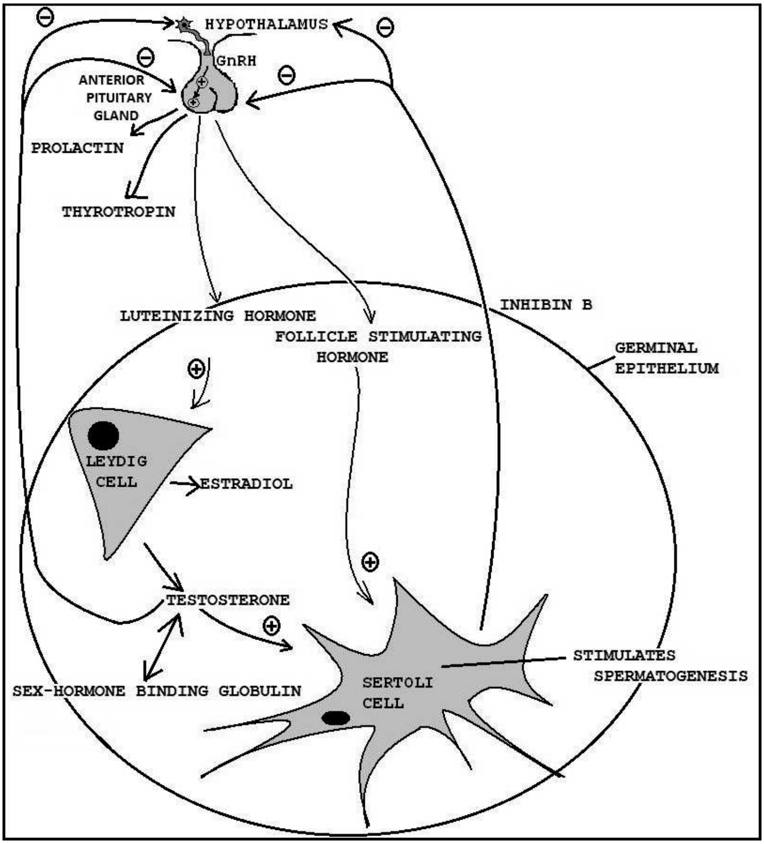

Figure 2: Pathways involved in the hormonal regulation of male reproduction
gnRH (gonadotropin Releasing Hormone)

Reproductive health concerns all factors involved in the process prior to and during conception, the pregnancy and finally the health of the newborn child. In males, one of the most important factors in reproductive health is the production and delivery of sperm. In addition to being dependent on a generally healthy status of the male, the process of producing sperm, spermatogenesis[31], is known to be highly dependent on a number of hormones, despite the fact that all their precise mechanisms of actions are still not known.

Androgen hormones are very important and the testis is the main site for androgen production in males, under strict control from regulatory pathways including the hypothalamus and the anterior pituitary gland in the brain[32] (Figure 2).

Testosterone is the primary androgen hormone in males. Other important androgen hormones are gonadotropin releasing hormone (gnRH), oestrogen, estradiol (E2), follicle stimulating hormone (FSH), luteinizing hormone (LH), inhibin B, activin, oxytocin, sex-hormone binding globulin (SHBG), prolactin (PRL), growth hormone, thyreotropin (TSH) and cholesterol[31]. Testosterone affects growth, differentiation and functions of the reproductive organs in males and it is also important for the features of masculinity (beard, hair growth, body form and muscle growth)[32]. Testosterone is produced in the Leydig cells and is stimulated by LH secretion from the anterior pituitary gland. Testosterone acts locally in the testis together with FSH, which is secreted from the anterior pituitary gland, to promote spermatogenesis in the Sertoli cells (Figure 2). A by-product in the secretion of testosterone from the Leydig cells is production of E2 which is important for the reabsorption of fluid in the rete testis and may also have implications on the production of normal sperm and their maturation[32]. Systemically most of testosterone is bound to plasma proteins, around 50 per cent to albumin, while slightly less is bound to SHBG, which also binds oestrogene. Systemically testosterone has numerous effects as mentioned earlier, but very important in reproduction is the negative feedback testosterone gives the hypothalamus and anterior pituitary gland in relation to production and release of LH and FSH.

Inhibin B is a main regulatory hormone in male reproduction. The systemic level of the hormone reflects the concentration of sperm and is a very good estimate of the exocrine influenced function of the Sertoli cells[32-34]. It is functioning as a negative feedback stimulus to the hypothalamus and pituitary gland.

TSH and PRL are also secreted by the pituitary gland. TSH regulates the biosynthesis and secretion of the thyroid hormones which are important in the growth of males and regulation of the autonomous nervous system[32]. PRLs role in males is not completely understood, but high levels are known to affect the libido in a negative way and cause impotence.

Fertility is a measure of successful reproduction in a couple or in a population and is a measure of the capability to produce children[35]. Infertility means you cannot conceive children. In epidemiological studies of reproduction infertility is often defined as having tried to get pregnant with his or her partner for more than one year without success[36]. The prevalence of infertility is difficult to assess, but a review by Skakkebæk et al.[37] suggests a total prevalence of 15 per cent for experiencing primary or secondary infertility as a couple during their reproductive life. A contributing male factor is thought to be present in 50 per cent of these cases. In developed countries, the 12-month infertility rate is estimated to be 3.5 – 16.7 per cent[38]. In Norway, female infertility is suggested to be 6.6 per cent[39].

Congenital anomalies or birth defects can be of different severity. The reported prevalence of anomalies is highly linked to the quality of registration of such defects. In Norway the MBRN monitors and registers the prevalence of congenital anomalies, and in 2010 the prevalence of any congenital anomaly was 4.202 per cent, and 2.125 per cent was considered as a serious anomaly[40]. Perinatal mortality is also monitored by the MBRN, and the prevalence in 2010 was 0.39 per cent. Perinatal mortality is defined as deaths within the first week of life.

A textbook of occupational and environmental reproductive hazards[35] states that around 20 per cent of the congenital anomalies are associated with gene mutations and 5 per cent with chromosomal aberrations. Less than 10 per cent of congenital anomalies are known to be due to teratogen agents, which are agents that can cause birth defects. Most teratogen agents known today are not tested adequately for developmental toxicity, but a principle does apply which states that any agent can be shown to have teratogen capacity when a large enough dose is given at a sensitive time in development (Karnofsky's Law)[41].

In males, reproductive health can be impaired by a number of factors[42, 43]. Among these factors are disease, trauma, surgery, allergy, drug or medication use, abnormal anatomy, low libido, psychological and environmental factors. Suggested environmental factors are for instance: stress at home, stress at work, exposures to metals, pesticides, solvents, hormone disruptors, ionizing EMFs, non-ionizing EMFs, heat, vibration and combined exposures. An article by de Fleurian et al.[44] investigates many of these factors through a questionnaire administered to men attending an infertility clinic showing relations between infertility parameters and heavy metals, solvents, fumes, polycyclic aromatic hydrocarbons, mechanical vibrations and excess heat.

Many of these factors may cause disruption in spermatogenesis leading to a suppression of sperm count or an increased proportion of abnormal sperm. Abnormal sperm may be caused by alterations in sperm production, sperm chromatin/DNA stability or epigenetic effects[35, 37, 45]. Another factor leading to impaired reproductive health caused by the male is if there are disturbances in the sperm-oocyte function. Also, there are unexplained causes which account for about 15 per cent of the infertility cases.

1.3.1 Reproductive health and radio frequency electromagnetic fields

The topic of RF EMFs and their possible influence on reproductive health is a controversial issue. Thermal levels of RF EMF exposure is known to affect sperm morphology and delay conception[46, 47]. In terms of non-thermal exposure there is uncertainty regarding the potential influence on reproductive health. A report by ICNIRP from 2009 states that "overall, problems with exposure assessment temper any conclusion regarding reproductive outcomes, and no adverse effects of RF have been substantiated"[10]. The conclusion from ICNIRP is also recently confirmed in a Norwegian report from 2012 stating that there is limited foundation for drawing any conclusion regarding RF EMF and reproduction[11].

Several studies relating to human reproduction and RF EMF have been performed (Table 1), and some have proposed mechanisms showing the impact of RF EMF on the reproductive health of men. Some pathways have been in specific focus; influence on hormonal balance, sperm parameters and DNA and/or gene transcription (Figure 3).

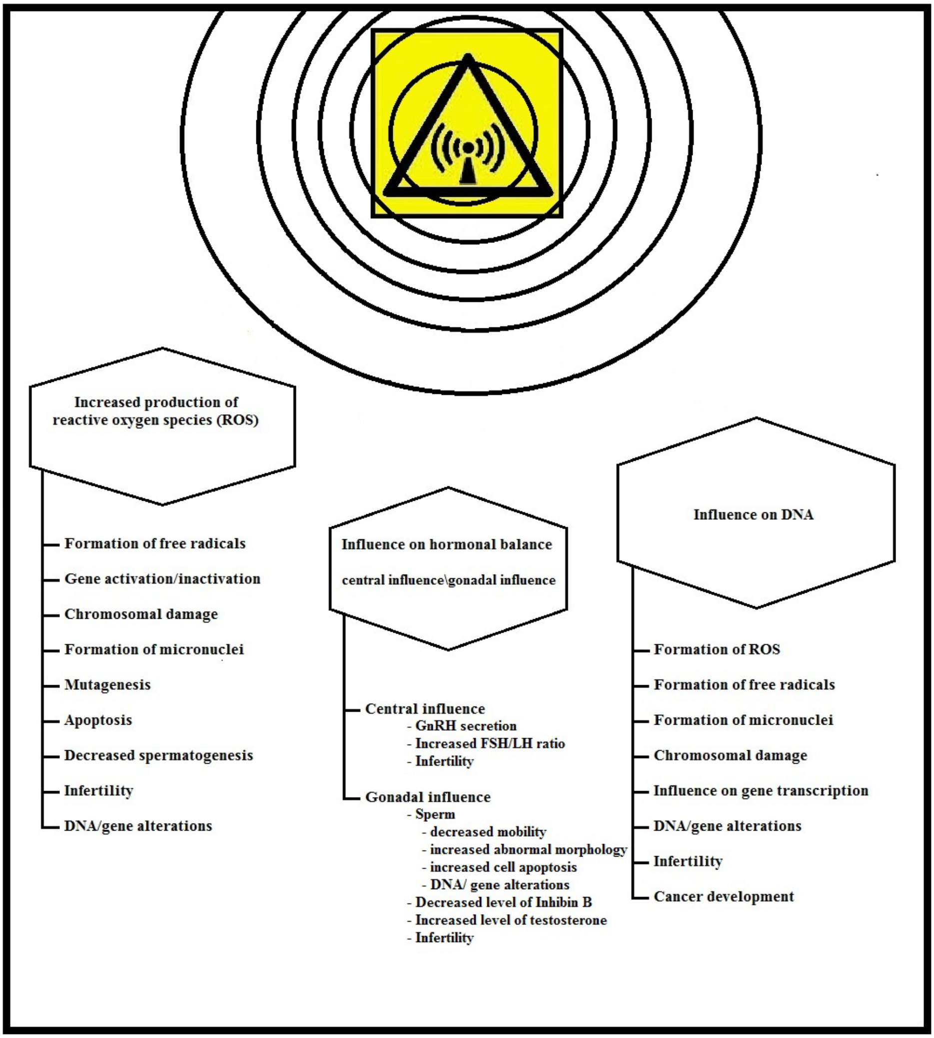

Figure 3: Suggested mechanisms in non-thermal EMF exposure on male reproduction.

Baste et al.[28, 48] and Mjøen et al.[49] have both investigated occupations involving exposure to non-ionizing EMF and reproductive outcomes. The first study by Baste et al.[48] investigated self-reported exposure to non-ionizing EMF in the RNoN and found a significantly linear association between self-reported exposure to non-ionizing EMF and self-reported one year of infertility. A significant linear trend was also found with a lower ratio of boys to girls at birth when the father reported a high degree of exposure to non-ionizing EMF. The study had no measurement of exposure. In the other study by Baste et al.[28] dose-assessment of the exposure to non-ionizing EMFs on-board the RNoN FPB was conducted based the Navy's previous conducted stationary measurements of these vessels. Reproductive outcomes were investigated through linkage with the MBRN. This study found that work on-board a FPB during the three months prior to conception was associated with a risk of perinatal mortality and preeclamptic pregnancies. Mjøen et al.[49] categorized paternal occupations in relation to exposure to RF EMF. The study found some increased risks, but the categorization was crude and no measurements were taken.

Gutschi et al.[50], Grajewski et al.[51], Schrader et al.[52] and De Seze et al.[53] have all analysed hormone levels in relation to non-ionizing EMF. The results are not consistent. Gutschi et al. proposed an influence from non-ionizing EMF, namely that non-ionizing EMF inhibits an enzyme responsible for converting testosterone into dihydrotestosterone. This would lead to higher levels of testosterone and lower levels of LH. This was proposed after having found increased levels of testosterone and lower levels of LH among men having a cell phone compared to men without a cell phone[50]. The study has important limitations, especially in regards to exposure assessment limited to merely having a cell phone or not. Also; the participants were men attending an infertility clinic, and the timespan of the survey was very long and did not account for changes in the society regarding for instance cell phone use. Grajewski et al.[51] investigated RF heater operators and found higher levels of FSH among these. This could indicate local damage to the germinal epithelium and a compensatory increase in FSH for maintaining semen quality. The study did not achieve the needed sample size and had limitations in blood sampling which made the results unreliable. Schrader et al.[52] investigated military personnel exposed for radar compared to personnel exposed to lead and personnel without any exposure, without finding differences in neither FSH, LH nor testosterone. They did not, however, perform any form of exposure assessment and exposure to radar was not clearly defined. The study also lacked information on how and at what time of day the blood sampling was done. De Seze et al.[53] investigated the possible influence that RF EMF emitted from a GSM cell phone could have on secretion of hormones from the anterior pituitary gland. Twenty healthy men were selected, and blood samples drawn prior to, during and after exposure. Exposure was given by GSM cellular phones with fixed output power, but no actual assessment of this exposure was done. No influence on hormones was seen. The participants had several requirements during the study period to avoid confounders, and also several inclusion criteria had to be met. The requirement of for instance not having used any type of radio cellular phone during the last three months prior to the study may have led to a selected and not representable group depending on the normal use in the population.

In regards to influence on sperm parameters the following studies have findings leading to theories of possible mechanisms. Weyandt et al.[54] investigated semen samples of military personnel associated with lead, radar or non-exposure. The group of men associated with radar microwave exposure displayed lower sperm counts/mL and sperm/ejaculate than the comparison group. There were no exposure measurements taken and no medical evaluation was done of the participants. Similar findings were seen in a study by Hjollund et al.[55] although later measurements did not reveal any exposure to microwaves. Another occupational group exposed to ELF EMF are arc welders. A study by Hjollund et al.[56] did not find any B ELF EMF's influence on semen parameters and hormones, but the sample size was small. Fejes et al.[57] assessed cell phone exposure by means of a questionnaire and analyzed semen parameters of different groups of exposure. They found that use of the cell phone was correlated with a decreasing proportion of rapidly progressing motile sperm and with an increasing proportion of slow progressive motile sperm which can lead to increased infertility. The population sample were men attending an infertility clinic because of infertility problems. No exposure measurements were taken, but they ranked cell phone usage into the categories of duration of possession, duration of standby close to patient and duration of daily transmission.

Lately there has been more focus on the possible genotoxic damage caused by non-ionizing EMFs on humans through ROS formation, chromosomal aberrations and micronuclei formation. Two studies, one from the Republic of Korea and one from Italy, have been conducted on MRI exposure and possible genotoxic damage[58, 59]. Both discovered increased formation of micronuclei in the cell cores, but the Korean study[58] also investigated and found significant DNA damage and chromosome aberrations.

Both studies used lymphocyte cultures which were exposed to MRI for different durations. The Italian study also investigated in vivo lymphocytes from individuals who had had a MRI cardiac scan and found similar results[59]. There have also been investigations of cell phone frequencies with inconsistent results in terms of genotoxic damage. Scarfi et al.[60] could not find evidence of genotoxic effects after exposing lymphocyte cultures from 10 healthy donors to a 900 MHz GSM signal. The study was very well designed and used a good model for exposure, giving them a solid exposure assessment. Schwarz et al.[61] also used an exposure model with solid exposure assessment and found a dose-dependent increase of micronuclei and comet tail after exposing fibroblasts to UMTS 1950 MHz.

Table 1: Overview of occupational studies of reproductive health among male workers with possible exposure to non-ionizing electromagnetic fields, cell phone studies on male reproduction and three exposure studies.

The table outlines the designs used, the exposure categorization and classification, the country, 1st author, year of publication, main outcome of the studies and the reference IDs corresponding with the reference list at the end of the thesis.

Study design	Exposure group	Exposure classification	Country	Author (year)	Main outcome
Register based cohort study	1. Paternal work on-board: A. Vessels in the RNoN B. Fast patrol boats 2. Related to RF dose assessment	Self-reported and dose assessment	Norway	Baste, V.[28] (2012)	Work on-board FPBs during the three months prior to conception was associated with risk of perinatal mortality and preeclamptic pregnancies (linkage with MBRN). This was also found when investigating RF dose assessment, but no clear dose response. No associations were seen for congenital anomalies, sex ratio, low birth weight, preterm births and small size for gestational age.
Cross-sectional	Men using cell phone (N=991) Men not using cell phone (N=1119)	Self-reported use or no use	Austria	Gutschi, T.,[50] (2011)	Sperm samples and blood samples revealed that the men using cell phone had a significantly increased proportion of pathological morphology and a reduced amount of rapidly progressive sperm. In addition they had a higher level of Testosterone and reduced level of LH. No differences were seen for sperm count, teratozoospermia, FSH and PRL.
Cross-sectional	Paternal service in the RNoN	Self-reported	Norway	Baste, V.[48] (2008)	Increasing self-reported work close to equipment emitting RF EMF was significantly linearly associated with both reported one year of infertility and lower ratio of boys to girls at birth.
Register based cohort study	Fathers who at work was exposed to RF EMF in various degree: -probably not (N=376837) -possibly (N=139871) -probably (N= 24885)	Expert categorization	Norway	Mjøen, G.[49] (2006)	The study found a small increased risk for preterm births and a small decreased risk for cleft lip in births where the father could have been exposed to RF EMF in his work. The study also investigated low birth weight, early and late stillbirths, male gender, birth defects when present, and in addition to cleft lip, seven other specific birth defects without finding any clear associations among these outcomes and exposure.

Cross-sectional	Cell phone usage > 60min/day (N=59) < 15 min/day (N=195) Phone close and Stb.by < 1 h/day (N=106) > 20 h/day(N=88)	Self-reported usage of cell phone	Hungary	Fejes, I.[57] (2005)	Sperm samples revealed a negative correlation between high usage of cell phone and proportion of rapidly progressive sperm and, coherently, a positive correlation with slow progressive sperm. No effects were seen for stand-by operating differences. Also, no effects were seen for the other parameters investigated (sperm volume and concentration, proportion of non-progressive and immotile sperm, total motility, total sperm count, total motile sperm count and total rapid progressive motile sperm count).
Cross-sectional	RF-heater operators (N=12) Unexposed workers (N=34)	Job titles and RF radiation survey with measurements	USA	Grajewski,B.[51] (2000)	Questionnaire, semen- and blood sampling revealed small differences. The viability of the sperm was higher in the exposed men, while the pH was lower and the s-FSH of the exposed men was higher. No differences were seen for sperm count, sperm concentration, semen volume, semen osmolality, sperm motility, sperm velocity, percentage of normal sperm, distribution of abnormal sperm morphology, total testosterone, LH, PRL nor sperm chromatin structure assay.
Cohort study	Arc-welders (N=36) Non-welders (N=21)	Job titles	Denmark	Hjollund,N.H.[56] (1999)	Time to pregnancy, semen quality and reproductive hormones displayed no consistent support for deleterious effects on human fertility.
Prospective cohort	Healthy volunteers (N=20) exposed to GSM RF EMF for 2 h/day, 5 days/week in 1 month	Use of mobile phone with fixed output power	France	De Seze, R.[53] (1998)	Blood samples drawn weekly and investigated for s-TSH, s-ACTH, s-GH, s-PRL, s-LH and s-FSH to investigate anterior pituitary function. No significant effects seen.
Cross-sectional	Military - radar operators (N=33) - artillerymen (N=57) - controls (N=103)	Job titles	USA	Schrader, S.M.[52] (1998)	Endocrine- and semen analysis did not reveal any significant differences.
Cross-sectional	Military - missile operators (N=19) Other occup groups (N=489)	Job titles	Denmark	Hjollund, N.H.[55] (1997)	Median sperm density was low compared to references with an adjusted difference of 23 million/mL (P=0.07). No differences were seen for semen volume, percentage of oligospermia, immotile spermatozoa, percentage of normal morphology.

Cross-sectional		Military - microwave exp. (N=20) - artillery men (N=30) - control (N=31)	Job titles	USA	Weyandt, T.B.[54] (1996)	Semen- and blood analysis. Microwave-exposed soldiers displayed a significant decline in sperm count (million/ml) and total sperm count (million). No differences were seen for thirteen other sperm parameters.
Exposure assessment	1	Fast patrol boats in the RNoN	Dose-assessment	Norway	Baste, V.[29] (2010)	RF EMF exposures on-board FPBs were generally low, except for a few cabins above deck for two classes.
	2	Hospital operating theatres	Measurements of E-field and calculation of B-field	Sweden	Liljestrand, B.[21] (2003)	The levels experienced by the surgeon exceed the limits given by ICNIRP. E-field exposures of 15 kV/m and B-field calculated to 16 µT.
	3	Radio officer's exposure to electric and magnetic fields. (85 measurements)	Measurements of E- and B-field.	Denmark	Skotte, J.[24] (1984)	Locations normally occupied by the radio officer on Danish merchant ships revealed low exposure during normal activity, well below the ANSI levels.

Abbreviations: ACTH(Adrenocorticotropic hormone), ANSI(American National Standards Institute), B(Magnetic), E(Electric), EMF(Electromagnetic field), FPB(Fast patrol boat), FSH(Follicle stimulating hormone), GH(Growth hormone), GSM(Global System for Mobile), ICNIRP(International Commision for Non-Ionizing Radiation Protection), ID(Identification number), LH(Luteinizing hormone), MBRN(Medical Birth Registry of Norway), N(Number), PhD(Philosophiae Doctor), PRL(Prolactin), RF(Radio frequency), RNoN(Royal Norwegian Navy).

1.4 Rationale and objectives of the study

1.4.1 Rationale of the study

The International Commission on Non-Ionizing Radiation Protection[10] describe still unanswered questions and unclear relationships between non-ionizing electromagnetic fields and reproduction. There is a lack of quality in the studies performed, especially with regard to occupational exposure assessment, making it difficult to draw conclusions at present. Recently, the World Health Organization and the International Agency for Research on Cancer classified radio frequency electromagnetic fields as class 2B "possibly carcinogenic to humans"[12]. An agent which may be carcinogenic may also have the capability of affecting reproduction through mechanisms such as epigenetics and by destabilization of DNA/ chromatins, and this underlines that questions remain unanswered in this area.

The lack of quality and the difficulty in drawing conclusions make it important to conduct high quality studies on non-ionizing electromagnetic fields and adverse effects on reproductive health. In addition, the male factor is more and more becoming a factor of interest in infertility. It is necessary to conduct studies with male reproduction in focus.

Nationally, the Royal Norwegian Navy working environment of the employees has been an area of concern for several years. The "KNM Kvikk" case received a lot of publicity, and although tremendous efforts were made, the studies failed to quell concerns among workers. There still is a concern among these workers that exposure to non-ionizing electromagnetic fields could have influenced reproduction and that this might happen even today. Investigation of these aspects is important to quell eventual myths, and it is equally important to improve the working conditions entailing potential risk through exposure to non-ionizing electromagnetic fields.

1.4.2 Main objective

The main objective of this thesis is to gain more knowledge regarding the possible link between exposure to non-ionizing electromagnetic fields and male reproduction.

1.4.3 Specific objectives

Paper I had the objective of investigating the prevalence of congenital anomalies, stillbirths and perinatal deaths in the children of workers who had served on-board the "KNM Kvikk" compared to the children of workers in the Royal Norwegian Navy who had not served on-board this vessel.

The hypothesis was that service on-board the "KNM Kvikk" was associated with an increased risk of adverse reproductive outcomes.

Paper II had the objective of investigating male personnel in the Royal Norwegian Navy, using expert categorization for non-ionizing electromagnetic fields, and to compare the frequency of infertility, the number of biological children, children with congenital anomalies, stillbirths, perinatal deaths and deaths within first year of life in exposed and unexposed groups.

The hypothesis was that exposure to non-ionizing electromagnetic fields in the Royal Norwegian Navy was related to negative reproductive outcomes.

Paper III had the objective of measuring radio frequency electric fields on-board Royal Norwegian Navy vessels during normal activity with personal measurements.

The hypothesis was that the exposures to radio frequency electric fields on-board vessels in the Royal Norwegian Navy were higher on deck than below deck. In addition we hypothesized that the exposure on-board vessels would be larger for personnel working close to non-ionizing electromagnetic field-emitting equipment than for other personnel.

Paper IV had the objective of investigating an acute exposure to non-ionizing electromagnetic fields and determining whether or not this exposure could cause any change in male reproductive hormones.

The hypothesis was that non-ionizing electromagnetic field exposure during magnetic resonance imaging would affect male reproductive hormones.

2. MATERIAL AND METHODS

The papers of this thesis are performed at different times and are part of different projects. An overview of the timeline with exposure paradigm and designs of the papers can be viewed below in Figure 4.

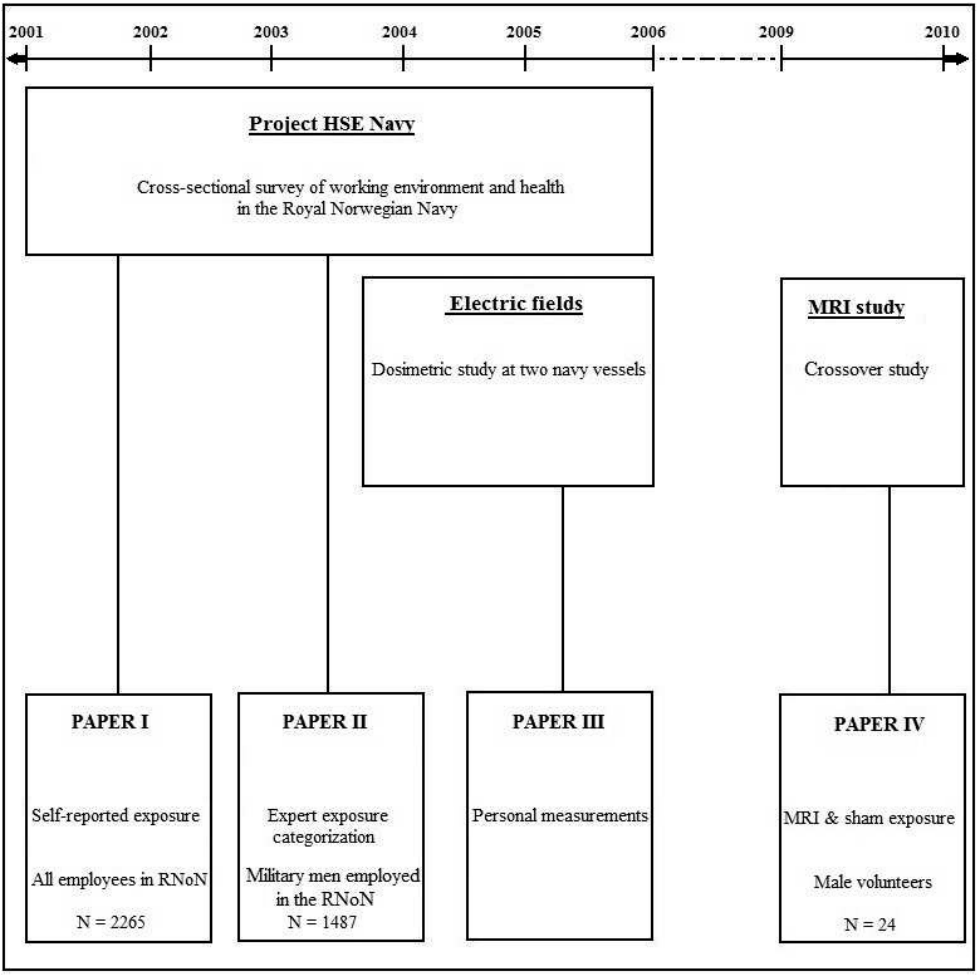

Figure 4: Timeline of the thesis, exposure paradigm and design of studies.
HSE (Health, Safety and Environment), MRI (Magnetic Resonance Imaging),
RNoN (Royal Norwegian Navy)

2.1 Cross-sectional study (Papers I and II)

A cross-sectional study among all employees who were employed in the RNoN in September 2002 was initiated by the RNoN and carried out by the University of Bergen.

2.1.1 Questionnaire (Papers I and II)

A questionnaire (Appendix I) was sent out to all employees in the RNoN (both military and civilian workers) in 2002 with the employee's name, address, and national insurance number pre-printed on the form. The form was returned directly to the University of Bergen. Total response rate was 58 per cent (N=2265) with a slightly higher rate for the military men at 63 per cent (N=1487). For the non-respondents, we knew the current workplace, gender and age, but had no information on previous workplaces. There were more civilian workers among the non-respondents. Men who responded were on average older than those not responding (38 years of age vs. 36 years of age respectively), while for the women it was the inverse (40 years of age vs. 43 years of age).

The questionnaire was part of a larger study (HSE Navy). Only questions relevant for the papers of this thesis are described here. Baseline variables were solicited, including years of age, weight, height, civilian and military education, duration of service in the RNoN, duration of work outside the RNoN and chronic diseases. Physical exercise was assessed both in service and outside the Navy. Smoking was assessed by asking if the respondents had ever smoked on a daily basis. If the respondents answered yes to this question, they were then asked to quantify the amount of smoking by pack years, type of tobacco and whether or not they still smoked. Alcohol usage was assessed by asking if they used alcohol or not. If the respondents answered yes to this question, they were then asked to quantify the amount of alcohol usage in number of "standard units of alcohol" per week.

All respondents filled in information about their past and present place(es) of service. The RNoN provided a list of 32 different places of service and a list of 18 work categories. The respondents gave information about what kind of service they had experienced, work category and the year he/she started their service at that place, and the year it ended. This was to be done for all years of service in the RNoN.

In addition, there was another question with nine different specific places of service, including work on-board the "KNM Kvikk" and 18 work categories. For this question also, the responders were asked to provide the year they began and the year they ended work in the specific place of service and work category.

The respondents also filled out two lists for different work exposures experienced, one for their service in the Navy and one for exposure elsewhere. The list included whether the respondents had been in contact with, worked with or been exposed to organic solvents and paint, skin contact with oil, gasoline or diesel and vapour from the same petroleum products, smoke from burning oil, exhaust gas, pesticides or herbicides, dust from grit blasting or sanding, welding or torch cutting or working with the hull, lead, explosives, noise, vibration or shaking, demolition work, heavy lifting, twisted work positions, work with arms above the shoulders, passive smoking and asbestos. Also it included questions regarding work closer to high frequency aerials than 10 m, closer to radar than 5 m, and closer to communication equipment than 3 m. The scoring on the exposure list was on a scale divided into never, very little, some, much, very much and do not know.

The respondents were also asked about their reproductive health in the questionnaire. We assessed infertility by asking the question "Have you and your partner ever tried for more than one year to get pregnant without success?" The response categories were "yes", "no" and "do not know". In addition it was asked whether they had biological children or not. For each child the respondents were asked to provide the year of birth, gender of the child, eventual anomalies and chromosome anomalies and to indicate whether the child was premature, stillborn or died within the first week or first year of life. The questions regarding children's health were selected and modified from the questionnaire used in the European Studies of Infertility and Subfecundity (ESIS)[36].

2.1.2 Reproductive outcomes and place of service (Paper I)

In paper I, the reproductive outcomes in the RNoN were studied in relation to different places of service in the RNoN. The father or mother who, in the questionnaire given in the cross-sectional survey of all employees in the RNoN, had informed about congenital or chromosomal anomalies for one child or more were sent a second one-page questionnaire to fill out for each child. This questionnaire included date of birth or abortion, the gender of the child, birth weight and gestational length, how the delivery had been or how the pregnancy ended, when the diagnosis was established, what the diagnosis was, who had diagnosed the child and a characterization of the consequences of the diagnosis for the child. There was no information in this questionnaire regarding previous places of service or self-reported exposures which had been given in the first questionnaire. All answers in the second questionnaire were summarized and sent to Haukeland University Hospital where two paediatricians decided whether the child most likely had a congenital anomaly or not based on the parents report. The paediatricians were blinded to the service the parent had done in the Navy. Response rate on the second questionnaire was 86.6 per cent (84 of 97 children). The paediatricians were able to evaluate 83 of the 84 children. The remaining 14 children (1 who could not be evaluated and 13 who did not respond on the second questionnaire) were divided, for analytical purposes, into having a congenital anomaly or not at the same fraction as the 83 children for which a decision had been made.

For a child to be exposed to a place of service, this exposure would have had to occur before the time of conception. To minimize exposure misclassification, it was decided that if the parents had served on-board a vessel for the first time during the year the child was born or later, the child could not have been exposed to that vessel. A child was classified as exposed to a place of service if the parent had served at that place the year before the child was born or earlier.

2.1.3 Non-ionizing electromagnetic field exposure categorization in the Royal Norwegian Navy and reproductive health (Paper II)

Based on the findings in paper I, paper II further investigated the possibility of any influence on male reproduction from ELF- and RF EMFs experienced during service in the RNoN. Paper II investigated infertility, number of biological children, children with congenital anomalies, stillbirths, perinatal deaths and deaths within first year of life in the RNoN. To investigate the influence of non-ionizing EMFs, we chose to evaluate the military men who had responded to the questionnaire, since many of these were known to be working with equipment causing exposure to non-ionizing EMFs.

2.1.3.1 Expert categorization

To reduce possible misclassification due to self-reported exposure to non-ionizing EMFs reported in paper I, we established an expert group for determining which work categories in the RNoN were related to non-ionizing EMF exposure.

The group comprised eight persons all of whom worked with protection from- or research on non-ionizing EMFs. Four of these were from the RNoN and were involved in the RADHAZ project and health services in the RNoN. One was from the Norwegian Radiation Protection Authority and three were doing research on non-ionizing EMFs. The group discussed all 18 work categories listed by the RNoN in the first questionnaire and grouped the categories “tele/communication”, “radar/sonar” and “electronics” as exposed to non-ionizing EMFs on at least a weekly basis. These three work categories, therefore, were listed under the title “exposed to non-ionizing EMF”. The workers in “tele/communication” were primarily workers who repaired communication equipment, radio operators or communication workers in the operating room on-board the vessels. The workers in “radar/sonar” were navigators on vessels or at land based installations that used radar and other navigation equipment. The “electronics” category comprised people that performed repairs on communication systems and produced electric parts for weapon- and communication systems. They worked mainly in workshops. All the other work categories in the RNoN, a total of 15, were grouped as “not exposed”.

2.1.4 Statistics (Papers I and II)

Paper I used the prevalence ratio (the ratio between the prevalence odds) with 95 per cent confidence interval as an estimate of the possible relationships between the places of service and prevalence of congenital anomalies and stillbirths/perinatal deaths. Results from the “KNM Kvikk” were compared with all other places of service combined, with service on other vessels and with service on other MTBs. In comparing groups, we used Pearson’s Chi square test or Fischer’s exact test for the categorical variables, while Student T-test was used for the continuous variables.

Paper II analysed the work categories “tele/communication”, “radar/sonar” and “electronics” separately compared to the “non-exposed” work categories. Student T-test was used for continuous variables and the Chi square test for categorical variables. In addition, Fischer’s exact test was used for numbers below 5 in one or more cells. Smoking was differentiated by the subject’s indicating whether he had ever smoked or not, and the use of alcohol was quantified by the number of “standard units of alcohol” below or above 15 per week[62]. Adjustments were made for the variables that differed between the groups (age, ever smoked, military education and physical exercise at work) using a logistic regression model. The statistical significance levels in both papers I and II were set at $P < 0.05$.

2.2 Exposure to electric fields in the Royal Norwegian Navy (Paper III)

Paper III presents the findings from a dosimeter study measuring RF E-fields on-board two vessels in the RNoN; a MTB of the “Hauk” class and a submarine of the “ULA” class. The “Hauk” class was the class replacing the “Snøgg” class to which the “KNM Kvikk” belonged. The vessels in the “Hauk” class are very similar to the “KNM Kvikk”, but with different equipment. The vessels have short distances between the field emitting equipment such as transmitters, receivers and antennas and the crew on-board compared to larger vessels. In the period available for measurement, a submarine was also available and was chosen for measurement. It is of similar size to the MTB, but has a different operating pattern. While the MTB operates above sea level and often uses radio- and navigation equipment, the submarine operates mostly below sea level and strives to be as silent as possible with regard to radio- and navigation equipment.

2.2.1 The measurements of electric fields

The MTBs of the “Hauk” class are very fast, small patrol boats of 36.5 m length and 6.2 m width. They are normally equipped with torpedoes, missiles and a canon. The submarines of the “Ula” class are small underwater combat vessels of 59.0 m length and 5.4 m width equipped with torpedoes. Both types of vessels have extensive amounts of navigational, communications and weapon guidance systems all of which emit non-ionizing EMFs when in use.

All measurements were done during normal activity on-board the vessels. For measurement of the E-fields, the NardAlert XT 8860 was chosen. NardAlert XT is a small instrument produced by Narda Safety Test Solutions that can fit in a breast pocket. It is primarily used as a battery-operated RF personal monitor for individuals working in areas with exposure to RF EMFs. It measures E-fields in the frequency range of 100 kHz to 100 GHz. In this study, the instrument was set to register the exposure to E-fields every second. The results of the measurement were later downloaded to a computer and viewed as an excel-file with the result as percentages related to the guidelines given by ICNIRP.

Each measurement lasted for one work period (typically 4 hours). During daytime, all measurements were primarily done while personnel carried the instruments, while during night-time the instruments were stationary and located where the personnel were normally found (i.e., sleeping quarters and mess). At the end of each measurement period the data were downloaded to a computer and the people monitored were interviewed about the main work location and movements during the shift. Also, to have the possibility of investigating influence from different sources on the E-fields measurements, the use of radio equipment and weapon systems use was plotted by time.

Nine officers and enlisted personnel were monitored in the MTB, and eight of these were measured twice for better accuracy. The personnel on-board the MTB were divided into those working primarily above deck and those working below deck to investigate if the exposures were different relative to position on-board. In the submarine, seven officers and enlisted personnel were measured.

2.2.2 Statistics

The data were given in percentages of ICNIRP guidelines and comparisons of these given percentages for the different locations were done by the non-parametric Kruskal-Wallis test in SPSS. Significance level was set at $P < 0.05$.

2.3 Magnetic resonance imaging study (Paper IV)

Paper IV investigated a known source of non-ionizing EMFs and the possible influence this could have on hormones relevant for male reproduction. An MRI investigation represents one of the most intense non-ionizing EMF exposures one can receive today on a "normal" basis[63]. Young male medical students were recruited for this study. Extensive information about the study was given both orally at information meetings and in writing by mail, and there were several inclusion criteria that had to be met. All subjects had to be healthy, non-smoking, Caucasian, male medical students in the age range of 18–40. They could not have had previous exposure to solvents or oil vapour, or have previously worked in areas with a risk of exposure to RF EMFs, such as in welding, work aboard FPBs in the Navy or as members of electronic warfare units in the army. They could not have been involved in amateur radio activity. The normal MRI exclusion criteria also had to be met with regard to the absence of metals in the body, no history of head-, eye-, ear- or heart surgery and no claustrophobia.

A total of 60 persons were interested in participating in the study and of these, 30 persons agreed to be on a calling list. We recruited 24 of these in the study. The participants had several requirements regarding their activity, sleep pattern, ability to drink coffee, alcohol and use of certain substances before each investigation in the study.

2.3.1 Design

A balanced crossover design was chosen in this study consisting of three sessions with an interval between each. Each session began with a 30-minute preparation period, during which the participants relaxed and filled out a questionnaire (Figure 5).

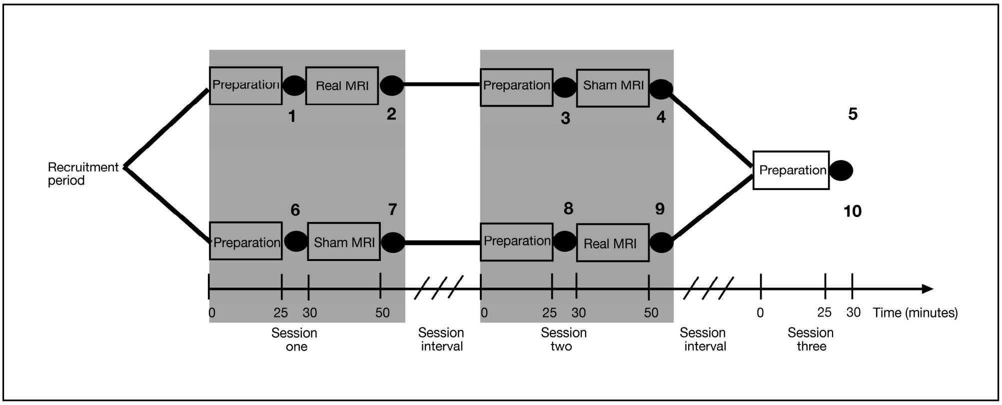

Figure 5: Cross-over design in the MRI study
MRI: magnetic resonance imaging
●: Blood sampling

In this study two different questionnaires were used. The first (which they filled out at the first session only) had background questions such as years of study, height and weight, number of biological children, use of cell phone (minutes and number of calls per day), hours of physical exercise per week and general health. The second questionnaire was filled out before every session (a total of three times) and had questions on transportation to the location, hours of sleep the preceding night and the extent of their physical activity and cell phone activity during the previous week compared to what they answered in the first questionnaire. In addition to this, the questionnaire also had questions on whether or not the participant had been sick during the previous week and if so what the nature of the illness was. The participant also had to confirm that they had not drunk coffee, tea, beverages containing caffeine and/or alcohol or taken any other central stimulating substances during the previous 12 hours. After this preparation period, a blood sample was immediately drawn and, at sessions one and two, the participant was guided into the MRI-area for either a real MRI investigation or a sham investigation. The investigation lasted for approximately 20 minutes, after which a new blood sample was taken immediately. At the third session only a blood sample was taken and no investigation with real- or sham MRI was done.

2.3.2 Magnetic resonance imaging exposure

A real MRI investigation was conducted in a 1.5 Tesla General Electric Signa EXITE scanner. The scanner had a transmitting body coil and a receive-only head coil; this means that all exposures in the MRI machine (B-fields and RF EMFs) were to the whole body. All pictures taken were examined by a neuroradiologist and revealed no pathology. The sham MRI was given by a MRI-machine copy produced and owned by Nordic Neuro Lab. The device is normally used for training children or persons with claustrophobia before a subsequent examination in real MRI, in addition to testing study designs for the MRI environment. The machine is basically produced of fibreglass with a movable body-board and a sound-stereo system simulating the experience in the real MRI.

2.3.3 Blood samples

Five blood samples were taken from each participant (Figure 5). The following hormones were analysed to assess a broad spectrum of male reproductive hormones: LH, FSH, testosterone, SHBG, inhibin B, PRL, E2 and thyreotropine. Due to diurnal variations in the normal hormonal profile, all blood samples had to be taken in the time period between 07:00–10:00 a.m.

We used three laboratories to conduct the analysis in this study. The Hormone Laboratory at Oslo University Hospital, Oslo, Norway is accredited as a sample laboratory and was responsible for analysing Inhibin B using the internationally approved method. The Hormone Laboratory at Haukeland University Hospital, Bergen, Norway is not accredited, but is responsible for performing hormonal analysis in the “Helse Bergen” regional health authority in Norway. The laboratory, for the purposes of this study, was responsible for analysing the hormones FSH, LH, E2, PRL, SHBG and testosterone using internationally approved methods. The Laboratory for clinical biochemistry at Haukeland University Hospital, which is accredited as a sample laboratory, was responsible for analysing the hormone TSH using the internationally approved method.

2.3.4 Statistics

To analyse the material, the word "pre" was related to the blood samples drawn immediately before receiving an exposure (real or sham). The word "post" was related to the blood samples drawn immediately after the exposure. The word "post2" was related to the first sample taken at the next session (Figure 5). Significance level was set to $P > 0.05$.

In the real and sham MRI paired samples, the T-test was used in separate analysis to investigate whether mean hormone levels changed:

- From the samples drawn at the beginning of the study and at the end of the study.
- From the "pre" to "post".
- From "pre" to "post2".

Paired samples T-test were used to investigate if there were differences between the real and sham MRI in terms of changes in the mean hormone levels:

- From "pre" to "post".
- From "pre" to "post2".

In addition to these tests, it was also investigated whether there was an effect associated with the order in which the participants had received their exposures. For this reason, all analyses were done separately for those receiving the sham MRI first and those receiving the real MRI first. There were no significant changes among the groups.

A power calculation was conducted beforehand giving us a needed sample size. Figures from a previous published study on inhibin B change among volunteers with normal and impaired spermatogenesis were used[33]. To detect a difference in inhibin B of 20 pg/ml, a sample of 24 participants were investigated, giving a statistical power of 96.9 per cent.

2.4 Ethics

The research programme HSE Navy was approved by the Regional Committee for Medical Research Ethics in Western Norway (89.02/2002 and 120.04/2004) and the Norwegian Data Inspectorate (2002/1224-3 and 2004/11286). The research programme was granted full freedom of publication through an agreement between the RNoN and the University of Bergen. Written consent was given by all participants, and all data containing personal identification at the University of Bergen were destroyed in 2008. The RNoN decided that the questionnaire survey had to have full personal identification on the forms to ensure storage in the Registry of the Norwegian Armed Forces Medical Services. An opportunity to decline participation and linkage with other medical registries was given. If the participants did not claim a reservation against linkage, the data are still stored in the Registry of the Norwegian Armed Forces Medical Services.

The research programme MRI study was approved by the Regional Committee for Medical Research Ethics in Western Norway (2010/1271) and written consent was given by all participants. All data containing personal identification will be destroyed by December 2015.

3. RESULTS

3.1 Cross-sectional study (Papers I and II)

3.1.1 Questionnaire (Paper I)

Paper I in the cross-sectional study investigated 2265 respondents and their reproductive outcomes.

3.1.1.1 Congenital anomalies

Of all 1438 parents and 3122 biological children there were 83 parents reporting a total of 97 children with congenital anomalies. Eleven children with congenital anomalies had a parent who had served on-board the “KNM Kvikk” as recently as one year prior to birth. This gave a prevalence ratio (PR) of having a child with congenital anomaly of 4.9 with a 95 per cent confidence interval (CI) 2.5 - 9.6 if the parent had served on the “KNM Kvikk” compared with respondents who had not served on-board the “KNM Kvikk”. Compared with respondents who had served on-board any vessel, the PR was 4.3 (95 % CI 2.2 - 8.7) and compared with respondents who had served on other types of MTBs, the risk was 4.0 (95 % CI 1.8 - 8.9). The parents were on average 30 years of age when the children with anomalies were born compared to 31 years of age when the children without anomalies were born.

3.1.1.2 Stillbirths and perinatal deaths

The PR of having a stillborn child or one that died within one week was 4.1 (95 % CI 1.7 - 9.9) if a parent had been working on-board the “KNM Kvikk”, compared to all other respondents. Compared with parents who had served on-board any vessel or MTB, the respective ratios were PR 3.6 (95 % CI 1.5 - 8.9) and PR 2.7 (95 % CI 1.0 - 7.5). Both sexes were present among parents who had served on-board vessels, and on average the parents who had experienced having a stillborn or perinatal child death was 30 years of age compared to 31 years of age for the parents who had not experienced this. All analyses were done separately for men only, with similar results. For women, such an analysis was not possible due to the small numbers of subjects.

3.1.1.3 Lifestyle and self-reported exposures

The personnel who had served on-board the "KNM Kvikk" did not differ from the other respondents with regard to use of alcohol, smoking, heavy lifting, work in twisted positions or body mass index.

During the investigation of the self-reported exposures, the personnel who had served on-board the "KNM Kvikk" reported a higher degree of exposure to oil/ gasoline/ diesel vapour, exhaust gas, noise, vibration and shaking, work close to high frequency aerials/communication installations and radars compared to other respondents. Most of these exposures are related to work on-board vessels, and especially smaller vessels. But also, when compared with other MTB crew members, the personnel who had served on-board the "KNM Kvikk" reported a higher degree of exposure to oil/gasoline/diesel vapours, exhaust gas and noise.

3.1.2 Expert evaluation of congenital anomalies (Paper I)

A total of 97 children of personnel in the RNoN had congenital anomalies, and extra information was obtained concerning 84 of these in the second questionnaire. An evaluation by paediatricians at Haukeland University Hospital reduced the number of children with congenital anomalies to a total of 70. Among those children having a parent influenced by the "KNM Kvikk" the reduction was from 11 with anomalies to 8. Taking this evaluation into consideration, the PR of having a child with a congenital anomaly among the personnel who had served on-board the "KNM Kvikk" at least one year prior to birth was 4.0 (95 % CI 1.9 - 8.6) compared with respondents who had not. Compared with respondents who had served on-board any other Navy vessel or only on an MTB, the risk was still elevated, respectively 3.5 (95 % CI 1.6 - 7.7) and 3.4 (95 % CI 1.4 - 8.6).

3.1.3 Non-ionizing electromagnetic field exposure categorization in the Royal Norwegian Navy and reproductive health (Paper II)

The workers in this study were military men, on average 36 years of age. Using the expert classified exposed work categories, both the “tele/communication” and the “radar/sonar” workers displayed a higher proportion of workers who answered yes to the question regarding whether they had ever experienced infertility compared to unexposed workers. Compared to the unexposed group, the odds ratio (OR) for experiencing infertility was 1.72 (95 % CI 1.04 - 2.85) for the “tele/communication” group and 2.28 (95 % CI 1.27 - 4.09) for the “radar/sonar” group. The results remained unchanged after logistic regression adjusting for possible confounding factors such as years of age, ever smoked, military education and physical exercise at work. The expert classified exposed work category “electronics” showed no increased risk of infertility. No differences in the number of biological children, paternal years of age at first child, occurrence of congenital anomalies, preterm births, stillbirths, perinatal deaths or infant deaths within the first year of life were seen when comparing the groups.

The workers in the exposed categories had graded their self-reported exposures to non-ionizing EMFs differently. The “tele/communication” and “radar/sonar” groups reported significantly higher exposures to non-ionizing EMFs compared to the unexposed categories while the “electronics” group did not report higher exposures. For all other factors, the expert classified exposed work categories generally reported lower exposures compared to the classified unexposed work categories.

3.2 Exposure to electric fields in the Royal Norwegian Navy (Paper III)

On the MTB, the measurements were done during training and drilling of a new crew at sea outside Bergen, Norway. In the submarine, the measurements were done during transport voyage from Edinburgh, Scotland, to Bergen, Norway, with occasional attack drills. The main sources of exposures in both vessels were the general E equipment, communication and navigation equipment.

3.2.1 Missile-torpedo boat

Twenty measurements were done on the MTB. The exposure to E-fields was generally low, averaging 0–10 per cent of the ICNIRP guidelines. Although low, the levels varied and some small differences did exist. A typical position below deck was that of the operation room officer, who seldom left his post; his levels varied between 0–6 per cent of the guidelines, averaging 1 per cent. The artillerist who was mostly above deck had a significantly higher exposure (Kruskal-Wallis test $P < 0.01$), varying between 0–10 per cent of the guidelines and averaging 4 per cent. Use of radio transmission equipment gave a small increase in exposure, but still low compared to the guidelines.

3.2.2 Submarine

Thirty-six measurements were done in the submarine, and the exposure to E-fields was low, averaging 0–10 per cent of the ICNIRP guidelines. There was no difference in E-field exposure when the submarine was submerged versus surface voyage. The position in front of the sonar screen was measured with peak levels up to 264 per cent of the guidelines, but this was related to a malfunction of the screen.

3.3 Magnetic resonance imaging study (Paper IV)

In paper IV, all 24 students who joined the study completed all sessions; real, sham and control. The participants were between 19 and 35 years of age; they reported fair health or better, had no children and had a body mass index (BMI) averaging 23.4 kg/m^2. The intervals between the sessions were planned to be seven days, but this became impossible to achieve and the final average was therefore 11 days. From a questionnaire on the volunteers' activities during the different weeks preceding the sessions, we found no systematic differences with regard to physical activity-, sleep patterns or use of cell phone during the different weeks.

3.3.1 Hormonal values

All values investigated in this study were within the normal range given in the respective laboratories. No differences were found in real or sham MRI sessions when analysing the mean hormone values:

- From the beginning of the study to the end of the study.
- From before the exposures compared with after the exposures
- From before the exposures compared with the sample drawn on average 11 days later.

Nor were any differences found when investigating whether the mean hormone levels changed differently in real compared to sham MRI sessions.

4. DISCUSSION

The focus of this thesis has been male reproduction and non-ionizing electromagnetic fields. The discussion in this thesis is based on the combined results from cross-sectional surveys in a working environment, a dosimeter study investigating the levels of exposures in that working environment today and an experimental study investigating a possible acute impact of non-ionizing electromagnetic fields on male reproduction.

4.1 Methodological discussion

4.1.1 Design

Different designs are used throughout this thesis. Papers I and II used cross-sectional study design; paper III used field measurement study design and paper IV used a prospective randomized balanced crossover design. The cross-sectional design has limitations in drawing causal conclusions; however such studies are useful in obtaining information quickly from large populations and for generating hypothesis. A large population was needed to study the prevalence of congenital anomalies, which is a relatively rare condition. However, to investigate further the possible causal relationships between non-ionizing EMFs and male reproduction, more information on the exposure to non-ionizing EMFs and reproductive outcomes were needed. Therefore a field measurement study and a prospective randomized balanced crossover study were conducted.

4.1.2 Questionnaires; reliability and validity

Papers I and II were based on the same questionnaire[64]. The majority of the questions used were from validated instruments. The questions on children health and infertility were selected and modified from the questionnaire used in ESIS, which also discussed the quality of the questionnaire information and how valid the retrospective information should be considered[36]. Although, differences in different cultures may exist, the ESIS found that it seems to be a good correspondence between information gathered retrospectively and information obtained from, for instance, hospital records with regard to periods of infertility and past pregnancies and events. The work history in the questionnaire was developed for the project in cooperation with the RNoN to ensure correct work categories, places of service and similar important issues to make it understandable for the employees of the Navy. The part of the questionnaire assessing different exposures had some limitations, especially related to assessing non-ionizing EMF exposure. The participants were to grade their contact with different exposures using a six-grade scale; never – very little – some – a lot – very much – and do not know. For the non-ionizing EMF exposure three different questions were asked; "Have you in your work, now or previously, worked closer to a high frequency antenna than 10 meters?" "Have you in your work, now or previously, worked closer to communication installations/ transmitting antennas than 3 meters?" And "Have you in your work, now or previously, worked closer to radar than 5 meters?" Non-ionizing EMF was not defined in the questionnaire and includes everything from E-fields to radar exposures. This may have led to misclassification of exposures.

The participation rates in papers I and II were 58 per cent and 63 per cent respectively. The low response rate could have influenced the results, especially in paper I since the number of cases of congenital anomalies was very low. The participation rates were consistent with what is seen in similar studies[65, 66]. Reasons for not achieving an even higher response rate could have been the pre-printed name, personal identification number and the extensive task of having to fill out 19 pages. The extensiveness was chosen as the project HSE Navy had many objectives and was designed to investigate several different aspects of the working environment. The low response rate might have meant that we got a higher, lower or similar proportion of responses from the workers with problems in the Navy when compared to workers without any problems. We are unable to determine this because we did not have complete information about the non-respondents. However, we did have information regarding the age, military or civilian employment and gender of the non-respondents[67]. More males responded than females (58.8 % compared to 52.4 %), the respondents were on average 2 years of age older than the non-respondents and, for the military personnel, they were 4 years older. For the military personnel, there was no difference in the sex distribution among respondents compared to non-respondents.

General information bias may be present in such a large questionnaire study due to wrong answers by the respondents and scanning errors. Therefore, a random selection of 10 per cent of the questionnaires was made, and these were inspected manually for errors[64]. This investigation revealed on average one error per 579 variables per scheme, which was considered acceptable. Also misclassification[68] regarding reproductive health might have occurred in paper I, as the parents from the "KNM Kvikk" could have reported more anomalies compared with the rest of the study population because of the publicity this vessel had received earlier. This might have given differential information bias. This was one main reason for doing the validity check at the hospital by means of information from a second questionnaire sent to all parents in the Navy who had answered that they had a child with a congenital anomaly in the initial questionnaire.

To have an opportunity to control for possible confounding factors, several questions on life-style factors were asked in the questionnaire. Smoking, years of age, alcohol, chronic diseases, BMI and environmental exposures can all affect the reproductive ability of man[35]. In paper II, the groups differed in number of workers who ever had smoked and this was adjusted for in the analyses. Paper I had no differences in smoking status among the respondents with exposure to "KNM Kvikk" compared to other respondents. Age is important in investigating reproductive ability in men, and decreased sperm quality is seen after the age of 35[43]. However, the participants' mean age in all papers was below 35 years of age and the small differences seen between the groups were deemed unimportant. The workers in the RNoN were generally very healthy[69] and the use of alcohol, BMI and incidence of chronic diseases did not differ among the groups in papers I and II. Environmental exposures were assessed through self-reporting in the questionnaires on both exposures at work and outside work. We used regression analyses to remove the effect of eventual differences in such exposures between the different groups.

Common method bias is of importance in our cross-sectional studies, especially in paper I, since both the exposure and the health outcome variables were collected from the same questionnaire[70]. In paper I, this might have been important since the parents who had a child with congenital anomaly and had served on-board the “KNM Kvikk” might have remembered this service better than the parents who had no children with a congenital anomaly, thereby seemingly creating an excess of children with congenital anomalies after service on-board the ”KNM Kvikk”. An overestimation of the risk might also have occurred if the parents who had served on-board the ”KNM Kvikk” reported the health of their children correctly but the rest of the employees in the RNoN underreported their children’s conditions. The overall prevalence of having a child with congenital anomaly was 2.6 per cent (after paediatric evaluation) in the questionnaire survey. This figure is consistent with the international prevalence of 1–7 per cent[71-73] and with the prevalence in Norway estimated to be 2–3 per cent in the period 1967–1996[74] and indicates that a large overrepresentation did not occur. In paper II, common method bias is less likely to be of importance since the classification of exposed and non-exposed was based on expert classification of work categories and not by the respondents themselves[75].

In paper IV, an effort was taken, during the inclusion of participants, to avoid participants with known environmental exposures that could be harmful to reproduction; in addition, questionnaires were given to quantify, for instance, the use of cell phones, physical activity, sleep and on-going diseases.

4.1.3 Exposure assessment to non-ionizing electromagnetic fields

Exposure assessment is one of the most important aspects in research on non-ionizing EMFs and health[10].

Self-reporting

Paper I uses self-reported exposure to describe the working environment on-board a specific vessel in the RNoN. Self-reported exposure to non-ionizing EMFs is a very crude measurement. There is considerable ignorance with regard to what non-ionizing

EMFs are and how one is exposed to them. The questions used in the questionnaires in papers I and II relate to how close to various non-ionizing EMF emitting equipment the employee had worked. For the employee, it would be easy to relate this to the antennas on-board the vessels, but few employees would have information on where the cables were located on-board and the questions had limitations. For the smaller vessels in the RNoN, all employees on-board would be within 10 m of the aerials most of the time. For the larger vessels, this discrimination of distance from equipment would be more suitable. Regarding the questions on radar exposure, a definition of radar would have improved the answers. An employee working with the radar screen on-board could report high exposure to radar, while in reality, he is little exposed due to the fact that the equipment emitting the radar beam is located at the top of the vessel.

Expert categorization

In paper II we tried to improve the shortcomings of the questionnaire. The exposure was classified by using expert classification of the self-reported job categories given in the questionnaire. However, this categorization also left doubt as to the extent of the exposure and what type of non-ionizing EMFs personnel had received, because non-ionizing EMF was not defined. The "electronics" group did not differ from the unexposed in terms of reproductive outcome, contrary to the other two groups. This group consists mainly of workers in workshops who will be mostly exposed to the ELF EMFs. On-board vessels the "tele/communication" and "radar/sonar" workers will receive exposure mainly from the RF EMFs. This could explain the differences seen.

Measurements

Paper III used objective exposure measurements done on-board two vessels with personal measurements through a dosimeter. Objective personal measurements of non-ionizing EMFs is considered the best way to describe exposure to non-ionizing EMFs[10]. The instrument was chosen as this was the only instrument at the time that could perform personal measurements of E-fields in a large frequency area (100 kHz–100 GHz), which is the RF part of the EMFs. However, the instrument could not measure the B-fields. For the far field, the B-fields can be calculated, while in the near field region it is recommended to measure both the B- and the E-fields because they behave independently of each other. The near field includes most of the surface of the vessels measured. However, given how small the E-fields measured were, the possibility of finding large B-fields on-board these vessels is unlikely.

The work activity of the personnel measured would influence the measurements and is a weakness[76]. A strict protocol must be followed, and preferably the researcher should supervise the personnel at all times. This was not always possible on-board the vessels, although a researcher was present. Specific activities could lead one to remove the dosimeter while the task was being performed. The personnel could also place the dosimeter in other positions than their own and get higher (for example adjacent to field emitting equipment like antennas) or lower (for example leaving it under deck while tasks are being performed above) readings. Also the activities of the vessels could influence the measurement. The levels may be higher if there is a higher level of use of radio and weapon equipment. This was not the situation during the period when measurements were taken.

The low levels of E-fields measured on-board the MTB and the submarine indicated that non-ionizing EMF exposure in the populations in papers I and II was low. However, the RNoN historically has had different types of equipment, and exposure levels may have varied. Regarding the “KNM Kvikk”, the level of use of radio and weapon equipment was most likely higher than on-board the vessels measured in paper III due to the usage of the vessel in electronic warfare in addition to its being differently equipped[1].

The dosimeter study was conducted on only two navy vessels, but comprised altogether 56 measurements. The measurement method has some uncertainty with regards to the measurement results, as the E-fields are highly fluctuating. Not many studies have been done measuring E-fields using personal measurements. Other studies conducted on B-field exposures have found instrumental uncertainty of 15 per cent[77]. However, even with an uncertainty of 50 per cent, the levels found in paper III would still be low. The study by Baste et al. also assessed the exposure levels on-board

FPBs as being low, with some exceptions pertaining to some of the cabins located above deck on the "Snøgg" and "Hauk" class of MTBs[29].

The numbers of measurement samples came about as a result of trying to accommodate the shift schedules on-board and the time given on-board. These were the maximum number of samples possible, given the available time. The study gave a good description of the E RF EMF conditions on-board during normal transport sailing.

A known high exposure environment

To investigate possible acute effects from non-ionizing EMFs and especially RF fields on male reproduction, a known source for RF fields was used in paper IV, namely the MRI. During a MRI scan, the subject is exposed to known quantities of static B-field, gradient B-field and RF field. The procedure is being used increasingly throughout the world, and there are now an estimated 20 000 MRI machines worldwide.

The MRI used was a 1.5 T GE Signa EXITE scanner from General Electric with Echospeed gradients (33 mT/m, 120 T/m/s). The scanner had a transmitting body coil; this means that the RF field given to the participant is delivered to the whole body, while it had a receive-only head coil. This is different from more modern MRI machines which often have a transmitting- and receive coil that can be placed over the area of interest (for example the head) thereby giving RF EMF exposure only to that part of the body and lowering the level of necessary exposure. The scanners estimate the SAR based on the subject's weight to estimate what RF dose it can deliver during the procedure to not exceed the ICNIRP guidelines. This calculation gave an estimated mean average whole body SAR of 0.29 W/kg in paper IV. The protocol chosen was an anatomical head scan lasting 20 minutes. This machine, and this protocol, was chosen because it is the most commonly used machine and protocol in the Western world.

There were uncertainties in the exposure assessment in the MRI because it was not measured independently during the different scans. The RF estimation produced by the machine was based on average exposure of the subjects. It did not take into account the intense peaks of exposure which were present in the MRI during scanning sequences. The machine estimates the RF dose by weight, not accounting for distribution of fat- contra muscular tissue. A large amount of fat tissue will give a larger SAR compared to the same RF dose given to a large amount of muscular tissue. The time also varied somewhat, giving some uncertainties concerning how the RF dose was delivered and finally how large an SAR the volunteers had gotten. In addition this SAR was underestimated as the machine did not give parameters and estimations of RF dose for the two longest sequences in the protocol.

The exposure duration given in paper IV could have been too short to cause any effect. In a similar study by Lee et al.[58] genotoxic effects were seen in lymphocytes, but not until the exposure time was more than 22 minutes. Also, the MRI used in the Lee et al. study had a larger B-field of 3 T and the protocol used was different. Another article showing the effects of MRI on micronuclei formation in lymphocytes derived from volunteers who had received a cardiac scan in MRI also had a longer exposure time in the MRI before seeing effects[59].

Blinding of the participants in paper IV was difficult to achieve due to the different locations of the real and sham MRI machine. An anticipated effect by the volunteers of the real MRI may have influenced the results. The persons doing the blood analysis at the laboratories were blinded as to what exposure the samples had received.

The MRI delivers three types of non-ionizing EMFs. Segregation of responsible field would have been important if effects had been found.

4.1.4 Blood samples

Blood sampling was performed by experienced researchers and analysed in high-quality laboratories. All samples were treated in the same way and according to the international guidelines. All samples were taken at fixed times in the morning, this, together with assessing several hormones relevant for male reproduction, is a strength in our study[78, 79]. Previous studies have assessed fewer hormones [50-52, 54]. The hormones measured in this study may have been affected by an influence of non-ionizing EMFs on the hypothalamus/ pituitary gland through FSH, LH, TSH and PRL. In addition a possible influence of non-ionizing EMFs on the testicles and on spermatogenesis itself could have affected inhibin B, testosterone and E2. Hormones change continuously, and the levels in the blood are therefore constantly changing due to diurnal rhythm and other influences[34, 78], thus making it important to assess hormones at fixed times.

In examining infertile couples, the males are investigated by semen samples and often also blood samples of FSH and LH. The hormones are used as indicators of possible syndromes leading to infertility[43]. Other examinations are often dependent on the findings in several semen samples.

Semen samples were not chosen as an outcome for male reproductive health in this study for two reasons. Firstly; semen is produced continuously and in a three month cycle. Therefore to assess semen correctly, there would be a need for repeated semen samples preferably every day for three months to investigate influence at all possible stages. Influences on the spermatogenesis at different stages may give alterations in the sperm after various durations of time with a maximum time of at least three months, making it practically very challenging to assess such changes.

Secondly; there are considerable methodological limitations entailed in the analysis of semen samples, which also makes it a very difficult variable to study[47]. Firstly, the normal limits given by the WHO on semen characteristics are not based on population samples of fertile men or unselected men. Laboratories analysing semen samples often use different limits and interpretations which result in large variations in the results. There is no clear-cut correlation between any single semen parameter and fertility. No single ejaculate sample can predict the fertility of a man. This also leads to the need for large sample size which is difficult to accomplish as the participation rate in studies on semen average on 50 per cent, often lower. The counting of sperm and evaluation of their motility and morphology has a large subjective component which is not removed even with computerized methods.

4.2 Main discussion

Not many studies exist which investigate the reproductive health of males in relation to their occupation, and especially not related to non-ionizing EMFs. In male reproduction, one effect on the father which could cause congenital anomalies, stillbirths or perinatal deaths in his offspring, or infertility, would most likely be a direct damage to the DNA in his sperm, damage that causes epigenetic (indirect) changes in the sperm, other damages to the process of spermatogenesis, a transmission of teratogen agents through the seminal fluid or a household contamination from substances brought home by the father (Figure 3)[3, 42, 43, 80].

Cross-sectional studies

Paper I found a significantly increased PR of having children with congenital anomalies among personnel who had served on-board the MTB "KNM Kvikk" compared to other employees in the RNoN; similar results were also seen for stillbirths and perinatal deaths.

The "KNM Kvikk", as previously mentioned, was a special MTB vessel in that it was a leading vessel and was used in electronic warfare. This meant that this vessel would have longer periods in service compared to other vessels, during which it would lie still to conduct electronic warfare. This could explain some of the increased self-reported exposure to vapour from oil, gasoline, or diesel and exhaust. It is known that several hydrocarbon compounds may affect reproduction[81, 82]. The amounts of exposure to hydrocarbon compounds on-board the "KNM Kvikk" and whether or not it was very different from the other MTB vessels is difficult to assess. However, it is unlikely that this exposure would be of the magnitude needed to affect reproduction.

The special tasks of the "KNM Kvikk" could also indicate that the personnel on-board this vessel were away from home for longer periods of time compared to personnel on-board other vessels; this is not known.

Also, since the levels of exposure to non-ionizing EMFs on-board the "KNM Kvikk" are not known, it is not possible to rule out that non-ionizing EMF exposure may have been high enough to cause thermal exposure levels at some point in time.

The findings in paper I are not contradictory to the previously published reports on the "KNM Kvikk". Both the report by "Sjøforsvarets forsyningskommando" (SFK)[1] and the NIOH report[3] has a non-positive conclusion in which they do not find direct documentation supporting an association, but neither can they rule out the association between service on-board the “KNM Kvikk” and reproductive outcomes. The main limitations mentioned especially in the NIOH report are the incomplete personnel lists from the RNoN at that time and incomplete exposure assessment which makes it difficult to draw a conclusion.

Paper II found an increased risk of having experienced infertility among personnel categorized as being exposed to non-ionizing EMFs in the RNoN through having worked in the categories “radar/sonar” and “tele/communication” compared to unexposed workers. No other reproductive outcomes were different among the groups.

Although few, there are some studies that have looked into the relationship between occupational paternal non-ionizing EMF exposure and reproductive health, but there are no consistent results between the studies.

Mjøen et al.[49] conducted a study in Norway investigating associations between the paternal occupational exposure to RF EMFs and adverse pregnancy outcomes using the MBRN and the Norwegian general population censuses which contain data on occupations coded according to the Nordic Classification of Occupations. An expert panel determined RF EMF exposure in the various occupations and graded these as being “probably not exposed”, “possibly exposed” and “probably exposed”. The study had no information on infertility, but had findings on reproductive outcomes which contradict our finding. Among the “probably exposed” occupations, they found an increased risk of preterm births (OR 1.08) and a decreased risk of total cleft lip (OR 0.63). Among the “possibly exposed” occupations, they found a slightly increased frequency of male gender (OR 1.01), increased risk of other defects (OR 2.40) and a decreased risk of other syndromes (OR 0.75) and upper gastro intestinal defects (OR 0.61). The study had no other information on exposure which could have caused misclassification of exposure.

Two previous papers have been published concerning reproductive health in the RNoN[28, 48]. One paper investigates groups of personnel in the RNoN by self-reported exposures to non-ionizing EMFs, and the findings were in accordance with the findings in this thesis. With increased self-reported exposures, the self-reported one-year infertility increased significantly. The study also found a higher boy-to-girl ratio among personnel reporting a higher degree of exposure to non-ionizing EMFs[48]. The weakness of self-reported exposure was a problem. The paper was based on the same data material as paper I and II in this thesis, but the exposure assessment was different. A second paper linked a RNoN cohort with the MBRN. This paper found that work on-board a FPB over the last three months prior to conception gave an increased risk of perinatal mortality and preeclampsia compared with work on-board other vessels in this period. The study found no associations between acute RF EMF exposure and congenital anomalies, low birth weight, preterm births, SGA or sex ratio[28]. The RF EMF exposure for the fast patrol boats was calculated through a dose assessment using the RADHAZ reports in the RNoN.

A study by Irgens et al. from 1999 supports our findings in paper II, finding reduced semen quality among men exposed to non-ionizing EMF attending an infertility clinic with their partners[83]. Exposure to non-ionizing EMF was assessed through a questionnaire. The exposure assessment was a weakness of the study and other confounding factors could have been of importance. Several other studies have also seen a possible influence of non-ionizing EMF on fertility, but they often have methodological limitations[51, 54]. The limitations especially concerned exposure assessment, study design, sample size and procedures regarding blood- and semen samples. Hjollund and Bonde wrote a letter to the editor regarding their semen analysis of personnel operating military radar equipment which also displayed changes in the sperm samples of the military personnel[55]. However, later measurement did not reveal any exposure to microwaves present. Another study by Hjollund et al. investigated the impact of ELF B-fields on human fertility[56]. The study investigated 36 male welders compared to 21 non-welders. There were measurements of ELF B-fields through measurements with personal exposure meters during 60 hours of both the male and female partner. The semen variables and hormones were unrelated to the exposure measurements, but the sample size was small.

The groups in paper II differed neither in number of children nor in the age at which they had their first child. This could indicate that the infertility was more a time-limited infertility. However, there was no information on when the period of infertility was experienced, so it was difficult to ascertain the relation in time to exposure. The study did not find any increased risk of any other adverse reproductive outcome from being categorized as exposed to EMFs.

Dosimeter study

Paper III investigated the RF E-fields on-board two RNoN vessels and displayed the low levels of RF E-field exposure on these vessels. The levels were mostly between 0-10 per cent of the guidelines given by ICNIRP [10]. The levels measured are in line with findings in another study on civilian vessels in Norway[23]. Most other previous studies have measured B-field in other environments than on vessels[84, 85]. The preferred assessment of B-field is often chosen due to difficulties and uncertainties in assessing E-fields[86]. However, personal measurements of E-fields should also be done despite the limitations they have. One could speculate that there is a dose-response relationship regarding exposure to non-ionizing EMFs and male reproduction. Large fields such as might have been experienced on-board the “KNM Kvikk” could have led to congenital anomalies, still- and preterm births through mechanisms earlier described, while lower exposures seen more generally in the RNoN could chronically influence fertility. However, these are only speculations.

Magnetic resonance imaging study

Paper IV found no differences in the level of FSH, LH, TSH, PRL, SHBG, testosterone, E2 or inhibin B after a real 20 min standard anatomical head scan in a 1.5 T MRI machine. The same was true for the sham exposure. In addition, there were no changes in the hormone levels after, on average, 11 days. The finding indicated that the exposure did not influence spermatogenesis in men.

Other studies looking at hormones in response to RF fields have shown inconsistent results[50-53] and all have important methodological limitations. The study by Schräder et al.[52] is mainly in line with our study, but there was no actual measurement of exposure from the potential RF source. The study by de Seze et al.[53] found no influence on TSH, LH, FSH, PRL, growth hormone and adrenocorticotropin after investigating possible influence by RF fields emitted from a GSM telephone on the secretion of hormones from the anterior pituitary gland. Two other studies[50, 51] are not in line with our study and had findings from RF field exposure on hormones relevant for male reproduction. The study by Grajewski et al.[51] displayed increased levels of FSH among RF heater operators, while Gutschi et al.[50] found higher levels of testosterone and lower levels of LH in men having a cell phone compared to men not having a cell phone. The limitations of these studies are especially associated with exposure assessment, blood and semen sampling procedures, sample size and control of confounders.

Two other studies also contrast with our study, one from Korea and one from Italia, both looking at other endpoints after MRI exposure[58, 59]. The Italian study[59] displayed a dose-dependent increase in micronuclei formation in lymphocytes which had been exposed for a considerable period of time in the MRI scanner. In addition, an acute increase in micronuclei formation was seen in lymphocytes derived from volunteers who had been exposed to a normal cardiac MRI scan. The Korean study[58] displayed significant DNA damage, increased formation of micronuclei and chromosomal aberration after MRI exposure. However the methods used in these studies were different from ours and the clinical consequences of the findings are not known.

The non-ionizing EMF exposures used in both of these studies were larger than in paper IV of this thesis. In the study by Simi et al.[59] the in vitro treatment used four different exposure times in a 1.5 T MRI scanner ranging from 686 seconds until 2188 seconds with significant increased frequency of micronuclei after all exposures. The mass of the blood sample which was exposed was 0.03 kg, thereby giving the blood sample a much larger SAR value than what was experienced in the exposure used in paper IV of this thesis. Also, the in vivo experiment used larger exposure than in our MRI study. The participants received a cardiac MRI scan which lasts for a much longer time, on a standard basis, than the scan used in paper IV in this thesis. The study by Lee et al.[58] displayed in their Figure 2 that they did not have any significant effect in their in vitro experiment until the MRI scan had exposed the cells for 45 minutes or more.

The lack of effects on hormones seen in paper IV is reassuring, and the study may be seen as a precedent for future safety studies in MRI. However, the study does not rule out other possible effects on reproduction and on other endpoints. This should be investigated in future studies investigating these other endpoints and/ or using different exposure classification.

4.3 External validity

The "KNM Kvikk" was a leading vessel in the fleet unit and had a special responsibility for conducting so-called electronic warfare. This specific vessel probably had higher RF EMF exposures on-board than other naval ships[1, 29]. One hypothesis is that the RF EMF exposures could have led to the effects seen in reproductive health, but this is difficult to ascertain. Other factors may also have contributed. The working environment on-board this vessel was very special, and it is difficult to apply the findings to other vessels in the RNoN. The importance of the findings on congenital anomalies and stillbirths/perinatal deaths is more difficult to generalize since the causes are unknown.

The RNoN as a workplace is changing rapidly, with continuous modernizing of the fleet as well as changes in their operating qualities. The work categories "radar/sonar" and "tele/communication" were related to increased OR of infertility compared to other work categories not exposed to non-ionizing EMFs. The work categories do not exist in the RNoN any longer, and the finding is not possible to generalize to land based work categories. But there might be navies in other countries that still use these work categories.

The majority of studies in this thesis were conducted in the RNoN (Papers I, II and III). Selection bias[68] was likely to occur in the RNoN since there were demands on the physical condition of all employees, especially when they are admitted to the Navy, but also continuously during their service in the Navy[64, 69]. Both selections for service due to good health and de-selection out of the service due to health problems were likely occurrences. The military personnel were regularly inspected by health authorities to insure that they were fit to serve. This would most likely have given them prevalence rates for diseases, for example, which were lower than for the general population and made it important to compare populations within the Navy. Despite these weaknesses, an increased risk of negative reproductive outcomes was found, but as previously mentioned generalizing from these findings is difficult when the causes are unknown and more research is needed.

The MTBs used when the project HSE Navy was performed have been sold and new and modern MTBs are in place with different constructions, numbers of crew and tasks. However, it is important to remember that similar vessels can be in service in other navies and equipped in similar ways. For these vessels, the findings of low exposure to E-fields are important. This finding of low E-fields on-board the RNoN vessels can also be generalized to other civilian vessels, as it is unlikely that the exposure on civilian vessels is higher than on military vessels due to a lower proportion of non-ionizing EMF emitting equipment.

The acute effects from RF EMF on male reproductive hormones were investigated after conducting an MRI investigation without finding any effects. This finding can be generalized to young males receiving a 1.5 T MRI investigation with regard to acute and short term effects on hormones relevant for male reproduction. Other endpoints were not studied, neither possible chronic effects from repeated low level exposures.

5. CONCLUSION

The main objective of this thesis was to gain more knowledge regarding the possible link between exposure to non-ionizing electromagnetic fields and male reproduction.

Paper I showed a significant increased risk of self-reported congenital anomalies, stillbirths and perinatal deaths among children of personnel who had served on-board the “KNM Kvikk” compared to other personnel in the Royal Norwegian Navy. The causes of these findings are unknown.

Paper II concludes with a significant increased risk of self-reported infertility found among male military personnel who were categorized by an expert panel as being exposed to non-ionizing electromagnetic fields when compared with other, non-exposed personnel in the Royal Norwegian Navy. There were no differences between the groups regarding the number of biological children, children with congenital anomalies, stillbirths, perinatal deaths or children who died within first year of life.

Paper III displays that the exposure to radio frequency electric fields on-board two Royal Norwegian Navy vessels was very low. There were minor differences in regards to location on-board, with higher exposure above versus below deck.

Paper IV could not detect any significant immediate or short term change in levels of hormones relevant for male reproduction among male volunteers who received acute exposure to non-ionizing electromagnetic fields in the form of a magnetic resonance imaging scan.

Overall conclusion

Based on the objectives and results of this thesis, and seen in light of the studies' limitations, this thesis concludes that:

The studies in this thesis could not establish non-ionizing electromagnetic fields as a cause for the findings in paper I and II, but neither could the thesis explain the findings.

Low levels of radio frequency electric fields on-board two vessels in the Royal Norwegian Navy have been documented, indicating low risk of high exposure to radio frequency electric fields in the Royal Norwegian Navy.

No support was found for an effect of acute exposure to non-ionizing electromagnetic fields on reproduction through influence on hormones relevant for male reproduction.

6. FUTURE PERSPECTIVES

The Royal Norwegian Navy

The low exposure levels to electric fields found in this thesis on the Royal Norwegian Navy vessels gives little cause for concern regarding non-ionizing electromagnetic field exposure and risk of effects on the male fertility of navy servicemen today. Awareness is nevertheless needed, as we do not know the full picture. Continued focus and work in the Royal Norwegian Navy through the project Radiation Hazard is important in this respect to control exposure levels, since vessels and equipment in the Royal Norwegian Navy are often changed.

Research

Other endpoints, exposure levels and durations of exposure than those studied in this thesis should be further investigated. Endpoints that have been focused on recently in relation to non-ionizing electromagnetic field exposure are;

- Experimental studies
    - The DNA stability of cells.

      This can be investigated in a number of ways, but what seems to be most important at the moment is the frequency of micronuclei formation after radio frequency exposure and eventual recovery time, the formation of ROS and chromosome aberrations.

    - Epigenetics.

      This relatively new area seems to be of increasing importance and opens up several new ways to investigate non-ionizing electromagnetic field exposure.

- Epidemiological studies
    - Chronic low time exposures.

      This can be studied further through follow-up studies; cohorts of exposed personnel could therefore be of interest. Magnetic resonance imaging personnel and surgeons involved in diathermy surgery are examples of such cohorts. A good exposure assessment through, preferably, personal dosimetry is of importance in such studies.

REFERENCES

1. forsyningskommando S. Mulig sammenheng mellom høyfrekvente elektromagnetiske felt og medfødte misdannelser: medisinske og tekniske undersøkelser i forbindelse med mulig sammenheng mellom høyfrekvente elektromagnetiske felt og medfødte misdannelser relatert til KNM Kvikk. . SFK/T - TKK - EMC & M; 1998.
2. Irgens LM, Lie RT, Baste V. Perinatale helseproblemer hos barn av tjenestegjørende i Sjøforsvaret. Medica birth registry of Norway; 1998.
3. Kristensen P. Medfødte misdannelser blant barn med fedre som hadde tjenestegjort på KNM Kvikk. STAMI; 2000.
4. Moen BE, Koefoed V, Bondevik K, Haukenes I. A survey of occupational health in the Royal Norwegian Navy. International Maritime Health. 2008; **59**(1-4): 9.
5. Lillestøl E, Hunderi O, Lien JR. Varmelære og elektromagnetisme; 2001.
6. Griffiths DJ. Introduction to electrodynamics. 3rd ed. San Francisco, Calif.: Pearson Benjamin Cummings; 2008.
7. Fysiske og biologiske arbeidsmiljøfaktorer, samt ulykker; 2003.
8. Henriksen T, Ingebretsen F. Stråling og helse. Oslo: Universitetet i Oslo; 1993.
9. Sekulic M, Hassunizadeh B, McGraw S, David S. Feasibility of early emergency room notification to improve door-to-balloon times for patients with acute ST segment elevation myocardial infarction. Catheter Cardiovasc Interv. 2005; **66**(3): 316-9.
10. Icnirp. Exposure to high frequency electromagnetic fields, biological effects and health consequences (100 kHz - 300 GHz): ICNIRP; 2009.
11. Nasjonalt folkehelseinstitutt. Svake høyfrekvente elektromagnetiske felt - en vurdering av helserisiko og forvaltningspraksis. Oslo: Folkehelseinstituttet; 2012.
12. Baan R, Grosse Y, Lauby-Secretan B, El Ghissassi F, Bouvard V, Benbrahim-Tallaa L, et al. Carcinogenicity of radiofrequency electromagnetic fields. Lancet Oncol. 2011; **12**(7): 624-6.
13. International Agency for Research on Cancer. Non-ionizing radiation, Part 1: Static and extremely low-frequency (ELF) electric and magnetic fields. Lyon: IARC; 2002.
14. Hansson MK, Alanko T, Decat G, Falsaperla R, Gryz K, Hietanen M, et al. Exposure of workers to electromagnetic fields. A review of open questions on exposure assessment techniques. IntJOccupSaf Ergon. 2009; **15**(1): 3-33.
15. Mantiply ED, Pohl KR, Poppell SW, Murphy JA. Summary of measured radiofrequency electric and magnetic fields (10 kHz to 30 GHz) in the general and work environment. Bioelectromagnetics. 1997; **18**(8): 563-77.
16. Hannevik M, Saxebøl G. "En undersøkelse om radiofrekvent stråling i plast- og møbelindustrien". SIS; 1983.
17. Alexander J, Brunborg G, Oftedal G, Hillert L, Feychting M, Moen BE, et al. "Mulige helseskader ved stråling fra mobiltelefoner, basestasjoner og trådløse nettverk.". 2012.
18. Acoustic neuroma risk in relation to mobile telephone use: results of the INTERPHONE international case-control study. Cancer Epidemiol. 2011; **35**(5): 453-64.
19. Hardell L, Carlberg M, Hansson Mild K. Re-analysis of risk for glioma in relation to mobile telephone use: comparison with the results of the Interphone international case-control study. Int J Epidemiol. 2011; **40**(4): 1126-8.
20. Sjømoen TM, Lervik H, Heimdal PE, Klæboe L, Hannevik M. "Radiofrekvente felt i våre omgivelser - målinger i frekvensområdet 80 MHz - 3 GHz". Norwegian Radiation Protection Authority: Norwegian Radiation Protection Authority; 2011 2011-06-10.
21. Liljestrand B, Sandstrom M, Hansson MK. RF Exposure During Use of Electrosurgical Units. Electromagnetic biology and medicine. 2003; **22**(2&3): 5.
22. King RW. The electric field induced in the human body when exposed to electromagnetic fields at 1-30 MHz on shipboard. IEEE TransBiomedEng. 1999; **46**(6): 747-51.

23. Tynes T, Hannevik M, Andersen A, Vistnes AI, Haldorsen T. Incidence of breast cancer in Norwegian female radio and telegraph operators. Cancer Causes Control. 1996; **7**(2): 197-204.
24. Skotte J. Exposure of radio officers to radio frequency radiation on Danish merchant ships. AmIndHygAssocJ. 1984; **45**(12): 791-5.
25. Guidelines for limiting exposure to time-varying electric, magnetic, and electromagnetic fields (up to 300 GHz). International Commission on Non-Ionizing Radiation Protection. Health Phys. 1998; **74**(4): 494-522.
26. van RE, Saunders RD, van Deventer ET, Repacholi MH. Static fields: biological effects and mechanisms relevant to exposure limits. Health Phys. 2007; **92**(6): 584-90.
27. Amendment to the ICNIRP "Statement on medical magnetic resonance (MR) procedures: protection of patients". Health Phys. 2009; **97**(3): 259-61.
28. Baste V, Moen BE, Oftedal G, Strand LA, Bjorge L, Mild KH. Pregnancy outcomes after paternal radiofrequency field exposure aboard fast patrol boats. J Occup Environ Med. 2012; **54**(4): 431-8.
29. Baste V, Mild KH, Moen BE. Radiofrequency exposure on fast patrol boats in the Royal Norwegian Navy--an approach to a dose assessment. Bioelectromagnetics. 2010; **31**(5): 350-60.
30. Baste V, Universitetet i Bergen . Institutt for samfunnsmedisinske fag. Radiofrequency electromagnetic fields and reproductive health : occupational exposure among men in the Royal Norwegian Navy. [Bergen]: University of Bergen; 2011.
31. Fleming S, Cooke S. Textbook of assisted reproduction for scientists in reproductive technology. 1st ed. China: VIVID; 2006.
32. Goodman HM. Basic medical endocrinology: Elsevier Inc.; 2009.
33. Klingmuller D, Haidl G. Inhibin B in men with normal and disturbed spermatogenesis. HumReprod. 1997; **12**(11): 2376-8.
34. Meachem SJ, Nieschlag E, Simoni M. Inhibin B in male reproduction: pathophysiology and clinical relevance. EurJEndocrinol. 2001; **145**(5): 561-71.
35. Paul M. Occupational and environmental reproductive hazards : a guide for clinicians. Baltimore, Md: Williams & Wilkins; 1993.
36. Karmaus W, Juul S. Infertility and subfecundity in population-based samples from Denmark, Germany, Italy, Poland and Spain. Eur J Public Health. 1999; **9**(3): 229-35.
37. Skakkebaek NE, Giwercman A, de Kretser D. Pathogenesis and management of male infertility. Lancet. 1994; **343**(8911): 1473-9.
38. Boivin J, Bunting L, Collins JA, Nygren KG. International estimates of infertility prevalence and treatment-seeking: potential need and demand for infertility medical care. Hum Reprod. 2007; **22**(6): 1506-12.
39. Rostad B, Schei B, Sundby J. Fertility in Norwegian women: results from a population-based health survey. Scand J Public Health. 2006; **34**(1): 5-10.
40. Medisinsk fødselsregister, Nasjonalt folkehelseinstitutt . Avdeling for Medisinsk fødselsregister. Årstabeller for Medisinsk fødselsregister ... : fødsler i Norge. [Bergen]: Nasjonalt folkehelseinstitutt, Divisjon for epidemiologi.
41. Johnson EM. Screening for teratogenic hazards: nature of the problems. Annu Rev Pharmacol Toxicol. 1981; **21**: 417-29.
42. Sheiner EK, Sheiner E, Hammel RD, Potashnik G, Carel R. Effect of occupational exposures on male fertility: literature review. Ind Health. 2003; **41**(2): 55-62.
43. Esteves SC, Hamada A, Kondray V, Pitchika A, Agarwal A. What every gynecologist should know about male infertility: an update. Arch Gynecol Obstet. 2012; **286**(1): 217-29.
44. De Fleurian G, Perrin J, Ecochard R, Dantony E, Lanteaume A, Achard V, et al. Occupational exposures obtained by questionnaire in clinical practice and their association with semen quality. J Androl. 2009; **30**(5): 566-79.
45. Tas S, Lauwerys R, Lison D. Occupational hazards for the male reproductive system. Crit RevToxicol. 1996; **26**(3): 261-307.

46. Thonneau P, Bujan L, Multigner L, Mieusset R. Occupational heat exposure and male fertility: a review. Hum Reprod. 1998; **13**(8): 2122-5.
47. Lahdetie J. Occupation- and exposure-related studies on human sperm. JOccupEnvironMed. 1995; **37**(8): 922-30.
48. Baste V, Riise T, Moen BE. Radiofrequency electromagnetic fields; male infertility and sex ratio of offspring. Eur J Epidemiol. 2008; **23**(5): 369-77.
49. Mjoen G, Saetre DO, Lie RT, Tynes T, Blaasaas KG, Hannevik M, et al. Paternal occupational exposure to radiofrequency electromagnetic fields and risk of adverse pregnancy outcome. EurJEpidemiol. 2006; **21**(7): 529-35.
50. Gutschi T, Mohamad Al-Ali B, Shamloul R, Pummer K, Trummer H. Impact of cell phone use on men's semen parameters. Andrologia. 2011.
51. Grajewski B, Cox C, Schrader SM, Murray WE, Edwards RM, Turner TW, et al. Semen quality and hormone levels among radiofrequency heater operators. JOccupEnvironMed. 2000; **42**(10): 993-1005.
52. Schrader SM, Langford RE, Turner TW, Breitenstein MJ, Clark JC, Jenkins BL, et al. Reproductive function in relation to duty assignments among military personnel. ReprodToxicol. 1998; **12**(4): 465-8.
53. de Seze R, Fabbro-Peray P, Miro L. GSM radiocellular telephones do not disturb the secretion of antepituitary hormones in humans. Bioelectromagnetics. 1998; **19**(5): 271-8.
54. Weyandt TB, Schrader SM, Turner TW, Simon SD. Semen analysis of military personnel associated with military duty assignments. ReprodToxicol. 1996; **10**(6): 521-8.
55. Hjollund NH, Bonde JP, Skotte J. Semen analysis of personnel operating military radar equipment. ReprodToxicol. 1997; **11**(6): 897.
56. Hjollund NH, Skotte JH, Kolstad HA, Bonde JP. Extremely low frequency magnetic fields and fertility: a follow up study of couples planning first pregnancies. The Danish First Pregnancy Planner Study Team. OccupEnvironMed. 1999; **56**(4): 253-5.
57. Fejes I, Zavaczki Z, Szollosi J, Koloszar S, Daru J, Kovacs L, et al. Is there a relationship between cell phone use and semen quality? ArchAndrol. 2005; **51**(5): 385-93.
58. Lee JW, Kim MS, Kim YJ, Choi YJ, Lee Y, Chung HW. Genotoxic effects of 3 T magnetic resonance imaging in cultured human lymphocytes. Bioelectromagnetics. 2011.
59. Simi S, Ballardin M, Casella M, De MD, Hartwig V, Giovannetti G, et al. Is the genotoxic effect of magnetic resonance negligible? Low persistence of micronucleus frequency in lymphocytes of individuals after cardiac scan. MutatRes. 2008; **645**(1-2): 39-43.
60. Scarfi MR, Fresegna AM, Villani P, Pinto R, Marino C, Sarti M, et al. Exposure to radiofrequency radiation (900 MHz, GSM signal) does not affect micronucleus frequency and cell proliferation in human peripheral blood lymphocytes: an interlaboratory study. Radiat Res. 2006; **165**(6): 655-63.
61. Schwarz C, Kratochvil E, Pilger A, Kuster N, Adlkofer F, Rudiger HW. Radiofrequency electromagnetic fields (UMTS, 1,950 MHz) induce genotoxic effects in vitro in human fibroblasts but not in lymphocytes. Int Arch Occup Environ Health. 2008; **81**(6): 755-67.
62. Aasland OG, Amundsen A, Bovim G, Fauske S, Morland J. [Identification of patients at risk of alcohol related damage]. Tidsskr Nor Laegeforen. 1990; **110**(12): 1523-7.
63. McRobbie DW. Occupational exposure in MRI. Br J Radiol. 2012; **85**(1012): 293-312.
64. Magerøy N, HMS Sjø. En Spørreundersøkelse om arbeid og helse blandt [sic] ansatte i Sjøforsvaret : en delrapport i prosjektet HMS Sjø. [Bergen]: Seksjon for arbeidsmedisin, Universitetet i Bergen; 2004.
65. Bridger RS, Brasher K, Dew A, Kilminster S. Occupational stress and strain in the Royal Navy 2007. Occup Med (Lond). 2008; **58**(8): 534-9.
66. Gray GC, Reed RJ, Kaiser KS, Smith TC, Gastanaga VM. Self-reported symptoms and medical conditions among 11,868 Gulf War-era veterans: the Seabee Health Study. Am J Epidemiol. 2002; **155**(11): 1033-44.

67. Magerøy N. Health among navy personnel : a cross-sectional study in the Royal Norwegian Navy. [Bergen]: University of Bergen; 2009.
68. Rothman KJ, Greenland S. Modern epidemiology. 2nd ed. Philadelphia: Lippincott-Raven; 1998. p. XIII, 737 s.
69. Strand LA, Martinsen JI, Koefoed VF, Sommerfelt-Pettersen J, Grimsrud TK. Cause-specific mortality and cancer incidence among 28,300 Royal Norwegian Navy servicemen followed for more than 50 years. Scand J Work Environ Health. 2011; **37**(4): 307-15.
70. Podsakoff PM, MacKenzie SB, Lee JY, Podsakoff NP. Common method biases in behavioral research: a critical review of the literature and recommended remedies. J Appl Psychol. 2003; **88**(5): 879-903.
71. Doyle P, Maconochie N, Davies G, Maconochie I, Pelerin M, Prior S, et al. Miscarriage, stillbirth and congenital malformation in the offspring of UK veterans of the first Gulf war. Int J Epidemiol. 2004; **33**(1): 74-86.
72. Richards ID, Bentley HB, Glenny AM. A local congenital anomalies register: monitoring preventive interventions. J Public Health Med. 1999; **21**(1): 37-40.
73. Czeizel AE, Intody Z, Modell B. What proportion of congenital abnormalities can be prevented? BMJ. 1993; **306**(6876): 499-503.
74. Medisinsk fødselsregister. Fødsler i Norge gjennom 30 år : 1967-1996. Bergen: Fødselsregisteret; 1997.
75. Kristensen P. [Bias from dependent errors in observational studies]. Tidsskr Nor Laegeforen. 2005; **125**(2): 173-5.
76. Bolte JF, van der Zande G, Kamer J. Calibration and uncertainties in personal exposure measurements of radiofrequency electromagnetic fields. Bioelectromagnetics. 2011; **32**(8): 652-63.
77. Johansen C, Raaschou-Nielsen O, Skotte J, Thomsen BL, Olsen JH. Validation of a job-exposure matrix for assessment of utility worker exposure to magnetic fields. ApplOccupEnvironHyg. 2002; **17**(4): 304-10.
78. Brambilla DJ, Matsumoto AM, Araujo AB, McKinlay JB. The effect of diurnal variation on clinical measurement of serum testosterone and other sex hormone levels in men. JClinEndocrinolMetab. 2009; **94**(3): 907-13.
79. Brambilla DJ, O'Donnell AB, Matsumoto AM, McKinlay JB. Intraindividual variation in levels of serum testosterone and other reproductive and adrenal hormones in men. ClinEndocrinol(Oxf). 2007; **67**(6): 853-62.
80. Chia SE, Shi LM. Review of recent epidemiological studies on paternal occupations and birth defects. Occup Environ Med. 2002; **59**(3): 149-55.
81. Wennborg H, Magnusson LL, Bonde JP, Olsen J. Congenital malformations related to maternal exposure to specific agents in biomedical research laboratories. J Occup Environ Med. 2005; **47**(1): 11-9.
82. De Celis R, Feria-Velasco A, Gonzalez-Unzaga M, Torres-Calleja J, Pedron-Nuevo N. Semen quality of workers occupationally exposed to hydrocarbons. Fertil Steril. 2000; **73**(2): 221-8.
83. Irgens A, Kruger K, Ulstein M. The effect of male occupational exposure in infertile couples in Norway. J Occup Environ Med. 1999; **41**(12): 1116-20.
84. Wenzl TB. Estimating magnetic field exposures of rail maintenance workers. AmIndHygAssocJ. 1997; **58**(9): 667-71.
85. Wilson BW, Lee GM, Yost MG, Davis KC, Heimbigner T, Buschbom RL. Magnetic field characteristics of electric bed-heating devices. Bioelectromagnetics. 1996; **17**(3): 174-9.
86. Kheifets LI, London SJ, Peters JM. Leukemia risk and occupational electric field exposure in Los Angeles County, California. AmJEpidemiol. 1997; **146**(1): 87-90.