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Robyn WINTERBOTTOM Rédactrice en chef

Cher lecteur, chère lectrice,

C'est avec beaucoup d'enthousiasme que je vous présente le deuxième volume de la Revue étudiante interdisciplinaire des sciences de la santé (RISS). Au premier cycle, on met de plus en plus l'accent sur l'apport et la participation à la recherche. Pendant leurs études, de nombreux étudiants de la Faculté des sciences de la santé de l'Université d'Ottawa font des recherches de grande utilité. La RISS a pour mandat de donner l'occasion aux étudiants de premier cycle de parfaire leur recherche en publiant et diffusant leurs travaux. En effet, lorsqu'un chercheur écrit pour un auditoire d'érudits, cela complète sa formation universitaire, facilite les débats scientifiques et ajoute de la crédibilité à ses travaux. Notre Journal s'est donc engagé à faciliter l'exploration intellectuelle parmi les multiples disciplines des sciences de la santé, et je suis certain que les douze articles choisis pour ces deux numéros reflètent adéquatement notre philosophie.

Ce Journal n'aurait pas pu être publié sans l'aide de nombreux intervenants. Le comité de révision des pairs se compose de professeurs de l'École interdisciplinaire des sciences de la santé (ÉISS), ainsi que de plusieurs professionnels du domaine. Grâce à leur expertise et à leur dévouement constant envers cette initiative, l'intégrité des documents publiés est garantie.

Je tiens aussi à remercier Dr. Raywat Deonandan, dont l'engagement et les conseils se sont avérés les piliers de la croissance et du développement de la RISS. L'enthousiasme et le soutien qu'il apporte aux étudiants de premier cycle vont bien au-delà des attentes normales vis-à-vis d'un professeur.

Pour conclure, je tiens à remercier aussi les étudiants qui font partie du comité de rédaction de cette année. Leur éthique de travail et leurs idées novatrices se sont avérées très précieuses dans le cadre du processus de publication.

J'ai apprécié au plus haut point mon travail au RISS, et je suis persuadé que la passion constante et le travail acharné des étudiants de premier cycle garantiront la réussite et la pérennité de cette initiative.

Amicalement,

Robyn Winterbottom
BHSc, Université d'Ottawa

MD Candidate, Université McMaster

Foreword

Robyn WINTERBOTTOM Editor-in-Chief

Dear Reader,

I am so thrilled to present the second volume of the Interdisciplinary Student Journal of Health Science (IJHS). Emphasis on scholarly development and participation in research has become a mainstream feature of undergraduate education. Many students in the Health Sciences faculty at the University of Ottawa have been, or are currently involved with, valuable research during their education. The aim of the IJHS is to offer undergraduates the opportunity to experience completion of the research process through publication and dissemination of their work. Writing for an academic audience complements scholarly development, facilitates scientific discussion, and adds credibility to students' work. The journal is committed to intellectual exploration across multiple disciplines in the health sciences; and I believe that the twelve articles selected for these two issues effectively represent our philosophy.

The publication of the journal would not have been possible without the support of numerous individuals. The peer review panel was composed of professors in the Interdisciplinary School of Health Sciences, as well as several professionals within the community. Their expertise and continued dedication to this initiative has been vital to the integrity of the literature within these pages.

I also extend my continued appreciation to Dr. Raywat Deonandan, whose commitment and guidance has been the cornerstone of the IJHS' growth and development. His enthusiasm and support for undergraduate students has gone above and beyond any expectations I could have for a professor.

Finally I would like to thank the students on this year's editorial committee. Their work ethic and innovative ideas have been invaluable to the publication process.

I have thoroughly enjoyed my work with the IJHS and I have no doubt that the continued passion and hard work of undergraduate students will enable success and longevity of this initiative.

Sincerely,

Robyn Winterbottom
BHSc, University of Ottawa

MD Candidate, McMaster University

Avant-propos

Raywat DEONANDAN Éditeur exécutif et superviseur académique

Il est de plus en plus admis par tous que l'éducation ne saurait être complète sans la communication de ses idées et le partage de ses observations. En vérité, pour beaucoup, la transparence est la marque de la science. C'est la raison pour laquelle les journaux scientifiques révisés par des pairs, quels que soient leur impact, leur diffusion et leur degré de sophistication, demeurent non seulement pertinents, mais également essentiels à la maturation de la science et de ses étudiants. Dans cette perspective, je suis fier que ce Journal ait survécu au-delà de son premier numéro, à titre d'initiative entièrement mise en œuvre par les étudiants. Je suis persuadé qu'au fil du temps, il s'avérera un pilier de l'enrichissement de l'éducation de tous les étudiants de premier cycle de la Faculté des sciences de la santé.

Je tiens à remercier du fond du cœur la rédactrice en chef de ce numéro, Robyn Winterbottom, dont le volume de travail équivaut parfois à un emploi à plein temps, ainsi que son impressionnante équipe éditoriale. Leur dévouement et leur passion pour cette initiative ont été pour moi une inspiration qui m'aide à demeurer humble.

Ce numéro a été subventionné en partie par le programme Mission Satisfaction de la Faculté des sciences de la santé de l'Université d'Ottawa. En outre, ce Journal ne pourrait pas exister sans la confiance constante des professeurs et de l'administration de l'Université, qui ont prodigué des conseils, et fourni des services de traduction, du mentorat étudiant et un excellent service de révision par les pairs.

Merci à tous,

Dr Raywat Deonandan
Professeur adjoint

École interdisciplinaire des sciences de la santé (ÉISS)
Faculté des sciences de la santé

Université d'Ottawa

Foreword

Raywat DEONANDAN Executive Editor and Academic Supervisor

Increasingly, there is recognition that there is no true scholarship without the communication of insights and the sharing of observations. Indeed, for many, routine transparency is the hallmark of science. Hence, peer-reviewed journals, at whatever levels of impact, sophistication and reach, remain not only relevant, but essential for the maturation of both science and science students. To that end, I am proud that this journal is being sustained beyond its first issue as a solely student-run initiative. I believe that, in time, it will prove to be an essential element for the enriched education of all undergraduate health science students.

I wish to express my profound gratitude to this issue's Editor in Chief, Robyn Winterbottom, whose workload was, at times, equivalent to a full time job, and to her impressive editorial team. Their dedication and passion for this endeavour have been both inspiring and humbling.

Aspects of the current issue were funded in part by a Mission Satisfaction grant from the University of Ottawa's Faculty of Health Sciences. This journal could not exist without the sustained confidence of the University's faculty and administration, who have contributed through advice, translation, student mentorship, and by serving as valued peer reviewers.

Thank you all,

Dr Raywat Deonandan
Assistant Professor

Interdisciplinary School of Health Sciences
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Angioplasty Used to Treat Multiple Sclerosis Patients: A Potential Revolution in Health Care Technology

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Résumé :

(traduction)

La sclérose en plaques (SEP) est depuis longtemps cataloguée comme une maladie neurologique à forte incidence chez les Canadiens, et en particulier chez les femmes. Cette maladie se manifeste initialement au début de l'âge adulte (entre 15 et 40 ans). On trouve des zones de démyélination avec une prolifération d'astrocytes, éparpillées dans la substance blanche des sujets atteints de SEP, et ceci provoque de la faiblesse musculaire, des engourdissements, du déséquilibre, des perturbations du sphincter, et d'autres dysfonctionnements neurologiques. Récemment, le Dr. Paolo Zamboni, un chirurgien vasculaire de l'Université de Ferrare, en Italie, a découvert que beaucoup de patients atteints de SEP présentent un rétrécissement de plusieurs des veines du cou chargées de drainer le sang du cerveau. Selon le Dr. Zamboni, ce rétrécissement des vaisseaux sanguins provoque un dépôt de fer dans les veines défectueuses, diminuant ainsi le flux sanguin et causant certaines complications liées a la SEP. Le Dr. Zamboni a réussi a débloquer ces veines grâce à l'angioplastie, une méthode normalement utilisée pour ouvrir les artères bouchées par l'artériosclérose. Dans le cadre d'un de ses projets de recherche, il a effectue cette procédure sur 65 patients, dont le taux de présence de lésions a diminue de 50% a 12%. Il a également constaté une amélioration de la qualité de vie de ces patients sur les plans mental et physique. L'auteur aborde aussi des questions éthiques dans son article. Les recherches du Dr. Zamboni suggèrent que la SEP peut être causée par des facteurs de patrimoine génétique. Les fournisseurs de soins de sante devraient-ils commencer à rechercher systématiquement ces facteurs chez les nouveaux nés? Ce dépistage devrait-il être obligatoire? Et serait-il gratuit?

Mots-clés :

Sclérose en plaques (SEP), angioplastie, insuffisance veineuse cérébrospinale chronique, fer, sclérose, neurodegeneration

Abstract:

Multiple sclerosis (MS) has long been labeled as a neurological disease with a high incidence among Canadians, women in particular. The disease first manifests itself in young adulthood (between the ages of 15 and 40 years). Areas of demyelination with a proliferation of astrocytes are found scattered in the white matter of MS patients, this leads to muscle weakness, numbness, disequilibrium, sphincter disturbance and other neurological dysfunctions. Recently Dr. Paolo Zamboni, a vascular surgeon at the University of Ferrara in Italy, found that many multiple sclerosis patients have a narrowing of some of the neck veins responsible for draining blood from the brain. According to Dr. Zamboni, this narrowing of the blood vessels leads to the deposit of iron in the defected veins, which restricts blood flow and is responsible for some of the MS complications. Dr. Zamboni achieved unblocking of the veins through angioplasty, a procedure normally used to open arteries affected by atherosclerosis. In one of his trials, 65 patients were given the procedure, which decreased the rate of occurrence of lesions, from 50 % to 12 % in patients. There was an improvement in mental and physical quality of life in most of the patients in this trial. Ethical questions are also discussed in this review. Dr. Zamboni`s studies suggest a genetic inheritance of factors that may lead to MS. Should health care providers institute a screening procedure in newborns? Would these screenings be mandatory? Would the screenings be free?

Keywords:

Multiple Sclerosis (MS), angioplasty, chronic cerebrospinal venous insufficiency, iron, sclerosis, neurodegeneration

Introduction

Multiple sclerosis (MS) is one of the most serious and common neurological conditions today. This disease is characterized by areas of degeneration of the myelin sheaths of nerve fibres in the brain and spinal cord. These degenerated areas heal through sclerosis (scarring), forming multiple sclerotic plaques (Crowley, 2010). For over a century, millions of young adults suffering from this disease have experienced severe disability and potentially reduced lifespan, as the scarring cannot be stopped, and the symptoms may only be managed. Epidemiologic studies indicate that MS is particularly prevalent in persons of western European descent, who live in temperate zones (McPhee, Papadakis, & Tierney, 2001); it tends to occur among young adults between the ages of 15 and 40 (Crowley, 2010). Canada has one of the highest incidence rates of MS in the world. Three Canadians are diagnosed with MS every day, and women are three times more likely to develop MS than men (MS Society of Canada, n.d.).

Multiple Sclerosis patients are separated into three groups based on the progression of the disorder. Relapsing-remitting patients develop new symptoms, or have the first episode reoccur, months or years after the first symptoms emerge. In some of these patients, the clinical course of MS changes into a steady deterioration, this type of progression is called secondary progressive. Finally, primary progressive MS is a less common type of progression, where the onset is early and the disorder develops at a steady pace from its onset (McPhee, Papadakis, & Tierney, 2001). Multiple Sclerosis is characterized by a series of symptoms, these include muscle weakness and spasms, numbness, disequilibrium, retrobulbar neuritis, double vision, and sphincter disturbances, which includes urinary incontinence (McPhee, Papadakis, & Tierney, 2001). Although partial recovery from acute exacerbations can be expected with current treatment, there is no way of preventing the progression of this disorder. Corticosteroids may hasten the recovery from acute relapses. High doses of prednisone (60 to 80 mg) may be given daily for a week, after which medication is tapered over the following two to three weeks (McPhee, Papadakis, & Tierney, 2001).

A treatment that could possibly alter the outcome of MS, this being ultimately death, would be hailed as a miracle in terms of health care technology, by the millions of individuals living with this condition. Dr. Paolo Zamboni, of the University of Ferrara in Italy, is possibly the man that has taken the largest step towards this “miracle” in years. His research suggests that MS is linked to a vascular condition, rather than an immune system dysfunction (Zamboni et al., 2009), as previously believed. The validation of Dr. Zamboni’s discovery, through extensive research and clinical trials, may potentiate the modification of medical textbooks worldwide.

Dr. Zamboni’s theory has been through extensive research. Trials were conducted, where sixty-five MS patients were divided into groups, based on the different classifications of MS progression; these groups were primary progressive, secondary progressive and relapsing remitting. In his work “A prospective open-label study of endovascular treatment of chronic cerebrospinal venous insufficiency”, he discovered that performing an angioplasty procedure in patients afflicted by chronic cerebrospinal venous insufficiency (CCSVI), associated with MS, is safe and effective in significantly improving MS clinical outcome (Zamboni et al., 2009). Venous pressure was decreased in the targeted vessels with only a minor and negligible complication rate (Zamboni et al., 2009). Some of the parameters observed were the rate of relapse-free patients, the presence of MS lesions, and the improvement in physical and mental quality of life (MS QOL questionnaire) (Zamboni et al., 2009). While results are promising, there is a difference between the groups evaluated; where certain MS types had more evident improvements in the mentioned parameters. Although angioplasty is relatively safe, any invasive procedure has risks associated with it. According to the National Heart Lung and Blood Institute, these risks include bleeding from the targeted vessel, damaging of blood vessel, potential allergic reaction to any of the materials used, arrhythmias, heart attack (3-5% of patients), and stroke (less than 1% of patients) (National Heart Lung and Blood Institute, n.d.).

Dr. Zamboni’s Research and Results

Dr. Zamboni’s study suggests that iron deposits associated with MS are the result of chronic insufficient venous drainage (high venous pressure), created by blockage of the vessels that drain blood from the brain (Singh & Zamboni, 2009). Iron has been deeply linked with senile toxicity and neurodegenerative disorders. Iron’s redox capability of switching between its ferrous and ferric states (its two ions forms: Fe^{2+} and Fe^{3+}) creates dangerous catalytic elements, which lead to neurodegeneration (Singh & Zamboni, 2009). He suggests that after vessels are damaged by

iron, they "leak" the iron and other unwanted cells into the brain through the blood-brain barrier – the barrier between blood and the cerebrospinal fluid (Crowley, 2010). Dr. Zamboni theorized that immune system cells, along with the iron, enter the brain (through the damaged vessels) and trigger neuron demyelination (the destruction of the

fatty sheaths along axons of neurons). This enables debilitating symptoms associated with MS, some of which were mentioned previously in this review. His breakthrough theory is that the blockage in the vessels may be eliminated by means of an angioplasty. This procedure consists of the insertion of a catheter into the patient's obstructed blood vessel, which has an inflatable balloon utilized to expand the blood vessels. This therapy substantially relieves venous pressure, reducing the damage to the myelin and alleviating the MS symptoms. Angioplasty procedures have long been applied to the treatment for atherosclerosis, which causes narrowing of arteries due to plaque build up (McPhee, Papadakis, & Tierney, 2001). However, Dr. Zamboni is the first to adapt the procedure to MS cases. In one of his trials, where 65 patients were given the treatment, there was a drop in the rate of occurrence of lesions, from 50% to 12% in patients (Zamboni et al., 2009). The study also indicated that the treatment had significantly decreased MS symptoms in certain patients. This was especially evident in MS patients who are prone to relapses (remitting relapsing MS). In this group, there was an increase from 27% to 50% of patients who were relapse-free after the procedure (Zamboni et al., 2009). There was an improvement in mental and physical quality of life for most of the patients in this study, especially the patients who presented primary progressive and relapsing remitting multiple sclerosis (Zamboni et al., 2009). Potential improvements in patients depend on how long they have had MS and how much brain damage had already occurred. Neurons do not regenerate once they are lost and myelin that has been severely damaged may remain scarred, which means that only partial recovery of function may be experienced by patients whom have had considerable neurodegeneration. Ideally, the procedure proposed by Dr. Zamboni would be performed early in the diagnosis, that is, before any significant neurodegeneration occurs in a patient, this way the potential to reduce symptoms associated with MS can be maximized.

Quality of life, well being and the "zone of maximum performance potential"

The competence-press model, which deals with an individual's performance, was introduced by Lawton in 1970. According to Lawton, there is an ideal equilibrium between competence and press, which must be maintained in order for individuals to function at an optimum level. Lawton named this zone of balance in the model the "Zone of maximum performance potential" ("Key Concepts and Issues", 2010). One defines "press" from this model, as any kind of obstacle or difficulty, which may be environmental, physical, emotional, occupational, and so forth. Symptoms are perhaps the biggest "press" that patients experience. In the case of MS, neuron degeneration causes blurred vision, muscle weakness, involuntary contraction of muscles, loss of co-ordination, and various other physical and cognitive symptoms which create impediments for individuals afflicted by this disorder (McPhee, Papadakis, & Tierney, 2001). As predicted by the model, symptoms faced by MS patients generate stress, or physical and/ or emotional press on the individual ("Key Concepts and Issues", 2010). The new procedure proposed by Dr. Zamboni may lessen, if not eliminate, the debilitating symptoms MS patients struggle with. According to Lawton's model, once the press that the symptoms create for the patient decreases, the individual becomes closer to the "zone of maximum performance potential". This zone, as the name suggests, is where the person is theoretically able to perform at his/her full potential. Dr. Zamboni's procedure allows for the patients to enter the zone of maximum performance and potential by relieving them of their symptoms.

The model "Conceptual framework for relating technology to improvement in quality of life and well-being" proposed by Jutai *et al* in 2009, depicts the diverse classifications of technology and their role of in improving quality of life (QOL) and well being. Technology is divided into medical and assistive technologies. Medical technology, also called life support technology, consists of substitutes for body structure or function, medical treatment, and measurement of living body functions. Assistive technology is divided into living support and social activity support technologies. The former consists of self and care support, while the latter consists of vocational and leisure support. This model enables patients dealing with stressful circumstances to educate themselves on techniques, which diminish strain, leading to a better quality of life. Consequently, an individual with a disability who passes from the medical to the assistive technologies his/ her QOL and well being

potentially increases, as according to this model. Dr. Zamboni's procedure may well be considered part of the medical treatment in the medical technology aspect of the model. Individual with MS may obtain Dr. Zamboni's procedure and retrieve body functions lost due to the disorder. Subsequent to body function restoration, the patient can seek self or care support to return to normal activities; and ultimately attain leisure or vocational support, so that he/she may participate in society more effectively and pleasurably, than otherwise possible ("Assistive Devices", 2010). Dr. Zamboni's procedure is perhaps the first significant stepping stone into the improvement of QOL and the well-being for MS patients. As the model by Jutai *et al* illustrates, as function and independence are regained, the patient's QOL and well being increases.

Ethical Issues are Raised

Western Medicine has incessantly progressed alongside technology. They have an important inter-reliant relationship in the western health care model. This dependence is a distinguishing feature of modern-western medicine, which separates it from medicine that is practiced in third world countries. For instance, North American doctors use nuclear imaging studies to diagnose tuberculosis, while World Health Organization (WHO) doctors working in Africa, use solely a stethoscope to reach the same diagnosis. North American health care relies on drugs, medical devices, and diagnostic and surgical equipment, amongst other types of technology, to deliver its services to the general public ("Key Concepts and Issues", 2010). There seems to be an insistent demand for innovations that might enhance or prolong life. Governments across nations spend millions of dollars in funding researchers undertaking the struggle to conjure the next "miracle drug" that will cure the deadliest diseases known. Many will fail in doing so, giving rise to an ethical issue. It may be said that the money used to fund researches would be more wisely spent if it were directed towards the creation of a greater accessibility to treatments of diseases, such as MS, to a greater number of people, perhaps in the form of more comprehensive health insurance coverage over the cost of treatment. Statistics Canada presents the average income of a family with 2 people or more, in 2007 in Canada, as $71 900, whereas the annual treatment cost for MS, according to the MS society of Canada, is as much as $40 000 (MS Society of Canada, n.d.).

Ethics is an essential factor when evaluating a new medical technology, as advancing technologies frequently result in moral debates. As previously discussed, Dr. Zamboni proposes that MS is instigated by the narrowing or partial blockage of blood vessels; causing an increase in pressure, and/or backflow of blood in these vessels, allowing unwanted materials to enter the brain and create damage (Singh & Zamboni, 2009). The narrowing of the vessels may be congenital to some people - the hereditary factor of MS. If Dr. Zamboni's theories are proven correct and there is a inherited basis to MS, government health legislators and health care providers will face numerous ethical questions relating to those that may be afflicted. Consequently, the government will be responsible for questions such as: whether there should be screenings for MS? Who should receive such screenings? Are they to be mandatory and free, or optional and not covered by health care plans? Will surgery be the only option for a positive screening test?

The MS society of Canada recognizes the breakthrough that Dr. Zamboni has accomplished; however, it is considered too hastily to reclassify MS as a vascular condition instantly, and so notifications to the public are made concerning follow-up research that must be completed in order for concrete conclusions to be made (MS Society of Canada, n.d.). Referring to the Medical Industrial Complex (MIC), where the state fosters and regulates private corporate interests in health ("Corporate Health and Regulation", 2010), one may reflect that Dr. Zamboni's new technique in treating MS does not follow the financial wishes of private health corporations. Considering that in 2006, 55 000 to 75 000 Canadians were estimated to suffer from MS (MS Society of Canada, n.d.), and that the annual cost for the MS treatment may strike $40,000, one may conclude that the drug companies world-wide, especially in Canada being one of the largest populations affected by MS - may not regard Dr. Zamboni's procedure as a scientific advance, but rather an economic nightmare. The MIC may include the numerous drug companies, who could potentially lose considerable amount of money annually if the treatment of MS was no longer needed.

Conclusion

In summary, MS has many underlying factors, which must be exhaustively researched in order for concrete conclusions to be drawn. Ethical guidelines ought to be determined when dealing with a discovery of this magnitude,

allowing for the appropriate issues to be questioned, and dealt with. Furthermore, if one considers the money that is generated by pharmaceutical companies dealing with MS treatments, it can be said that Dr. Zamboni might not only be fighting the disease, his recent discoveries may need to stand against corporate greed as well. Ultimately, researchers around the world will have the challenge of testing Paolo Zamboni's theory with an ample number of MS patients in order to validate this new treatment method. If it becomes scientifically proven and accepted by medical societies as a promising way to decrease symptoms, or a definite way to end the disease, this would most certainly revolutionize modern medicine. Such advancements will save potentially millions of lives, inspire innovative researchers to discover treatments, and review existing practices concerning illnesses that are presently considered "death sentences", due to the lack of a cure, or inadequate treatments that only subside symptoms. Future discoveries and pioneer techniques may greatly contribute to solving conditions, such as, Multiple Sclerosis, Lou Gehrig's Disease (also known as ALS), Muscular Dystrophy, Huntington`s Chorea, and many others which currently lack a cure or effective treatment to prolong life.

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Effects of Bisphenol A and Diethylstilbestrol on Estrogen Receptor Expression and Male Fertility

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Résumé :

(traduction)

On définit l'infécondité comme l'incapacité d'un couple à concevoir un enfant après un an de rapports sexuels sans protection. Les pathologies masculines de reproduction sont la principale cause d'au moins 20% des cas d'infécondité, si bien que l'infécondité masculine est un problème important pour la santé globale de la population. Les agents perturbateurs endocriniens (APE) peuvent provoquer une dégradation de la spermatogenèse en provoquant des déséquilibres hormonaux et des changements morphologiques. Le DES et le BPA sont tous les deux des œstrogènes exogènes, également appelés xéno-œstrogènes. L'œstrogène joue un rôle important au niveau de la fertilité des hommes, ainsi que des femmes, car il influe sur l'équilibre endocrinien global requis pour permettre la spermatogenèse. On peut surveiller ses effets sur l'axe hypothalamique-pituitaire-gonadal en évaluant la sur-régulation des récepteurs des œstrogènes α et -B (ERα et ERβ), ainsi que le récepteur 30 couplé à une protéine G (GPR30), qui est un nouveau récepteur des œstrogènes. Il y a une controverse à propos des mécanismes de perturbation endocrinienne associés à ces produits chimiques, pour savoir si leurs effets négatifs sur la fertilité apparaissent à faible dose, ou seulement à forte dose, ce qui est systématiquement toxique. Une analyse de la documentation associée à cette recherche nous permettra de mieux comprendre les bases moléculaires de la dégradation de la spermatogenèse et de la fertilité masculine, associée à l'exposition aux APE, et en particulier au DES et au BPA. Les résultats de cette étude viendront améliorer les connaissances dans les domaines de la santé de la population, de la salubrité de l'environnement et de la génétique moléculaire. Nous espérons que, grâce à une connaissance plus approfondie de l'impact des APE sur la fertilité, les gouvernements pourront empêcher que les gens y soient exposés, en réglementant mieux l'emploi de produits comme le DES ou le BPA.

Mots-clés :

Bisphénol A, diéthylstilbestrol, Agents Perturbateurs Endocriniens (APE), xéno-oestrogènes, infécondité masculine, spermatogenèse, Récepteur des Œstrogènes Alpha (ERα), Récepteur des Œstrogènes Beta (ERβ), Récepteur couplé à une Protéine G (GPR30)

Abstract:

Infertility is defined as a couple's inability to conceive after one year of unprotected intercourse. Male reproductive pathologies are the predominate cause of at least 20% of cases of infertility; making male infertility is an important issue in overall population health. Endocrine disrupting chemicals (EDCs) can impair spermatogenesis by creating hormonal imbalances and morphological changes. DES and BPA are both exogenous estrogens, also known as xenoestrogens. Estrogen has an important role in fertility of males as well as females: it has a role in the overall endocrine balance required to allow spermatogenesis. Effects on the hypothalamic-pituitary-gonadal axis may be monitored by assessing for upregulation of estrogen receptors α and -B (ERα and ERβ), as well as the novel estrogen receptor g-protein coupled receptor 30 (GPR30). Controversy surrounds the mechanisms endocrine disruption associated with these chemicals, and whether the negative effects on fertility are relevant at low doses, or only at high doses which are systemically toxic. Analysis of literature associated with this ongoing research will enrich our understanding of the molecular bases for impairment of spermatogenesis and male fertility associated with exposure to EDCs, specifically DES and BPA. Once completed, this study will contribute to knowledge in the fields of population health, environmental health, and molecular genetics. With a more thorough understanding of the impact of EDCs on fertility, it is hoped that governments will further prevent exposure by better regulating the use of compounds such as DES and BPA.

Keywords:

Bisphenol A, diethylstilbestrol, Endocrine Disrupting Chemicals (EDCs), xenoestrogens, male infertility, spermatogenesis, Estrogen Receptor Alpha (ERα), Estrogen Receptor Beta (ERβ), G-protein Coupled Receptor (GPR30)

Introduction

One of the underlying causes of the decreasing fertility rates among the developed world in a decrease in fecundity, or the ability to conceive. While a number of factors may take part in this trend, endocrine disruptors have been shown to play a significant role. Male infertility is an important component of the overall issue; in fact it is the sole cause of 20% of cases of human infertility, and a contributor in 30-40% of cases (Phillips & Tanphaichitr, 2008). Factors affecting fertility in males must be studied distinctly from the female causes. While the role of estrogen in females is commonly well understood, estrogen is also an important hormone in the hypothalamic-pituitary- gonadal axis of males, which is the endocrine basis of reproductive capacity. Interest in this field has evolved since male mice with knock-out status for estrogen receptor α (ERα) were demonstrated to have impaired fertility (O'Donnell, Robertson, Jones, & Simpson, 2001).

BPA is a known endocrine disruptor. It acts as an exogenous estrogen, or a xenoestrogen. Exposure in humans may occur through occupational exposure, or environmental exposure (Li et al., 2009). BPA is used in industry for the manufacturing of epoxy resins and polycarbonates for food packaging (Merck Sharp & Dohme Corp, 2006a). BPA has been associated with impaired spermatogenesis and steroidogenesis. Public awareness of adverse health effects of exposure to BPA is rising, and governmental legislation is increasing aimed to reduce exposure.

DES is a synthetic, nonsteroidal estrogen which also falls into the category of endocrine disruptor and more specifically xenoestrogens. It is a known human carcinogen, and is used in some cases as an androgen suppressor in combined antineoplastic therapy (Merck Sharp & Dohme Corp, 2006b). DES was administered to pregnant women in the 1940's—1970's to prevent miscarriages and spontaneous abortions, as well as pre- mature deliveries (Adamsson, Brokken, Paranko, & Toppari, 2008; Hong et al., 2010). Attention to the negative effects on the human endocrine system arose when women exposed to DES neonatally, several years after it was administered to their mothers during pregnancy, developed rare vaginal and uterine cancers at a significantly elevated rate (Hong et al., 2010). Effects on the male reproductive system have more recently come to light. Exposure to DES has been shown to disrupt steroidogenesis and spermatogenesis in rodents (Cederroth, Schaad, Descombes, Chambon, Vassalli, & Nef, 2007; Hendry, Weaver, Naccarato, & Khan, 2006). Most of this research has been done based on in-utero and neonatal exposure (Hong et al., 2010). While few studies have examined the effects of exposure in adults, such as in the case of antineoplastic uses, it has been shown to drastically increase apoptosis in spermatocytes and spermatids (Ma, Yang, Wang, Shi, & Chen, 2010).

ERα was the first of the estrogen receptors to be implicated in male fertility. Expression of ERα has been demonstrated to be reduced by up to 50% in human embryonic testicular cells with exposure to high doses of BPA, and up to 75% with high doses of DES (Benachour, Moslemi, Sipahutar, & Seralini, 2007). ERβ has a similar functionality as ERα, but through a different mechanism. This is an example of redundancy in genetics, which may help compensate when one system is working inadequately.

GPR30 has only very recently been implicated as an estrogen receptor of the plasma membrane cells in the brain (Funakoshi, Yanai, Shinoda, Kawano, & Mizukami, 2006). Research by Otto *et al.* (2009) however, has indicated that GPR30 doesn't seem to be required for male reproductive function in mice. The novel nature of this ER necessitates further research before sufficient evidence is available to accept or reject a role for GPR30 in male fertility.

Materials and Methods

Inclusion Criteria

Only original journal articles, such as original cohort studies, case-control studies and review articles were included. Human, rodent and in vitro studies were all used. Only articles from the past 5 years (published in 2005 or later) were included. Articles were eliminated if they did not focus on 1) the male reproductive system, 2) BPA and/or DES specifically, and 3) increase in estrogen receptor expression as a potential means of impairment of fertility. Studies focusing mainly on brain function (ex: the role up dopamine uptake), and reproductive cancers were eliminated as they are beyond the scope of this review.

PubMed Search

Between the two searches on PubMed, 20 articles meeting the inclusion criteria were obtained. The search terms were as follows:

- ("bisphenol A "[Substance Name] OR "Diethylstilbestrol" [Mesh]) AND ("Estrogen Receptor

alpha" [Mesh] OR "Estrogen Receptor beta" [Mesh] OR "GPR30 protein, mouse "[Sub- stance Name] OR "GPER protein, human "[Sub- stance Name])

A total of 280 results were returned, 157 of these were from the past 5 years

- ("bisphenol A "[Substance Name] OR "Diethylstilbestrol" [Mesh]) AND ("Testis" [Mesh] OR "Vas Deferens" [Mesh] OR "Seminiferous Tubules" [Mesh])

A total of 428 results were returned, 62 of these were from the past 5 years

SCOPUS Search

Only 1 of the articles met the inclusion criteria, but it was an editorial commentary. The primary article on the qualitative study was accessed through PubMed and included in the systematic review. The search terms used to retrieve articles from this database were as follows:

- (Bisphenol A OR Diethylstilbestrol) AND ((Estrogen receptor alpha OR Estrogen receptor beta OR G-protein coupled receptor 30) OR (Testes OR Vas deferens OR Seminiferous tubules))

A total of 5 results were returned, all of which from the last 5 years

Ovid Search

The vast majority of these were eliminated because they were excerpts from textbooks rather than scientific journal articles. Each of the results meeting the inclusion criteria was already included in the PubMed collection. This indicates a high degree of data saturation, meaning that the likelihood of the existence of articles not included in the review collection which met the inclusion criteria is quite low. The search terms used to retrieve articles from this database were as follows:

- (Bisphenol A OR Diethylstilbestrol) AND ((Estrogen receptor alpha OR Estrogen receptor beta OR G-protein coupled receptor 30) OR (Testes OR Vas deferens OR Seminiferous tubules))

A total of 2069 Results were obtained, which was decreased to 1484 by deduplication. 665 of these results were published within the last 5 years.

Results

Of the 20 studies included in the systematic review, only 1 was inconclusive. Hong *et al.* (2010) demonstrated effects of DES on gene expression, but did not provide insight into the injurious effects, or lack thereof, on male fertility. Three other studies revealed a statistically insignificant relationship, or a complete lack of correlation. Kato *et al.* (2006) found no statistically relevant difference in semen analysis, fertility, copulatory rate or preputial separation in rats exposed to as much as 95mg/kg/day of BPA. Likewise, Tyl *et al.* (2008) found no change in sperm motility of percent of normal sperm in mice exposed to as much as 600mg/kg/day of BPA. Finally, Adamsson *et al.* (2008) were unable to prove impairment of androgen receptor (AR) protein synthesis resulting from exposure to DES. They concluded that perhaps the difference seen in previous studies were due to high doses that were cytotoxic (Anahara et al., 2006). In the case of endocrine disrupting chemicals, such findings can help prevent unnecessary public hysteria.

Conversely, from a public health perspective it is often preferable to err on the side of caution. Significant impairments to male fertility were described in 17 of the 20 studies included in this review. During a qualitative study of men with occupational exposure to BPA, Li *et al.* (2009) demonstrated that exposed factory workers reported a 4-fold decrease in sexual desire, a 4-fold increase in erection difficulty, and a 7-fold increased risk of ejaculation difficulty. With such results coming from interviews with people, it is important to use animal studies to determine possible mechanisms that would cause these effects. One such suggested mechanism is the disruption of steroidogenesis. Hendry, Weaver, Naccarato, and Khan (2006) describe an earlier, longer lasting pubertal testosterone surge. According to Cederroth *et al.* (2007) this occurs due to repression of ERα. Findings from Mikkilä, Toppari, and Paranko (2006) and Nakamura *et al.* (2010) demonstrate decreased intratesticular steroidogenesis, which they believe to be due to decreased testicular mass associated with exposure to both BPA and DES.

Besides testosterone, decreased production of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) was also observed (Shin et al., 2009; Warita et al., 2006). Kobayashi et al. (2009) conceded to the negative impact of steroidogenesis, but suggested that there was an increase

in androgen receptor (AR) expression to compensate. Salian, Doshi, and Vanage (2009a) associated BPA exposure with impaired intra-testicular expression of steroid receptor co-regulators; steroid receptor coactivator-1 (SRC-1) and nuclear receptor corepressor (NCoR). Likewise, steroidogenic acute regulatory protein (StAR) is inhibited by exposure to DES, allowing for an increase in ARs (Kobayashi et al., 2009; Warita et al., 2006). Mikkilä et al. (2006) also observed a decrease in stAR levels, which they determined was due to a 41-44% increase in anti-stAT antibodies. Similarly, Volle et al. (2009) demonstrated an increase in orphan nuclear receptor small heterodimer partner (NrOb- 2) which is a transcriptional repressor of ERs.

Another observed means of impairment of male fertility is disruption of spermatogenesis (Hendry et al., 2006; Salian, Doshi, & Vanage, 2009b). Two of the studies demonstrated a "sloughing" off of germ cells in the seminiferous tubules, following neonatal exposure to BPA or DES (Koh et al., 2006; Salian et al., 2009c, Warita et al., 2006). Hypoplasia of Leydig cells was also observed (Warita et al., 2006). Salian *et al*. (2009c) proposed that this effect is caused by disturbance to the blood-testes barrier. Reduced sperm count was also observed in an additional, separate study by Salian *et al*. (2009a). A significant increase in apoptosis of spermatocytes and spermatids was recorded by Ma, Yang, Wang, Shi, and Chen (2008) in DES exposed adult hamsters was extremely increased compared to control samples. Anahara *et al*. (2006) demonstrated a decrease in actin binding necessary for sperm motility, via a decrease in cortactin expression in the testes.

Overall, there seems to be sufficient evidence of impairment of male fertility by exposure to DES and BPA to warrant avoiding these EDCs. In terms of understanding the breadth of influence of these chemicals, it is important to note that synergistic and transgenerational effects have been observed. Human exposure to continuous low-doses of EDCs seldom occurs with one chemical in isolation. It is important to study the confounding effects EDCs present when one is exposed to more than one at a time (Benachour, Moslemi, Sipahutar, & Seralini, 2007).

Discussion

Once the issues are well understood, the presence of these chemicals in our environmental may be controlled and the problems arising from exposure may be treated. In this study, estrogen receptor expression was used as a parameter for measurement of fertility. Increased estrogen receptor expression in male reproductive tissues has been associated with negative impacts on fertility. The reproductive outcome parameters affected by upregulation of estrogen receptors in males include sperm count (Ma et al., 2008), reduced sperm quality (altered morphology (Kato et al, 2006)), reduced sexual desire/copulatory rate (Li et al., 2009; Kato et al., 2006), erectile dysfunction and ejaculatory difficulty in humans(Li et al., 2009), preputial separation (Kato et al., 2006), and serum testosterone levels (Cederroth et al., 2007; Kato et al., 2006; Kobayashi et al., 2009; Mikkilä et al., 2006; Nakamura et al., 2010).

A multitude of options for future research exist in this growing area of environmental and population health. First of all, downstream gene products may be studied with PCR, to determine if these receptors are being activated and not just expressed. This will give indication of the effect on the cell as a whole, by including the internal signalling pathway.

Important knowledge gaps include the role of GPR30 which has only recently been implicated in the effects of EDC exposure on male fertility. Further, many studies have assessed the effects of EDCs on gestation; however few have examined their pathophysiological effects on female fertility. For example, ER expression could be studied in female mice neonatally exposed to BPA and DES. The impacts on their ovulatory capacity, hormone levels, litter sizes, frequency of resorption of fetuses, and number of pregnancies could be examined. Other interesting avenues of research include methods of correcting the effects of BPA and DES exposure. Since the effects of these EDCs appear to permeate through several generations following exposure, the future impact on human reproductive health cannot be reduced solely by eliminating exposure to these chemicals. Preliminary research has been done on therapies for those affected by EDC exposure. For example, Vitamin A has been linked with re-establishing sperm motility and decreasing the number of malformed sperm following neonatal exposure to BPA (Hendry et al., 2006). Likewise, the use of ginkgo biloba as a possible therapeutic agent for testicular injury caused by DES exposure is currently being studied (Hong et al., 2010).

Conclusion

The role of EDCs on male fertility is not well under- stood. Molecular mechanisms have not been well- examined in-

cluding possible epigenetic changes following EDC exposure. With the characterization of novel estrogen receptor subtypes and isoforms more study is required into the role and mechanisms of EDCs on male fertility.

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The Risk of Prostate Cancer from Occupational Exposures in Male Firefighters

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Résumé :

(traduction)

Le cancer de la prostate est le cancer le plus fréquemment diagnostiqué chez les hommes. Étant donné qu'il se développe lentement, on peut prévenir la mortalité si on détecte et traite la tumeur alors qu'elle n'en est encore qu'à ses premiers stades de développement. On a démontré que des facteurs environnementaux pouvaient augmenter le risque de cancer de la prostate. Quelques recherches ont été effectuées sur les niveaux de cancer de la prostate chez les pompiers, mais peu d'articles ont été publiés à ce sujet. Cette étude vise à trouver une corrélation entre le métier de pompier et le niveau de cancer de la prostate. L'article indique des agents cancérigènes potentiels liés au métier de pompier. Cette étude analyse cinq articles ayant utilisé différentes méthodes d'obtention des cas et des cohortes étudiés, ainsi que diverses méthodes de comparaison. Néanmoins, les articles étudiés ont conclu à une corrélation positive entre le niveau d'exposition des pompiers dans le cadre de leur métier et le niveau de cancer de la prostate. Les produits chimiques suspectés d'être des agents cancérigènes par ces études sont les hydrocarbures aromatiques polycycliques (HAP) et la fumée d'incendie. Cependant, les études ultérieures devront être plus rigoureuses dans le calcul des niveaux de cancer de la prostate, en tenant compte de facteurs liés au style de vie, et d'autres variables confondantes comme le tabac et la durée estimée de l'exposition.

Mots-clés :

Pompier, exposition professionnelle, néoplasme de la prostate

Abstract:

Prostate cancer is the most commonly diagnosed cancer among men. Since prostate cancer is a slow developing cancer, mortality can be prevented if the tumour is detected and treated in its early stages. There is proof that environmental exposures can increase the risk of prostate cancer. Many papers have performed data analyses on prostate cancer levels in firefighters. There has been some research on firefighter prostate cancer levels but few reviews on the topic. This paper focuses on finding whether there is a correlation between firefighting occupation and levels of prostate cancer. As well, this paper notes potential carcinogens within the firefighting occupation. Five papers were included in this review; these papers used different methods to obtain the cases and cohorts for the study. The papers also used different controls for comparison. Nevertheless, the papers found in the search supported a positive correlation between exposures in firefighting occupations and the level of prostate cancer. The two chemicals that were suspected carcinogens in these studies were Polyaromatic hydrocarbons (PAH) and fire smoke. However, future research can be more rigorous in calculations of prostate cancer levels by including lifestyle factors, other confounders such as smoking, and estimated length of exposure.

Keywords:

Firefighting, occupational exposure, prostate neoplasm

Introduction

Prostate cancer is the most commonly diagnosed cancer among men and the second most common cause of cancer mortality among men (Haas & Sakr, 1997). Each year, 25,500 Canadian men are diagnosed with prostate cancer (Prostate Cancer Canada, 2009). Both biological and environmental factors have been correlated with prostate cancer. Studies have shown that the main risks for prostate cancer cannot be altered: age, race and genetics. Many prostate cancer diagnoses occur in men over 60 years of age. More African-American males than Caucasian Americans are diagnosed with and die of prostate cancer. In addition, first degree family members with prostate cancer is a positive indication of the risk of developing prostate cancer. The risk is higher if the father's side of the family has a history of prostate cancer than if the mother's side has a family of history of prostate cancer (Flinton & Walters, 2005; Hsing & Chokkanlingam, 2006; Cancel-Tassin & Cussenot, 2005). Although the main risks are biological, and thus cannot be changed, the pathogenesis of prostate cancer is also linked to environmental exposures which can be altered.

Ninety percent of prostate cancer can be cured if it is treated early (Prostate Cancer Canada, 2009).. Identifying the chemicals that increase the risk of prostate cancer; exposures to these chemicals typically occur at workplace and are, therefore, occupational in nature. Firefighters are exposed to a number of chemicals in their work environment which is dynamic and the chemicals range from innocuous to known carcinogens (Kang, Davis, Hung, & Kriebel, 2008). During an "overhaul" procedure where firefighters extinguish hidden fires, self-contained breathing apparatus are not used. During the "overhaul" procedure which can last hours, and during actual firefighting the nature of exposure depends on the type of fire and the material that is burnt (Bolstad-Johnson, Burgess, Crutchfield, Storment, Gerkin, & Winston, 2000). Some of these exposures among firefighters include exposures to vapours and fumes of metals and organic chemicals, some of which are carcinogens. Typical exposures among firefighters are exposures to lead, antimony, cadmium, uranium, benzene, methylene chloride, polyaromatic hydrocarbons (PAH), perchlorethylene, toluene, and noncrystalline silica (Brandt-Rauf, Fallon, Tarantini, & Andrews, 1988; Fabian et al., 2001; Jankovic, Jones, Burkhar, & Noonan, 1991; Austin, Wang, Ecobichon, & Dussault, 2001).

Firefighters are at risk of developing a range of cancers among other health problems and these include leukemia, bladder cancer, brain cancer, colon cancer, kidney cancer and non-Hodgkin's lymphoma (Kang et al., 2008; Golden, Markowitz, & Landrigan, 1995; Guidotti, 1995; Guidotti, 2007; Youakim, 2006). A preliminary search of the scientific literature on prostate cancer and occupation indicated that prostate cancer among firefighters was underreported. Prostate cancer is the most commonly diagnosed cancer in men and occupational exposures have been reported to be associated with cancer development (Pukkala et al., 2009). Considering the extent of carcinogenic exposure and the prevalence of prostate cancer among firefighters, there may be a likely correlation between firefighting as an occupation and prostate cancer. The prevalence of prostate cancer among other cancers among firefighters has been reported to be higher (LeMasters et al., 2006; Bates, 2007).This study focuses on the development of prostate cancer among firefighters and its association with occupational exposures in firefighting. We also hope to identify potential chemicals and other burning substances that may be associated with the development of prostate cancer.

Methodology

A literature search was conducted to find relevant articles that reported of the risk of prostate cancer among firefighters. The search strategy was developed in Medline with the help of the reference librarian and once developed it was used to search all the relevant scientific databases. The search terms used were: "firefighters, prostate neoplasm, risk, occupational and environmental exposures." MeSH terms were used when possible otherwise text words in title and abstracts were searched. The search was conducted on the following databases: Ovid, Toxline, PubMed, Scopus and CINAHL. The time frame for the search was since inception to May 2010 and only articles on humans were included.

The inclusion criteria were case studies, cohort studies or cross-sectional studies reporting on the incidence and prevalence of prostate cancer among firefighters and its association with occupational exposures. The exclusion criteria were articles in languages other than English, animal experimentation studies and studies not reporting occupation as a risk factor for prostate cancer. The search results produced 185 articles in Ovid, of which fourteen articles fit the inclusion criteria. Toxline yielded no results.

PubMed showed two results, of which one was new. Scopus yielded 6 results, of which two were relevant. CINAHL yielded 1 review article. The review article on firefighters and the other original research articles are the basis of this paper.

All the searched articles were initially reviewed by reading the title and abstract and the ones that meet the inclusion criteria were retained for further scrutiny. At this stage the full article was reviewed and the relevant ones were included in this review. The selected articles were reviewed and relevant data on population demography, exposures, risk estimates, major findings and overall inferences was extracted using the PICO strategy (Hassig, 2009).

Results

From the many articles searched, fourteen articles met the search criteria and 5 were included: 3 case studies, 2 cohort studies, and no cross-sectional studies. The studies feature firefighters who were diagnosed or died of prostate cancer. These studies included between 981 and 60,878 cases of prostate cancer. Statistical tests were employed, by the studies, to find the correlation between exposures during firefighting and levels of prostate cancer.

Bates (2007) analysed records of all male cancers registered in California between the years of 1988-2003 and found 3,659 had firefighting (not administrative work in fire department) in the "occupation and industry" text fields. The data also shows that 1,144 of these firefighters had prostate cancer. A logistic regression was done in this case study using other cancers as a control to generate an odds ratio. The logistic regression models were controlled for age (5 categories), year of diagnosis (4-year categories), ethnicity, and socioeconomic status (5 categories). The results show a statistically significant positive odds ratio (OR) between firefighting and prostate cancer (OR = 1.22; 95% CI: 1.12–1.33) (Bates, 2007).

Krstev, Burgess, Crutchfield, Storment, Gerkin, and Winston (1998a,b) performed two case studies on prostate cancer: a smaller study based on 981 pathologically confirmed prostate cancer cases (Krstev et al., 1998a) and a larger study based on 60,878 American men who died of prostate cancer (Krstev et al., 1998b). The smaller case study by Krstev et al. (1998a) which was a case study on 981 new pathologically confirmed prostate cancer cases included 479 blacks and 502 whites who were diagnosed between 1986 and 1989, and 1,315 population controls (594 blacks and 721 whites). All of the cases and controls resided in either: Atlanta, Detroit, or in 10 counties in New Jersey. Data on cancer history was obtained through cancer registries. Information on occupation, including lifetime work history, was collected by in-person interview. In this small case-control study, the authors calculated odds ratios (ORs) with 95% confidence intervals (95% CI). The results indicated that firefighters had an increased risk of developing prostate cancer (chi2 trend, p = 0.02) (Krstev et al., 1998a). Due to the dependence on recall, the interviews can only show patterns of chemical exposure without scientific validity. Thus no chemical exposure can be conclusively linked to increasing risk of prostate cancer. Under the Standard Occupational Classification (SOC) by the U.S. Department of Commerce in 1980, Firefighters with and SOC of 512 had an OR = 3.85; 95% CI : 1.34-11.1. Firefighters with an SOC of 5123 had an OR = 3.34; 95% CI : 1.13-9.91 (Krstev et al., 1998a).

In a study of death certificates in 24 states, Krestev *et al.* (1998b) performed another case study that included 60,878 U.S. men with prostate cancer as underlying cause of death. The subjects were matched with controls that had died of all other causes except cancer, from 1984 to 1993. The industrial and occupational information were obtained from death certificates. Risk of prostate cancer mortality were shown to increase with increasing years of employment in firefighting (chi2 trend, p=0.02). Krstev *et al.* (1998b) notes the prevalence of the chemical PAH in firefighting. There were 140 cases of prostate cancer among whites, yielding a mortality odds ratio (MOR) of 1.2, 95% CI : 1-1.4 (Krstev et al., 1998b). There were 13 cases of prostate cancer among African Americans yielding a MOR = 2.2; 95% CI : 1.2-3.9 (Krstev et al., 1998b). The authors noted a significantly increased MOR of prostate cancer.

Ma *et al.* (1998) performed a cohort study using data from the National Cancer Institute, the National Institute for Occupational Safety and Health, and the National Center for Health Statistics. These institutions collected data on cause of death and occupation since 1984 on 24 states (Colorado, Georgia, Idaho, Indiana, Kansas, Kentucky, Maine, Missouri, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, North Carolina, Ohio, Oklahoma, Rhode Island, South Carolina, Tennessee, Utah, Vermont, Washington, West Virginia, and Wisconsin). The data was coded by the Bureau of Census Index of Industries and Occupations using death certificates. Among the firefighters, there were 1883 cancer deaths of which 1817 occurred in whites and 66 in blacks. The MOR was calculated for black

and white firefighters in which all deaths except cancers were used as the reference for the occupation. Then the MOR was adjusted for year and age of event. The only cancer that was elevated in both black and whites was prostate cancer (whites: MOR = 1.2; 95% CI : 1.0- 1.3; blacks: MOR = 1.9; 95% CI : 1.2-3.2) (Ma et al., 1998). However, the authors noted that this study lacks information on lifestyle, specific exposures, and other confounders related to disease outcome; therefore, more research is needed.

Demers, Checkoway, Vaughan, Weiss, Heyer, and Rosenstock (1994) performed a cohort study to determine if fire smoke increased the risk of prostate cancer. A cohort of 2,447 male firefighters in Seattle and Tacoma was used for the study. The population was followed for 16 years (1974-89). Incidence of cancer was ascertained using a population-based tumour registry; the control was the local rates among 1,878 policemen from Seattle and Tacoma. The 66 incidences of prostate cancer among firefighters was slightly elevated compared to the policemen (standard incidence ratio [SIR] = 1.4; 95% CI : 1.1-1.7) (Demers et al., 1994). Nevertheless, the sample was small; the correlation was not strong and was not related to the number of years of exposure.

Discussion

This review supports the hypothesis that prostate cancer is correlated with the firefighting occupation, however, the exact chemicals which are involved are not known, but a number of putative occupational exposures are reported. In this review the required information on incidence and mortality of prostate cancer among firefighters in the selected studies were obtained from death certificates, tumour registries and other confirmed cases. In these studies controls were selected from the population, other cancers, or other occupations. The studies could have included exposure matrices in their calculations to account for cumulative exposure. These results only show an overall correlation without information on the relationship between the length of work as a firefighter and the degree of risk of prostate cancer. A review by LeMasters *et al.* (2006) supported the positive correlation between firefighting occupations and prostate cancer and reported a summary estimate risk of SRE = 1.28;95% CI:1.15-1.43 following a systematic review and meta-analyses of thirty two studies on cancer risk among firefighters. It is believed that firefighters by virtue of their occupation are susceptible to a number of cancers including multiple myeloma, non-Hodgkin's lymphoma and testicular cancer (LeMasters et al., 2006).

PAH (Krstev et al., 1998b) and fire smoke (Demers et al., 1994) are suspected carcinogens but the relationship has not been confirmed although believed to be plausible. The main reason for the inability to confirm the carcinogens is because the chemical identification is based on estimates of chemical exposures within different occupations. Nevertheless, fire smoke and PAH are correlated with increased rates of prostate cancer among firefighters but the relationship is not proven to be causal. Moreover, it is also believed that firefighters at work are exposed to fumes, vapours and contaminated air in places where fire is burning. These fumes and vapours that emerge from burning materials are harmful substances comprising benezene, n-hexane, vinyl chloride, polycyclic aromatic hydrocarbons, polychlorinated biphyenyls, N-nitroso compounds, lead, arsenic and mercury among others (Bates, 2007). Firefighters are exposed to mixtures of chemical substances some of which are carcinogenic. The routes of exposure and delivery to target organs include skin, respiratory system and ingestion. These exposures at the site of contact or target organs produce direct and indirect effects associated with modulation of biochemical or physiologic pathways and other pathways of toxicity (LeMasters et al., 2006). Although firefighters use standard protective equipment which include thermal gear, respirators and face shields the exposures transcend these barriers and impose undue body burden on the firefighters (Coca, Williams, Roberge, & Powell, 2010). Heavy physical activity during firefighting enhances the exposure of the firefighter in spite of all the protective equipment.

Firefighters are susceptible, because of occupational exposures, to a number of cancers and prostate cancer is one of the major cancers. A number of exposures occur during the firefighting "overhaul" procedures. Firefighters are exposed to carcinogenic toxicants which increase the risk of cancers. Although this review shows that there is a positive correlation between prostate cancer and firefighting, individual substances have not been identified, more rigorous research is, therefore, needed. In particular, more information is needed on potential carcinogens present in the workplace of firefighters. It is also necessary to evaluate exposures more efficiently by quantifying exposure into exposure matrices and identifying the nature and the intensity of exposures through dosimetry. The duration of exposure for an individual during ones tenure as a firefighter and the latency period also needs to be considered. Appropriately designed protective equipment would cer-

tainly help in protecting the firefighters on their job. Confounders such as lifestyle factors should also be accounted for in the calculations of future research.

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Appendix: Data Collected

Study Title and Reference	*Population*	*Exposures*	*Prostate Cancer Risk*	*Major Findings*
Krstev, S., 1998a	981 new cancer cases (479 blacks and 502 whites) diagnosed between 1986 and 1989, and 1,315 population controls (594 blacks and 721 whites); in Atlanta, Detroit, and 10 counties in New Jersey.	No occupational exposures were identified as potential risk factors	Firefighters with an SOC of 512 had an OR = 3.85; 95% CI : 1.34-11.1. Firefighters with an SOC of 5123 had an OR = 3.34; 95% CI : 1.13-9.91. *SOC= Standard Occupational Classification (SOC)	Occupation was not a major determinant of prostate cancer risk.
Krstev, S., 1998b	60,878 U.S. men with prostate cancer as underlying cause of death was selected and matched with controls who died of all other causes except cancer, from 1984 to 1993.	PAH-possible carcinogen	(MOR) of 1.2, 95% CI 1-1.4. There were 13 cases of prostate cancer among African Americans yielding a MOR = 2.2; 95% CI : 1.2-3.9.	An excess of prostate cancer risk was observed in low social economic status occupations
Bates, M. N., 2007	Searched male cancers registered in California (1988-2003); 3,659 firefighters, 1,144 had prostate cancer		OR = 1.22; 95% CI: 1.12-1.33	Supports hypothesis that firefighting exposures may increase risk of cancer
Ma, F., 1998	1,883 male firefighters in 24 states who had died of cancer.		Prostate cancer risk was elevated in both groups (whites: MOR = 1.2; 95% CI = 1.0-1.3; blacks: MOR = 1.9; 95% CI = 1.2-3.2).	The overall cancer mortality was slightly elevated among white firefighters but the increase was not significant among black firefighters. Only prostate cancer was elevated in both groups. More research is needed to confirm the existence of differential rates of cancer mortality risks among firefighters of different race/ethnic subpopulations.
Demers, P. A., 1994	2,447 male firefighters in Seattle and Tacoma, (Washington, USA). The study population was followed for 16 years (1974-89).		(SIR = 1.4, 95 percent confidence interval [CI] = 1.1-1.7) (incidence density ratio [IDR] = 1.1, CI = 0.7-1.8)	The correlation was not strong but an increased risk was found.

Extreme Male Brain Theory of Autism

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Résumé :

(traduction)

Les troubles du spectre autistique (TSA) sont une catégorie de troubles de la neurologie du développement présentant des symptômes de dégradation sociale et des communications, ainsi que des comportements restrictifs et répétitifs. Ils sont davantage présents chez les hommes que chez les femmes, et cette différence entre les sexes a beaucoup influencé les hypothèses au sujet de leur étiologie. La théorie du cerveau mâle extrême (CME) est un modèle cognitif proposé par Simon Baron-Cohen pour expliquer les différences entre les sexes et les causes potentielles des TSA susmentionnés. Elle repose sur sa théorie d'empathisation-systématisation, qui consiste à classer les sujets dans cinq profils cognitifs (Type S, Type E, Type B, Type S extrême et Type E extrême). Ces profils cognitifs déterminent la capacité du sujet de systématiser et d'être en empathie avec. La systématisation est la capacité de comprendre un système et d'en déduire les règles. Elle exige des capacités de déduction et d'analyse. L'empathie a trait à la compréhension des émotions et des comportements humains, ce qui exige des capacités sociales et de communication. Les hommes ont tendance à mieux systématiser, tandis que les femmes présentent le profil opposé. Selon la théorie du CME, les autistes auraient un profil de Type S extrême, car on peut expliquer leurs troubles de communication sociale par leur déficit d'empathie, alors qu'on peut relier à leur fort niveau de systématisation leur préoccupation au sujet des patrons et leur comportement axé sur les détails. Ensemble, ces modèles cognitifs ont conduit à la théorie de la testostérone fœtale (Tf), qui stipule qu'un niveau élevé de testostérone prénatale est un facteur de risque pour le profil cognitif hypermasculinisé des sujets atteints de TSA. Dans cet article, les auteurs évaluent la validité des théories du CME et de la Tf, en étudiant la documentation portant sur la Tf avec des caractéristiques autistes dans l'ensemble de la population. Ces sept études ont confirmé une corrélation entre des niveaux élevés de Tf et une augmentation des caractéristiques autistes, mais il faut envisager d'y mettre des limites au moment de généraliser ces informations à un échantillon de sujets atteints de TSA.

Mots-clés :

Troubles du spectre autistique, théorie du cerveau mâle extrême, théorie d'empathisationsystématisation, théorie de la testostérone fœtale

Abstract:

Autism spectrum conditions (ASCs) are a category of neurodevelopmental disorders with symptoms of communication and social impairment, and the exhibition of restrictive and repetitive behaviours. Their occurrence is greater in males than females and this sex difference has played an important part in hypothesizing their etiology. The Extreme Male Brain (EMB) theory is a cognitive model proposed by Simon Baron-Cohen to explain the aforementioned sex differences and potential cause of ASCs. It is based upon his Empathizing -Systemizing theory, which classifies individuals into one of five cognitive profiles (Type S, Type E, Type B, Extreme Type S and Extreme Type E). These cognitive profiles determine an individual's ability to systemize and empathize. Systemizing is the ability to understand and derive the rules of a system, and requires deductive and analytical skills. Empathizing relates to understanding human emotion and behaviour, thus requires social and communication skills. Males tend to systemize better than empathize while females have an opposite profile. Based upon the EMB theory, autistic individuals would possess an Extreme Type S profile as their impairments in social communication can be explained by a deficit in empathizing, while their preoccupation with patterns and detail-oriented behaviour can be related to their high systemizing. Together, these cognitive models have resulted in the Foetal Testosterone (fT) Theory, which implicates high prenatal testosterone as a risk factor for the associated hypermasculinized cognitive profile of individuals with ASCs. This review paper assesses the validity of the EMB and fT theories by reviewing the literature relating fT with autistic traits in the general population. The seven studies confirmed a correlation between higher fT levels and an increase in autistic traits, but limitations need to be considered when generalizing this information to an ASC sample.

Keywords:

Autism spectrum disorders, extreme male brain theory, systemizing– empathizing theory, foetal testosterone Theory

Introduction

Autism spectrum conditions (ASCs) or autism spectrum disorders (ASDs) are a category of neurodevelopmental conditions characterized by impairments in the domains of communication, social interaction, and repetitive behaviours and interests (Faras, Al Ateeqi, & Tidmarsh, 2010; Hill & Frith, 2003; Knickmeyer & Baron-Cohen, 2006). Classical autism, Asperger Syndrome (AS) and Pervasive developmental disorder-not otherwise specified (PDD-NOS) are the three main types of ASCs and they differ in their number and severity of symptoms from each of the three domains (Hughes, 2008; Jones, Cork, & Chowdhury, 2006) Specific features of each type of ASC are described in Table 1.

The incidence of autism is greater in males than females (4:1) with an even greater sex difference for AS (10:1 males to females) (Baron-Cohen, 2009; Manson, 2008). Earlier reports showed a prevalence of 0.4/1000 in the general population, but recent rates for these disorders now range from 1-6/1000 (Marco & Skuse, 2006). Although ASCs appear to be on the rise, many attribute this phenomenon to improved diagnostic methods or expanded diagnostic criteria (Hughes, 2008; Jones et al., 2006; Marco & Skuse, 2006; Baron-Cohen, Knickmeyer, & Belmonte, 2005). However with little known about the etiology of these disorders, it is difficult to make this conclusion with any certainty. Changes in maternal and neonatal exposure to important environmental factors cannot be excluded from consideration. There appears to be a genetic component to these disorders as exemplified by the higher recurrence rate in siblings (2-8%) and twins (10-90%) (Marco & Skuse, 2006). And, while the spectrum of disorders is not directly heritable, recent molecular genetics studies have implicated multiple chromosomal loci (specifically chromosomes 15, 16, and 17) in their etiology (reviewed in (Hughes, 2008)). Thus, a multifactorial explanation involving both the environment and genetics contribute to the complex neurological mechanisms underlying ASCs (Faras et al., 2010; Hughes, 2008).

A variety of theories have been put forth that attempt to relate the symptoms of autism to existing cognitive concepts, such as the Theory of Mind Deficit, Executive Dysfunction, and Weak Central Coherence Theory (Hill & Frith, 2003). Others have taken these a step further by overlaying biologically relevant changes and exploring how these relate to cognitive deficits observed in autism and how together they might explain the important sexual dimorphism in the incidence rate. One such theory is the Foetal Testosterone (fT) Theory proposed by Simon Baron-Cohen (Baron-Cohen et al., 2009; Manning, Baron-Cohen, Wheelwright, & Sanders, 2001). It derives from the Ex-

Table 1 Characteristics of three main Autism Spectrum Conditions

Type of ASC	*Symptoms*
Classical autism	• deficits in social abilities and empathizing • deficits in communicative language • cognitive impairment (usually lower than average IQ) • delay of speech development • restrictive interests and behaviours • detectable before the age of 3
Asperger Syndrome	• poor social skills and lack of insight • restrictive interests and behaviours • IQ over 70 • no delay in speech
PDD-NOS	• individuals who do not meet the criteria of autism or AS, although still displaying symptoms in the 3 domains

(Adapted from: Jones A, Cork C, Chowdhury U. (2006). AUTISTIC SPECTRUM DISORDERS: Presentation and assessment. Community Pract. 2006 Mar;79(3):97-8)

treme Male Brain (EMB) theory that relates to the Empathizing-Systemizing (E-S) theory (Baron-Cohen, 2009; Baron-Cohen, 2002; Baron-Cohen, Richler, Bisarya, Gurunathan, & Wheelwright, 2003). The goal of this work is to review the Foetal Testosterone Theory of autism by delving into the cognitive models that define it; a review of the Empathizing-Systemizing and Extreme Male Brain theories will first be presented.

The Empathizing-Systemizing Theory

The premise of the Empathizing-Systematizing Theory (E-S) is that within the population, there are generally five brain types: Type S, Type E, Type B (balanced brain), and the Extreme Type S and E brains. Table 2 shows the cognitive profile of individuals with each brain type. A higher proportion of males tend to have a Type S brain as compared to other types and thus Type S brains can be considered a "male brain" whereas a higher proportion of females have Type E, which signifies a "female brain" (Baron-Cohen, 2009; Baron-Cohen et al., 2003; Goldenfeld, Baron -Cohen, & Wheelwright, 2005).

Males tend to systemize better than empathize, which relates to their Type S brains whereas females are superior at empathizing compared to systemizing (Baron-Cohen, 2002; Baron-Cohen et al., 2003). Systemizing is the ability to generate rules for a system and understand the processes underlying those rules. Individuals who can systemize tend to be very detail-oriented, understand patterns and thus can predict input and output relationships (ie: variable A correlates with outcome B). Such examples include memorizing the patterns of a train timetable (numerical system), understanding how to operate a video recorder (mechanical system), understanding a computer logarithm (abstract systems) or differentiating between types of stones (collectible system) (Baron-Cohen, 2009). Stronger systemizing in males may also relate to their appeared superior spatial abilities, specifically those of 2D and 3D mental rotation tasks and targeting (Voyer, Voyer, & Bryden, 1995; Collins & Kimura, 1997). For contextual-based systems such as social interactions, systemizing cannot be easily applied, as human emotions and behaviour tends to be highly variable. Empathizing is in opposition to systemizing with females tending to outperform males in this domain. A Type E brain appears to impart the ability to understand others via interpretation of their mental states and requires skills in empathy and communication in order to respond appropriately (Baron-Cohen, 2009; Baron-Cohen et al., 2005). Females tend to possess better social skills, language abilities, and verbal fluency as compared to males (Hines et al., 2003; Knickmeyer et al., 2006a) which may be related to their capacity to better understand and predict human behaviour (Baron-Cohen, 2009; Baron-Cohen, 2002; Knickmeyer, Baron-Cohen, Raggatt, Taylor, & Hackett, 2006b). Studies using the Empathizing and Systemizing Quotients (the EQ and SQ) have shown that in a sample of 114 males from the United Kingdom and Canada, the Type S profile was most prominent at 53.5% followed by Type B at 23.7%, Type E at 16.7%, Extreme Type S at 6.1% and no males displaying Extreme Type E profiles. In a related sample of 164 females, 44.2% of females had a

Table 2 Cognitive profiles and attributes that best describe them according to the Empathizing-Systemizing theory

Type of Cognitive Profile	*Attribute*
Type E (E > S)	Individuals who have stronger empathizing than systemizing abilities
Type S (S > E)	Individuals whose systemizing is stronger than their empathizing
Type B (S = E)	Individuals whose empathy is as good (or as bad) as their systemizing (B stands for "balanced")
Extreme Type E (E >> S)	Individuals whose empathy is above average, but who are challenged when it comes to systemizing
Extreme Type S (S >>E)	Individuals whose systemizing is above average, but who are challenged when it comes to empathy

(Adapted from: Baron-Cohen S. Autism: the empathizing-systemizing (E-S) theory. Ann N Y Acad Sci. 2009 Mar;1156:68-80)
S= systemizing ability; E= empathizing ability

Type E profile, 35% with Type B, 16.5% with Type S, 4.3% with Extreme Type E and none having an Extreme Type S profile (Baron-Cohen et al., 2003; Goldenfeld et al., 2005). Although individual variations are apparent, there is still a strong sex difference in systemizing and empathizing abilities.

The Extreme Male Brain Theory

Baron-Cohen's Extreme Male Brain (EMB) theory of autism is an extension of his E-S theory. It contends that individuals with ASCs have an Extreme Type S cognitive profile which results in higher than average systemizing with impaired empathizing (Baron-Cohen, 2009; Baron-Cohen et al., 2009). Lowered empathizing would then be responsible for their social and communication deficits, exemplified by the difficulties these individuals have in understanding and responding to others, while superior systemizing abilities would be attributed to their detailed and pattern-oriented behaviour and inability to predict human emotions and behaviours (Baron-Cohen, 2009). Results of a Japanese study showed that from a sample of 38 males and 10 females, 31.6% of ASC individuals have an Extreme S type brain, whereas 36.8% had a Type S brain, 28.9% a Type B, 2.6% a Type E and none had Extreme Type E (Wakabayashi et al., 2007). Similar results were found in a separate sample of high functioning autistic individuals (33 males, 14 females): 46.8% had an Extreme Type S brain and 40.4% had a Type S profile (Baron-Cohen et al., 2003; Goldenfeld et al., 2005). Note, however, that ASC individuals in these studies were predominantly male, a caveat typical of this work given the higher incidence rate of these disorders in males. Taken together the results of these studies further support the EMB theory (Baron-Cohen, 2009;Wakabayashi et al., 2007; Goldenfeld et al., 2005) in that a large proportion of autistic individuals fall within the range of Extreme Type S to Type S cognitive profiles, indicative of even higher systemizing ability than the typical male profile.

The Foetal Testosterone Theory of Autism

The Foetal Testosterone (fT) theory of autism is rooted in the sex difference that exists in ASCs. It relates to the EMB and E-S theories because androgens are hypothesized to play a role in foetal brain development (Geschwind & Behan, 1982; Geschwind & Galaburda, 1985; Pomerantz, Fox, School, Vito, & Goy, 1985; Chura et al., 2010) and high fT might thus be a risk factor for the hypermasculinized cognitive profile (Extreme Type S brain) in ASC individuals (Knickmeyer & Baron-Cohen, 2006). In animal studies, changes in prenatal testosterone have been shown to influence neuronal differentiation and postnatal cognitive behaviour (Phoenix, Goy, Gerall, & Young, 1959; Goy & McEwen, 1980). The results of studies with rodents and non-human primates show that the removal or addition of testosterone in males and females in utero during androgen-sensitive critical periods leads to changes in sexually dimorphic behaviour such as spatial abilities, play patterns, grooming, and sexual behaviours (Phoenix et al., 1959; Goy & McEwen, 1980; Wallen, 2005; Goy, Bercovitch, & McBrair, 1988; Casto, Ward, & Bartke, 2003). Indirect evidence stems from observations of androgen receptor binding in key areas of the foetal primate brain such as the hypothalamus, the amygdala, the cerebral cortex, the corpus callosum and the cerebellum (reviewed in 9). Thus, it is proposed that if levels of testosterone change significantly during critical periods, development of these key brain areas would be altered as would be the behaviours they underlie (Baron-Cohen et al., 2009; Hines, 2006). Animal work has shown modulation in the levels of circulating testosterone by maternal stress or alcohol consumption in male offspring (Skuse, 2009; Ward et al., 2003) and in fact, recent work has shown an important positive correlation between cortisol and plasma testosterone levels in the fetus (Chakrabarti et al., 2009; Gitau, Adams, Fisk, & Glover, 2005), further supporting environmental factors as capable of altering circulating testosterone during development.

The organizational effects of testosterone are found within critical periods. The current literature defines one of these periods between weeks 8 and 24 of gestation given that this is when the sex difference in fT is the greatest (Finegan, Bartleman, & Wong, 1989). Some implicate postnatal testosterone in influencing neural development, since there is a surge that occurs immediately after birth. However, no link has yet been reported between postnatal testosterone and sexual dimorphism in behaviour (Wallen, Maestripieri, & Mann, 1995). Part of the difficulty in assessing which behaviours are impacted by changes in foetal testosterone is our inability to alter foetal testosterone levels for ethical reasons. Therefore research with humans consists of evaluating the normal variations in fT levels in the general population and relating these to specific behavioural phenotypes. The direct method of assessing the relationship between fT and autistic traits is to measure fT in

umbilical cord blood, maternal blood, or amniotic fluid in a sample of children and to determine if androgen levels positively correlate with certain male-typical behaviours also seen in ASCs. If ASCs are an extreme of the male-typical brain, and this effect is influenced by surges in prenatal testosterone, then one would expect individuals with higher than average fT to have more male-typical traits and cognitive abilities. For example, males tend to excel at spatial abilities and studies have shown a high male dominance in tasks such as targeting and mental rotation. Females have better social skills, language abilities, and verbal fluency as compared to their male counterparts (Hines et al., 2003; Knickmeyer et al., 2006a). Thus, studies assessing the relationship between fT and cognition would be expected to reveal that individuals with high levels of testosterone would be superior at mental rotation and targeting tasks, while more impaired at empathizing and language abilities (Knickmeyer & Baron-Cohen, 2006). Those individuals with higher fT levels would also demonstrate more autistic traits, such as having problems in social interaction as well as impairments at verbal and non-verbal communication, as compared to people with lower fT levels (Baron-Cohen, 2009; Baron-Cohen et al., 2009).

Most of the studies assessing fT and autistic traits were from the Cambridge Foetal Testosterone Project, which used amniotic fluid samples from 235 women who underwent routine amniocentesis during their second trimester of pregnancy (Auyeung, 2009). This time period represents weeks 14-20 of gestation, which encompasses the critical period mentioned above when surges in fT are reportedly observed (Manson, 2008; Ward et al., 2003). Testosterone levels were analyzed by radioimmunoassay and participants were excluded from the study if the amniocentesis carried chromosomal abnormalities, if twins were the outcome, if the pregnancy led to birth defects, or if medical information was missing (Auyeung, 2009). The healthy children born to these women were enrolled in various studies to evaluate the presence of autistic traits and/or systemizing and/or empathizing traits at different stages of postnatal development. Descriptions and summaries of the results from these studies are detailed below.

When 129 typically developing toddlers aged 18-24 months from the Cambridge Foetal Testosterone Project were assessed using the Checklist for Autism in Toddlers (Q-CHAT) as an outcome measure of autistic traits, the authors found a positive correlation between fT levels and Q-CHAT scores (higher scores indicate more autistic traits), with a significant difference in scores between the males and females (males: 28.09 ± 7.30, females: 24.94 ± 6.52, $p < 0.05$ Cohen's $d = 0.46$, Appendix A, 36). While both foetal oestrogen and testosterone were assessed in their amniotic fluid samples, no relationship with oestrogen was observed (Auyeung, Taylor, Hackett, & Baron-Cohen, 2010).

In another study, a sample of 4-year-olds (24 males, 14 females) was assessed for a relationship between fT and skills of empathy and social interaction – animations of geometric figures were used to assess their ability to understand intentional human interactions. No correlation was found between fT and rates of mental or affective state, whereas fT was negatively correlated with intentional propositions and positively correlated with frequency of neutral propositions (Appendix A, Knickmeyer et al., 2006b). Sex differences in these results were also observed, but no correlation was present when sexes were analyzed separately (Knickmeyer et al., 2006b).

Using the Child's Communication Checklist (CCC), 35 males and 23 females aged 4 years were tested to explore the relationship between fT and quality of social relationships, communication skills, and presence of restricted interests in children of the same age. The results show a negative correlation between fT and scores for quality of social relationships and a positive correlation for restricted interests (Knickmeyer, Baron-Cohen, Raggatt, & Taylor, 2005). Males scored higher on the restricted interests subscale (Cohen's $d = 0.64$), whereas females scored higher for quality of social relationships (Cohen's $d = 0.47$; Appendix A, Knickmeyer, 2005). Further probing reveals no relationship between fT and quality of social relationships for each sex evaluated separately, whereas a correlation between fT and restricted interests was found exclusively in males. Subscales assessing speech, syntax, and pragmatics scores did not show sex differences or a correlation with fT (Knickmeyer, 2005).

In children 6-8 years of age, Chapman et al (2006) evaluated capacity to empathize using one of two tasks; study 1 used an Empathy Quotient (EQ) whereas study 2 used the Reading the mind in the eyes task (Eyes-C). The Eyes-C test involves looking at photos of eye regions, while the remaining facial features are covered, and discerning the emotional state of the photo's subject. In the first study, males scored lower than females on the EQ, interpreted to demonstrate poorer empathizing abilities (mean males' score: 32.62 ± 9.57, females' score: 39.12 ± 7.44, $p<0.01$); Cohen's $d = 0.76$; Appendix A, 38) and fT was negatively correlated with EQ scores ($r = -0.28$, $p< 0.01$). To exclude

sex as a potential confound, the scores for males and females were evaluated separately and the correlation between fT and EQ scores remained in males but was no longer apparent in female subjects.

A negative correlation between fT and Eyes-C scores was reported in the second study (Chapman et al., 2006), thus suggesting that individuals with higher fT levels had more difficulty correctly identifying emotions on the Eyes-C test. This effect remained when analyzing data from males ($r = -0.42$, $p<0.01$) and females ($r = -0.29$, $p<0.05$) separately, further supporting the notion that these differences are due to fT levels and not sex (Chapman et al., 2006).

The relationship between fT levels and sex-typical play was assessed in children aged 6-10 years in the Auyeung et al study (2009). Using the Pre-school Activities Inventory (PSAI), where higher scores reflect male-typical behaviour, the authors found a positive correlation between fT and sex-typical play behaviour in both males ($r = 0.20$, $p<0.05$) and females ($r = 0.42$, $p<0.001$) (Appendix A, Auyeung et al., 2009).

In another study from the Cambridge Foetal Testosterone Project, the authors employed the Childhood Autism Spectrum Test (CAST) and the Child Autism Spectrum Quotient (AQ-CHILD) to assess for autistic traits in 6-10 year-old children. Both instruments are parent-report questionnaires and higher scores translate to increased presence of autistic traits. The results found fT levels to be correlated with CAST ($r = 0.25$, $p < 0.01$) and AQ-Child scores ($r = 0.41$, $p < 0.01$). Males scored higher than females for the combined AQ-Child score (male mean score: 48.75 ± 17.96, female mean score: 34.42 ± 15.01, $t233 = 6.64$, $p < 0.01$) and the CAST score (male mean score: 5.22 ± 4.35, female mean score: 4.65 ± 3.87, $t226.25 = 2.12$, $p < 0.05$; Appendix A, Auyeung, 2009). When analyzing male and female scores separately to determine the correlation between fT and test scores, only the AQ-Child was found to correlate with fT. The CAST was positively correlated with fT in males but not in females (Auyeung, 2009). The authors attributed the negative finding in females to the narrower range in CAST scores and fT levels.

The results of a recent study by an unrelated group using data from the Western Australian Pregnancy Cohort showed a positive correlation between free fT levels (measured from umbilical cord serum) and Pragmatic Language Scores (PLS) ($r = 0.3$, $p < 0.01$) (Appendix A, Whitehouse et al., 2010). Note that higher PLS scores indicate greater difficulty in social communication, a trait typically associated with ASD individuals (Whitehouse et al., 2010). Further details of the six studies from the Cambridge Foetal Testosterone Project and the study from the Western Australian Pregnancy Cohort are presented in Appendix A.

Overall, the results of these studies show a positive correlation between fT levels and autistic traits. The outcome measures assessed different domains of autistic traits such as social skills, attention switching, attention to detail, communication and imagination, thus increasing the comprehensiveness of the findings. Instruments used to measure autistic traits included the Childhood Autism Spectrum Test (CAST), the Autism Spectrum Quotient-Child Version (AQ-Child) and the Checklist for Autism in Toddlers (Q-Chat), which are questionnaires that detect the amount and intensity of autistic traits in a general population (Auyeung, 2009; Auyeung et al., 2010). Note that test-retest reliability and validity studies for these instruments are currently ongoing. Also used was the Pragmatic Language Score (PLS), as verbal communication is known to be affected in ASC individuals (Whitehouse et al., 2010). Social interaction, including quality of social relationships, and presence of restricted interests were also assessed in age appropriate children (Knickmeyer et al., 2006b; Knickmeyer, 2005). Two studies focused on sextypical play (Auyeung et al., 2009) and empathizing (Chapman et al., 2006), both known
to be somewhat sexually dimorphic in children. Thus, the male-typical and autistic traits that were found to correlate with fT levels, such as reduced verbal communication, reduced social interaction, increased restricted interests, male-typical play, and reduced empathizing abilities lend further support to the EMB theory.

Limitations/Evaluation of the Foetal testosterone theory

The fT studies reviewed above appear to strengthen the fT theory of autism. However, an important limitation requiring consideration is that the studies did not assess fT in an ASC sample. Although fT levels were normally distributed and were shown to correlate with autistic traits, the sample was from the general population and not an autistic one. The ideal next step for this group would be to look specifically at children from their population for whom fT was assessed but who now have a diagnosis of ASC to compare to children without this diagnosis or even to children with

a diagnosis of another neurodevelopmental disorder. In fact, Baron-Cohen and his colleagues are currently using the Danish Biobank, where a large number of amniotic fluid samples were collected from pregnant women, in order to evaluate fT levels that they will compare to clinical cases of ASCs within the offspring of the mothers from whom fluid was collected (Baron-Cohen, Auyeung, Ashwin, & Knickmeyer, 2009). The results of this work are highly anticipated.

Another important limitation is that results are correlational, thus fT levels may not directly cause autistic traits, nor does it necessarily account for all of the variability observed. Other researchers suggest that there may be a third unknown factor responsible for both the effects of fT as well as the autistic traits (Barbeau, Mendrek, & Mottron, 2009). For example, Skuse (2009) notes that the fT theory cannot explain whether high fT levels cause ASCs or whether these increase susceptibility to ASCs via genetic factors. Recently, an association between clinical cases of AS, autistic traits, and genes that regulate sex steroids was reported (Chakrabarti et al., 2009). The present data are promising but are, as of yet, inconclusive as the etiological basis of ASCs.

Further criticism of the Cambridge group studies is the single assessment of fT levels and whether they were taken at the same time during development in all individuals (weeks 8-24 being a large range); thus, it is difficult to deem these levels as representative of foetal levels as hormone levels fluctuate over foetal development. Similarly, amniocentesis is generally carried out in women who are older and thus the foetus may be at risk for multiple insults during development. Maternal age, however, was controlled for in all amniotic fluid studies, and there was no correlation between age and outcome measures. Thus, despite its limitations, amniotic fluid is still a valid and the most ethical method for obtaining measures of fT, and may be superior to other methods such as using umbilical cord serum. Umbilical cord testosterone may contain maternal testosterone (as it contains maternal blood), thus may not reflect an accurate measure of fT (Auyeung et al., 2010).

Conclusion

The studies presented herein using direct measurements of fT yielded consistent correlations between higher fT levels and increased ASC characteristics, with effects being more prominent in males, thus supporting the EMB theory. While recognizing that most studies were conducted by a single group as part of the Cambridge Foetal Testosterone Project and that the psychometric properties of the evaluation instruments have been a point of contention for some researchers in this field (Skuse, 2009), these studies are nonetheless an important first step in exploring how biology can affect cognition. Future studies of the EMB theory may help us better understand how biologically relevant events underlie important sex differences in neurodevelopment and behaviour and why one sex appears to be more vulnerable to insults during this critical developmental period.

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Appendix 1: Studies Assessing Foetal Testosterone and Autistic Traits

Study	Sample	Outcome variables	Outcome Measures	Results
Auyeung, B., 2010	N = 66 N = 63	Q-CHAT, amniotic fT and fE levels	fT vs autistic traits in toddlers 18-24 months	Males: fT = (0.80 ± 0.36), Q-CHAT = (28.09 ± 7.30/ for a max. of 100 points) Females: fT = (0.34 ± 0.23), Q-CHAT = (24.94 ± 6.52 for max. of 100 points) Sex-difference effect size: fT (d = 1.36), Q-CHAT (d = 0.46), no effect of fE
Whitehouse, A. J., 2009	N = 78	PLS, fT in umbilical cord serum	TT vs free testosterone and pragmatic language ability in 10 year old females	PLS: mean = 1.06 (SD = 1.72, range: 0–7 out of max of 20 points) FAI = 7850.73 (SD = 22.05, range =6.93–123.53) Free testosterone, but not TT was positively correlated with PLS (R = 0.3, p = 0.009)
Auyeung, B…. Hines, M., 2009	N = 112 N = 100	PSAI, amniotic fT	fT vs sex-typical play in children aged 6-10	Males: fT (m = 0.83, SD = 0.83), PSAI scores (m = 68.95, SD = 10.73 Females: fT (m= 0.33, SD = 0.32), PSAI scores (m = 34.95, SD = 12.48) fT correlated positively with PSAI scores for both girls (r = .42, p < .001) and boys (r = .20, p < .05).
Auyeung, B….Hackett, G., 2009	N = 118 N = 117	CAST, AQ-CHILD, amniotic fT	fT vs empathizing in children aged 6-8	Males: fT (m=0.84, SD=0.41), AQ-CHILD (m=48.75, SD=17.96), CAST (m=2.36, SD=0.82); within sex, positive correlation between fT and AQ-Child and CAST scores Females: fT(m=0.32, SD=0.20), AQ-CHILD (m=34.42, SD=15.01), CAST (m=2.15, SD=0.69); within sex, positive correlation between fT and AQ-Child (no correlation with CAST scores) Between sexes: positive correlation of fT and AQ-Child and CAST scores
Chapman, E., 2006	N = 100 N = 93	EQ-C, Eyes-C Task (N = 40 males, N = 38 females), Amniotic fT	fT vs empathizing in children aged 6-8	Experiment 1: fT vs EQ scores • Males: fT (m=0.81 SD =0.37), EQ (m=32.62 SD =9.57) • Females: fT (m=0.31 SD=0.18), EQ (m=39.12, SD =7.44) • Effect size of sex differences, fT: d = 1.85, EQ scores, d = 0.76 Experiment 2: fT vs Eyes-C task • Males: fT (m=0.79 SD =0.41), Eyes-C (m=15.23, SD = 3.5) • Females: fT (m =0.38 SD =0.27), Eyes-C (m=16.29 SD =3.29) • Effect size of sex differences, fT: d=1.21, Eyes-C: 0.31
Knickmeyer, R., 2006	N = 24 N = 14	Animations showing social interactions (measures empathy) amniotic fT and fE	fT vs ability to disseminate visual stimuli in intentional and human terms in children aged 4	Sex differences: • Males = more neutral propositions (d =0.63) • Females = more affective state terms (d = 0.82), intentional propositions (d = 0.62), more mental state terms (d= 0.49) fT Correlations: fT not associated with mental or affective state terms (within or between sexes), negatively correlated with intentional propositions (between sexes and within sexes for males only), negatively correlated with neutral propositions (between sexes only) No sex differences in fE

Appendix 1 continued: Studies Assessing Foetal Teststerone and Autistic Traits

Study	Sample	Outcome variables	Outcome Measures	Results
Knickmeyer, R., 2005	N = 35 N = 23	CCC, amniotic fT	fT vs quality of social relationships and restricted interests in children aged 4	Sex differences: • Males: fT (m= 1.04 SD = 0.4) • Females: fT (m= 0.40 SD =0.19) Sex differences in effect size: • fT: d = 2.0 CCC subscale on quality of social relationships: Females > Males, d = 0.47 CCC subscale on restricted interests: Males > Females, d= 0.64 for males fT = positively correlated with restricted interests between and within sexes, negatively correlated with quality of social relationships between sexes only

*TD = typically developing, fT = foetal testosterone (measured in nmol/L), fE = foetal oestrogen, Q-CHAT =checklist for autism in toddlers (revised), m = mean, SD = standard deviation, d = Cohen's d, PLS = pragmatic language score (higher scores = more difficulty), FAI = free androgen index (pmol/l), TT = total testosterone, PSAI = Pre-school activities inventory (higher score = more male-typical behavior), CAST = Childhood Autism Spectrum Test, AQ-CHILD = Child Autism Spectrum Quotient, ASC = Autism Spectrum Condition, CPQ = Child's Play Questionnaire, CM = control males, CF = control females, EQ-C = Empathy quotient, Eyes-C task = Reading the mind in the eyes task, CCC = Child's Communication Checklist

A Review of Chlorine in Indoor Swimming Pools and its Increased Risk of Adverse Health Effects

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Résumé :

(traduction)

Contexte : Le chlore est un agent communément utilisé pour désinfecter l'eau des piscines. La ventilation inadéquate des piscines intérieures et les produits dérivés de la désinfection au chlore (DDC) provenant de la matière organique favorisent l'augmentation des risques de conséquences nuisibles pour la santé. On doit surveiller la qualité de l'eau et une ventilation adéquate pour éviter que les jeunes et les adolescents courent des risques.

Méthodes : Les auteurs ont étudié des recherches menées sur des enfants et adolescents âgés de 2 à 18 ans qui nagent dans les piscines intérieures. Toutefois, ils ont seulement étudié celles parues dans les journaux des années 2000 à 2010, et contenant des statistiques globales. Ils ont aussi passé en revue des articles scientifiques de collègues, et fait la méta-analyse de trois bases de données scientifiques différentes : PubMed, Web of Science et Google Scholar.

Résultats et Conclusions : Les enfants de moins de cinq ans, les maîtres-nageurs et les nageurs d'élite courent un risque accru de symptômes des voies respiratoires supérieures et inférieures, tels que l'asthme, parce qu'ils sont exposés fréquemment à de l'eau chlorée. Mais les nageurs récréatifs qui ne nagent que modérément ont moins de risques de contracter de l'asthme professionnel.

Conséquences : Si on réduit l'exposition au chlore des piscines intérieures, cela peut diminuer les risques de contracter des infections des voies respiratoires supérieures et inférieures.

Mots-clés : Chlore, effets nuisibles pour la sante, piscines intérieures

Abstract:

Background: Chlorine is a commonly used agent for water disinfectant in swimming pools. Inadequate ventilation in indoor swimming pools and chlorination disinfectant by-products (DBP's) caused by organic matter promote the increased risk of adverse health effects. Water quality and proper ventilation must be monitored to avoid health risks in youth and adolescents.

Methods: Studies were researched on children and adolescents from 2-18 years old who swim indoors. Articles were limited by only including journals from the year 2000 through 2010 and contain global statistics. Peer reviewed scientific articles were reviewed and a meta-analysis of three different scientific research databases, PubMed, Web of Science and Google Scholar, was conducted.

Results and Conclusions: Children under five years of age, lifeguards and elite swimmers are at an increased risk of upper and lower respiratory symptoms, such as asthma, when exposed to chlorinated swimming frequently. Recreational swimmers who swim moderately are at a lower risk for developing occupational asthma.

Implications: Reducing exposure to chlorine from indoor swimming pools may limit the risk of developing upper and lower respiratory infections.

Keywords:

Chlorine, adverse health effects, indoor swimming pools

Introduction

Physical activity, such as swimming, is highly beneficial for overall health and well being because it reduces and relieves pressure on joints, improves endurance and develops muscle strength (Bougault, Turmel, Levesque, & Boulet, 2009). However, chlorine based disinfectants, including chlorine, hypochlorite, and chloroisocyanurates are the most common water disinfectants for the prevention of water borne diseases (Bernard, Carbonnelle, de Burbure, Michel, & Nickmilder, 2006). When disinfectants react with organic amino compounds, disinfection byproducts (DBP's), commonly referred to as trihalomethanes, are formed (Nemery, Hoet, & Nowak, 2002). Organic compounds, for example chloramines and hypochlorous acid, are powerful oxidants, which destroy tight junctions in epithelial tissue and increase lung epithelium permeability (Bernard et al., 2006). Frequent exposure of these agents triggers the development of asthma and potentially allows the passage of allergens (Nemery et al., 2002).

Exposure of chlorination and organic matter and decreased ventilation from indoor swimming pools may have detrimental acute and chronic effects on the respiratory system (Bernard et al., 2006). Children, lifeguards, pool attendants and elite swimmers are at an increased risk for developing upper and lower respiratory problems (Lourencetti et al., 2008). Epithelial and mucosal damage caused by the exposure to chlorine products in children less than five years of age, pool attendants and competitive swimmers causes an early onset of asthma (Bernard et al., 2006). Children and youth are most susceptible to developing health effects because of the increasing use in youth for physical activity (Bougault et al., 2009) and they are likely to be swimming in water which is warmer and have higher levels of disinfectant (Weisel et al., 2009).

Chlorine levels are usually between 1.0 – 3.0 ppm in public swimming pools, both indoors and outdoors, and are increased upon water and surface contamination. The recommended chlorine levels are mandated by government agencies to avoid recreational water illnesses (Centers for Disease Control and Prevention, 2010). To ensure water facilities minimize contamination and are safe for public use, safety standards and guidelines for public pools must be implemented by officials and pool operators (Canadian Center for Occupational Health and Safety, 2003). These standards for indoor swimming pools include, but are not limited to, water disinfectant and temperature levels, and proper ventilation (Health Canada, 2009; see also Bernard et al., 2006). Consumers should continually review current information about safety standards and proper sanitation practices to minimize health hazards from chlorine and related agents from indoor swimming pools (Health Canada, 2009).

Methods

Search Strategies

Pubmed, Web of Science, and Google Scholar were three scientific databases used to search for related articles using the keywords: child, adolescent, swimming pool, chlorine, and asthma.

Inclusion and Exclusion Criteria

This systemic review only included human studies conducted on children and adolescents from the ages of 2 to 18. Studies included all geographical locations, which allowed for diversity among subjects and regulations. Data was collected from both indoor and outdoor public swimming pools. Articles included: Belgium, Italy, Spain, England, the US, Japan, Germany and Canada. Original research articles published after 2000 were included in this review. Some articles not included within the defined scope include articles found for "Protection and Action" section that dealt with policy and recommendations. Many of the studies included in our review were quasi-experimental research and association studies.

Data Extraction

Information that was extracted included statistics as well as quotations and conclusions. The purpose of the data extraction table was to illustrate the various methodologies researchers used to collect their data.

Data Synthesis

The data was reviewed and general trends emerging from the scientific literature were identified. These trends and relationships from the systemic review are presented in the results section.

Results

Environmental Hazard

Indoor swimming pools contain numerous chlorine-based

oxidants, which can be found in the water. These oxidants are located in not only the swimming pool, but in hot tubs, as well as whirl pools. The concentration of these oxidants in the air vary based on several factors such as the chlorine dosage in the water, bathing load, mode of swimming, the temperature of the air and the quality of ventilation (Bernard, Carbonnelle, Dumont, & Nickmilder, 2007). Within the environment, the most concentrated oxidants include trichloramine in the gaseous phase and the hypochlorous acid, as well as mono-and dichloramine, which can be found in aerosols (Bernard et al., 2007).

Human Exposure and Internal Dose

The main route of exposure for swimmers is through inhalation of aerosols that are actively floating in the air on the surface of the water. There is a shift from nose breathing to combined nasal and mouth breathing when the pulmonary ventilation exceeds a level of 30 L per minute (Bernard, 2007). This change in breathing allows the aerosols to bypass the nasopharynx filter and penetrate deeper within the lungs. Asthma is more prevalent in indoor swimming pools due to the decreased ventilation and concentrated inhalation of chemicals (Bernard et al., 2006).

Within children, aged 6 and 7, who have to attend the smaller pools and swim primarily in the shallow end, they are being exposed to the most polluted area of the pool. When looking at the concentration of trichloramine (refer to Figure 1) in the air around the small pool, the level of trichloramine is about 50% higher than levels in the large pool (Bernard, 2007). When children are first learning to swim, they inhale and swallow aerosols containing chloramines, which are soluble and can be carried to deep levels of the respiratory tract (Weaver et al., 2009). Due to the fact that children have a greater surface area, they absorb higher levels of chlorine products across the surface of their skin, in proportion to their body weight.

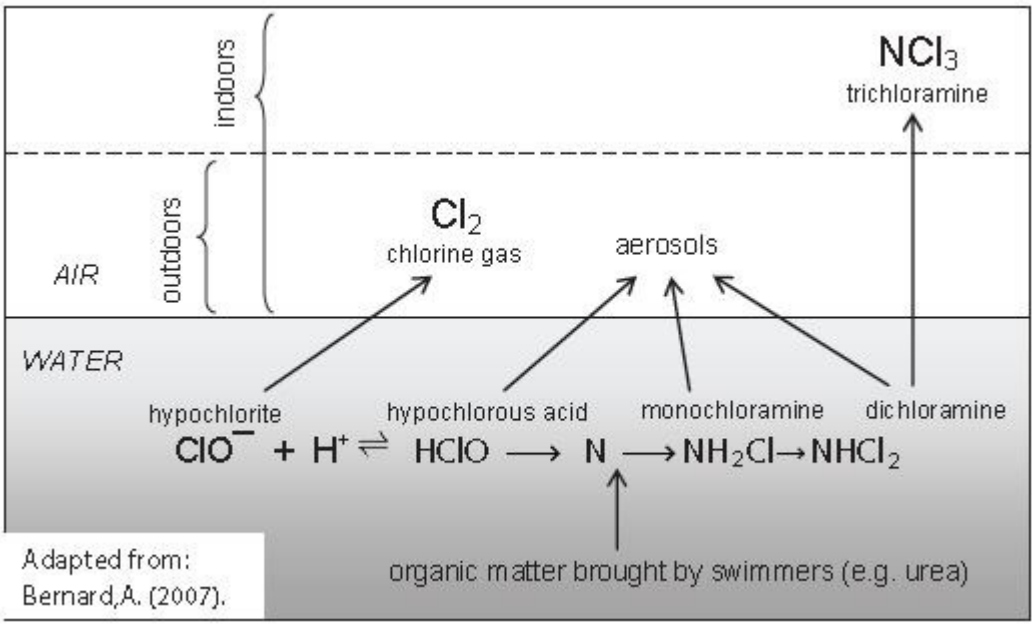
Health Effects

A common problem from the use of chlorinated swimming pools is the pungent smelling 'chlorine' water This smell, which is irritating for the eyes and upper respiratory system, is due to the presence of chloroamines (Weaver et al., 2009). Chloroamines, such as monochloroamine (NH2Cl), and dichloroamine (NHCl2) are synthesized from hypochlorite and ammonia compounds, which originate from the sweat and urine of swimmers (Weaver et al., 2009). The risks of exposure from chloroamines are determinant among the level of chlorine used, contamination of water from swimmers and their personal hygiene and air circulation (Lourencetti et al., 2008).

Risks

Figure 1

The diagram below illustrates potent chemicals which are found in the air of indoor swimming pools. Children in industrialized countries are exposed to trichloramine frequently, which has been shown to be one of the most concentrated air pollutants. Swimmers and competitive swimmers are most frequently exposed to chlorination products.



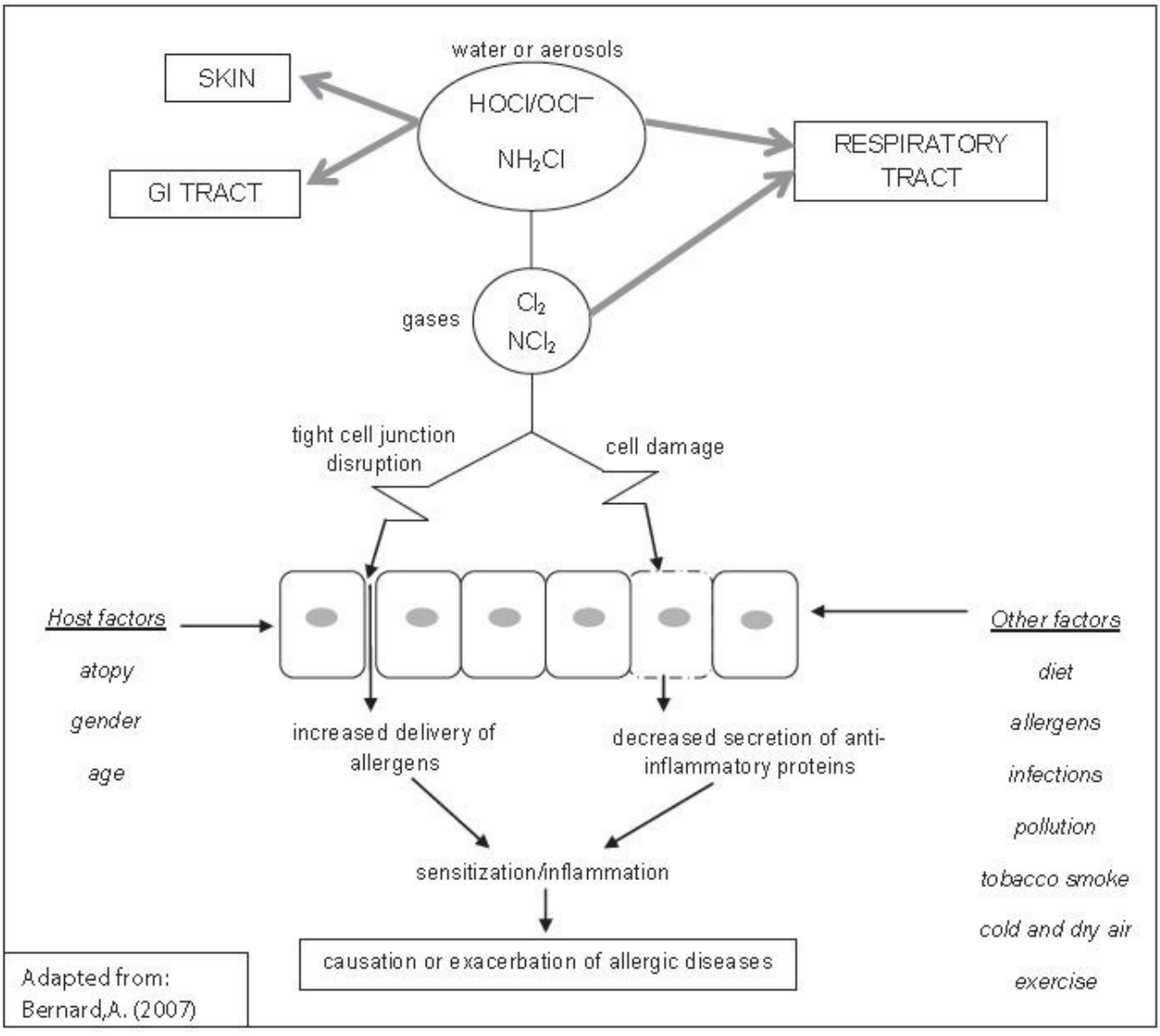
Malfunctioning of chlorine disinfection installations is a potential problem, which may cause serious side effects from acute exposure (Bernard et al., 2006). Asthma attacks, laryngeal oedema (swelling of the larynx) and upper and lower airway mucosa damage may result (Nemery et al., 2002). Reactive Airways Dysfunction Syndrome (RADS) and hyperventilation are linked to serious effects from prolonged chlorine exposure (Nemery et al., 2002). Individuals who routinely swim are at risk of chlorine exposure, especially competitive swimmers who are typically swimming up to two times a day (Bernard et al., 2006). The greater number of years individuals swim in an indoor chlorinated pool, the greater risk for developing wheezing and early onset of asthma (Bernard, Nickmilder, Voisin, & Sardella, 2009). Lifeguards, swim instructors and other personnel exposed to DBP's have an increased risk for developing occupational asthma, which is activated by inadequate ventilated facilities (Bernard et al., 2009). Drowning and chemical hazards are factors, which contribute to creating an unsafe aquatic environment. Air and chemical quality in indoor swimming facilities affect exposure levels in individuals (World Health Organization, 2006).

Protection and Action

The exposure of environmental toxins can be reduced by preventative measures, which are reinforced through education programs. Adults and children alike will continue to swim for leisure and physical activity, however, a reduction

Figure 2

The illustration above shows how chlorine based oxidants, which can be found in the air or water can enter the body through the respiratory tract or penetrate through the skin to cause either acute or chronic effects.



and/or avoidance of going to indoor swimming facilities that are disinfected using chlorine will decrease the inhalation of contaminants (Voisin & Bernard, 2008). Many studies have reported of the risk of exposure of young children (under 7 years of age) to the effects of chlorination, when young children use chlorinated pools, especially pools that emit a potent odor of chlorine (Bernard et al., 2006; Bernard et al., 2007). There are many ways in which a swimming facility can take action to reduce the harmful effects of chlorine and its by-products. Firstly, pools can maintain strict procedures regarding the control and supervision of free chlorine levels in water. Pool operators should receive training on how to measure the chemical content of water with periodic review trainings (Weisel et al., 2009). The World Health Organization (WHO) has published guidelines stating that levels of free chlorine in public pools should not exceed 3 mg/L or 3ppm (Voisin & Bernard, 2008). Health Canada advises a free residual of 1.0 to 3.0 ppm of chlorine (Health Canada, 2009). Secondly, encouraging improved swimmer hygiene in pools can reduce the production of DBP's, which are produced when chlorine combines with organic compounds (natural organic matter and bather load input) (Zwiener et al., 2007). Persuading pool patrons to shower before entering the pool, using toilet facilities, and applying watertight diapers will reduce bather load input in pools (World Health Organization, 2006; Zwiener et al., 2007). Thirdly, pools should maintain adequate ventilation around the pool's surface to reduce the inhalation of volatile by-products. The creation of volatile disinfection by-products, such as chloroform and nitrogen trichloride, is inevitable and will escape into the air, which become hazardous toxins in contained airtight facilities (World Health Organization, 2006). The WHO (2006) recommends appropriate ventilation rates of at least 10 litres of fresh air/s/m2 of water surface area. Proper ventilation will not only reduce the toxic by-product load on swimmers but also on lifeguards and other pool workers (Voison & Bernard, 2008). The management of pools has a responsibility to its patrons to balance the preservation of "the positive health effects of swimming through exercise while reducing other potential adverse health risks." (Zwiener et al., 2007).

Discussion

It is evident that the most vulnerable populations effected by chlorine exposure include children, lifeguards and elite swimmers. The exposure to chlorination by-products affects their upper and lower respiratory systems leading to either acute or chronic conditions such as asthma. In a 2006 study, research suggested that regular indoor pool attendance beginning at an early age in life could promote the development of asthma (Spivey, 2006). The main route of exposure to chemicals inducing a respiratory reaction occurs from the inhalation of aerosols that are actively floating in the air on the surface of the water. In order to reduce the burden placed on the body, the best way to reduce exposure is through avoidance and prevention.

The most recent studies conducted on adverse health effects of chlorine use in indoor swimming pools obtained a collection of accurate findings. The use of the data collected from association studies illustrated the relationship between the rate of exposure to chlorine and the prevalence of upper and lower respiratory symptoms. A positive correlation was shown between exposure to chlorine and the prevalence of childhood asthma in a 2007 study, in which more than 180,000 individuals participated (Nickmilder & Bernard, 2007). However, the unknown strength of the correlation cannot allow a conclusion on childhood asthma and other subsequent respiratory conditions to directly link to an increased exposure to chlorine. Studies suggest that further research is required to assess the relationship of exposure to chlorine and its adverse health effects.

Government agencies, such as Health Canada, set regulations for the mechanical and chemical maintenance of public swimming pools (Health Canada, 2009). These guidelines are needed in order to ensure the safety of both pool users and staff (Voisin & Bernard, 2008). Regulations set forth in public pools, include maintaining safe water quality, such as disinfectant and pH level, and filtration systems. Additionally, the proper use of handling chemicals, testing equipment following pool log documentation and routine inspection are critical for safety (Health Canada, 2009; Voisin & Bernard, 2008). Violations to swimming pools from routine inspection, which threaten public health, should be temporarily closed until proper guidelines are adhered to.

Conclusion

Children, elite swimmers, lifeguards and employees of indoor swimming pools are at the highest risk for developing respiratory conditions, such as asthma, due to their increased exposure to chlorine. The use of chlorine continues to be the main source for water disinfection, but the formation of disinfectant by-products such as chloramines from chlorine and organic substances proves to be hazard-

ous to health. Poor ventilation in swimming pools, the production of chloramines and mouth breathing from swimmers are all contributing factors to the development of upper and lower respiratory conditions.

Scientific research indicates that the early onset of asthma is associated with exposure to chlorinated swimming pools; however, more research needs to be conducted on the link between exposure and other health risks. Allergies and bronchitis are two health conditions that have yet to be linked to exposure from chlorinated swimming pools. In order to reduce the strain on the health care system and health professionals, funding for additional research needs to be provided. With further research, individuals will be able to determine at what level of exposure a specific health condition occurs. Furthermore, it will allow the ability to link a condition with the individual's involvement in swimming.

In order to reduce health hazards related to exposure from indoor swimming pools, actions by individuals, communities, governments and industries need to occur. At the individual level, there needs to be increased education and awareness about the effects of chlorine from indoor swimming pools on the body. Communities need to work with one another to advocate for policies and preventative strategies that the government would implement in the future. At the industrial level, substitution of water disinfectants that would decrease heath risks for the vulnerable populations need to be further researched. Bromination, which has several similar properties to chlorine, is an alternative method for water disinfectants.

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SmartHand: A Sense of Assistive Devices

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Résumé :

(traduction)

Les amputés doivent souvent affronter une stigmatisation sociale parce qu'il est évident aux yeux de tous qu'ils ont perdu un membre ou qu'ils utilisent une prothèse. Cependant, l'utilisation de prothèses a fait beaucoup de progrès au cours des dernières années, surtout en ce qui concerne les prothèses sensorielles. Plusieurs réseaux d'information ont récemment fait des reportages à propos d'un appareil de ce type, un nouveau prototype appelé la SmartHand. Dans la discussion, l'auteure analyse la SmartHand et la compare avec les plateformes existantes, et notamment avec les prothèses myo-électriques et avec la ré innervation musculaire ciblée. L'auteure conclut que la SmartHand offrait un niveau plus élevé de compétences à ses utilisateurs et améliorait leur qualité de vie. Toutefois ses conclusions soulignent aussi les obstacles scientifiques qui se posent, surtout au niveau du rejet tissulaire. L'analyse coût-avantage d'un tel appareil risque aussi de produire des données contradictoires, ce qui pourra nuire à sa mise en œuvre à une plus large échelle. Malgré ces problèmes, la SmartHand est un des appareils fonctionnels disponibles aujourd'hui les plus avancés sur le plan scientifique, et son utilité pour les amputés est indéniable.

Mots-clés :

Technologie d'appareils fonctionnels, invalidité, amputés, prothèses myoélectriques

Abstract:

Amputees have often faced social stigma attributable to their visible limb loss or use of artificial substitutions. In recent years, the use of prosthetics has become much more advanced, particularly in the field of sensory prostheses. One such assistive device, a new prototype technology known as the SmartHand, has recently been featured on several news networks. It is through this discussion that the SmartHand will be reviewed and compared with existing platforms that include myoelectric prostheses and targeted muscle reinnervation. Use of the SmartHand has been noted as having increased levels of competence in and improved the quality of life of its users. These conclusions also bring to light the scientific barriers that are faced, primarily with respect to tissue rejection. The cost benefit analysis of such a device may also produce conflicting data, thereby making it difficult to implement this device on a larger scale. Despite these problems, the SmartHand represents one of the most scientifically advanced assistive devices available in today's market, whose usefulness for amputees is undeniable.

Keywords:

Assistive device technology, disabled living, amputees, myoelectric prostheses

Introduction

One of the fundamental characteristics that define us as human beings is our hands. The complexity of motion and sensation made achievable through them is an unparalleled way in which people are able to interact with and experience the world. As such, the loss of these limbs from accidents or disease processes is a devastating loss to both a person's psyche and quality of life. In accordance with the International Classification of Health, an amputation represents a loss of body structures, wherein the consequent implication on an individual's level of activity and participation in society are enormous (Scherer, Jutai, Fuhrer, Demers, & Deruyter, 2007). To this end, amputee assistance is imperative as over two million people with lost limbs currently live in North America (Ziegler-Graham, MacKenzie, Ephraim, Travison, & Brookmeyer, 2008). Artificial limbs have long been the primary means of response for amputees. These substitutions are classified as assistive devices because they increase the ability of these individuals to perform daily tasks with greater proficiency (Scherer et al., 2007). The first prosthetics began as hook attachments and cable limbs but have since progressed to prostheses that allow for multifunctional control (Parker, Engelhart, & Hudgins, 2006). Subsequently, the current state of prosthetic technology regarding lower arm and hand functioning revolves around myoelectric prostheses. This type of device allows for the transmission of electromyographic (EMG) signals along remaining neurons to allow for possible motion (Weir, Troyk, DeMichele, & Kerns, 2005). In this capacity, residual muscle nerves are kept packaged within the remaining portion of the salvaged limb, wherein these nerves are then appropriately connected to proximal muscles and controlled by stimulation of electrodes in the prosthetic hand (Weir et al., 2005).

Over the past decade, most substantial refinement and marked progress in myoelectric prostheses has steadily continued in the area of complex movements. Comparatively, a desired function that is often overlooked by the majority of disabled individuals is improved sensation feedback (Pylatiuk, Schulz, & Doderlein, 2007). It is apparent that the inability to distinguish between the two areas of feedback, force and temperature, can be crippling to amputees (Pylatiuk et al., 2007). The significance of feeling includes motor functions; as movements become more precise, an individual requires responsive pressure feedback to execute skills with greater accuracy. A recent development to meet this need is provided by the SmartHand, which allows for in-depth "feeling". This device is still in the prototypic stages but has been in production for over a decade and is expected to be released within two years (Tutton, 2009). There have been minor advancements in sensory prosthetics in the past, especially using a system known as targeted muscle reinnervation (TMR) that uses chest muscles to permit feeling and movement (Miller, Stubblefield, Lipschutz, & Kuiken, 2008). Nonetheless, no existing technologies provide pressure feedback and feeling comparable to the SmartHand (Antfolk, Balkenius, Rosen, Lundborg, & Sebelius, 2010). As a prosthetic living support technology, the usefulness of the SmartHand needs to be judged on its ability to balance this novel innovation without comprising other functions. Aspects such as size, expenses, maintenance, and applicability to the amputee population are all areas that must be considered. One of the complaints of TMR technology was the perception of less natural- seeming sensations (Antfolk et al., 2010). As a result, if new technology such as the SmartHand cannot restore function in a practical way, it will not necessarily be of any benefit to the recipient. The SmartHand represents a tentative and intriguing advancement for the existing self-support technology of powered prosthetics.

Summary of the SmartHand

In a recent news article by Cable News Network (CNN) published in November 2009, the SmartHand is touted as a revolutionary piece of technology that will be amongst the most advanced prosthetic limbs available. The basis for the technology relies on the use of EMG signals from current myoelectric prostheses to activate motors found in the robotic fingers. The crucial distinction is that the SmartHand also allows for sensory information to be detected and transmitted from numerous sensors within each finger that permit for the actual sensation of touch. The sensory motors are then able to sense both pressure and force and transmit that information to actuators in the arm. Actuators must be targeted in order to match a given area of the finger with the correct nerve. In doing so, it allows for direct transmission to and activation of the part of the brain associated with that muscle. The brain then interprets the neuroelectrical impulse as a sensation of feeling in the "hand". A limitation is that the SmartHand will only be available for amputations done below the elbow as any limb lost above that point does not have enough muscles remaining to control the prosthetic with a sufficient degree of precision (Tutton, 2009). A second, more pertinent, limitation is the difficulty of attaching several electrodes to the

nerves remaining in the stump, known as the residuum. Since the placement requires exact measurements, any discrepancies make it difficult to discern between the feelings of two adjacent fingers. The appropriate solution under such circumstances is a neural interface similar to the current myoelectric system, which utilizes direct nerve attachment as opposed to focusing on muscles (Tutton, 2009). Moving away from larger muscles thereby allows for increased accuracy. Currently, the project uses an external transmitter fitted onto the arm as a prototype (Antfolk et al., 2010). If a neural interface method were implemented, it would have to be implanted into the individual causing concerns over biocompatibility.

Analysis

The SmartHand must initially be analysed on the basis of scientific evidence. The basis for the SmartHand pertains to its objective of directly routing nerve signals to the brain, which forms the critical point of difference from the competing technology in TMR signals. Targeted muscle reinnervation deinnervates muscles that are rarely used, specifically the pectorals. A subsequent redirection of nerves to that area produces the sensation of being touched on the arm when pressure is applied to the corresponding area of the chest (Marasco, Schultz, & Kuiken, 2009). Unlike the SmartHand, the difficulty in TMR lies in harnessing this sensory capacity into a more practical medium. Tutton (2009) stresses that the mechanism by which the nerve signals can be received by the SmartHand lies in the phantom limb. This is the basis of the TMR framework. More specifically, this phantom phenomenon describes the sensations that individuals experience originating from the lost body part (Hunter, Katz, & Davis, 2005). Tutton's news article (2009) also emphasizes the exploitation of these phantom experiences, as an amputee will continue to send nerve signals to corresponding neurons as if the limb was still present. The parallels between the two technologies can be difficult to distinguish, as Tutton (2009) further suggests that TMR methodology was considered prior to the neural interface. However, SmartHand technology is focused on attaching electrodes to nerve bundles in the residuum as opposed to regenerating nerves in the pectoral muscles. With a line of attachment through a neural interface, the nerves can be stimulated directly. Since phantom limb experiences indicate that the correct sensory motor cortex areas remain active, the brain can continue to receive these signals. An important problem to highlight is that every individual interprets phantom limb pain in a unique way, and some individuals do not experience the phenomenon to any degree (Hunter et al., 2005). Tutton (2009) fails to address this point, which makes it increasingly difficult to apply this technology on a broader scale. Each individual not only has to have the prosthetic matched with the correct nerves but must also have it calibrated to match the phantom limb sensory map. As such, the resulting use of this technology may be disproportionate in the population.

As a neural model is required for the SmartHand to perform optimally, unique challenges are presented. Since the interface requires a direct implantation into the human body, an initial claim of biocompatibility needs to be discussed. Similar to transplants or tissue related technologies where biological tissues need to be combined with synthetic materials, the possibility of rejection remains important to consider (Peramo & Marcelo, 2010). If the body is not compatible with such a device, illness will be observed in addition to the prosthetic being rendered nonfunctional (Tutton, 2009). An additional challenge to placing a device inside the body is that unlike tissues or stem cells, which can be autologous, the machine is a completely foreign object (Peramo & Marcelo, 2010). In this sense, this challenge is the largest scientific barrier to the full implementation of the SmartHand in the health care market. What is more is that the news report notably fails to discuss the sociological implications of implanting the interface. In Canada, any implanted product would automatically be classified as a Class III device, posing a moderate risk should the device fail to function correctly (Canadian Agency for Drugs and Technologies in Health, 2007). This would likely be an upgrade in classification as most prosthetic devices are non-invasive with the exception of initial reinnervation surgery. Any increase in risk to the patient should always be taken seriously and a cost-benefit analysis must be completed accordingly. Given the rigorous procedure associated with neural implantation, a higher associated cost would be expected. As the average price of a prosthetic limb in North America can reach upwards of twenty thousand dollars, the SmartHand would likely surpass current prices (Chung, Oda, Saddawi-Konefka, & Shauver, 2010). This cost would be further compounded by costs associated with routine and surgical maintenance to replace or alter the prosthetic as it ages with the patient. Providing an alternative to the neural model is impossible since Tutton (2009) states that the interface must be refined before the system can be considered commercially viable, which reflects that the neural model is not only nec-

essary for optimal functioning but is a foundational requirement of the SmartHand. The financial cost in acquiring and maintaining the SmartHand would become one of the major factors inhibiting the growth and spread of this new technology (Scherer et al., 2007). The possibility of regaining feeling in one's limbs is significant, but whether or not it is worth the price tag over a less expensive and invasive substitute remains unclear. Consequently, providing this device to all members of society may profoundly limit its use in the amputee population.

A final point of discussion pertains to the convenience and utility of the SmartHand in daily life as an assistive living technology. As previously reported by the news report, the device is grounded in myoelectric prostheses. To this end, the SmartHand is at least as functionally valuable as the current motorized limbs in allowing an individual to perform basic movements. The vast majority of current prostheses are generally one single degree of freedom or multimovement machines that are slow and limited (Weir et al., 2005). Although the news report does not provide commentary on the speed of the SmartHand, it does note the allotment of individual finger control. Coupling this ability with exceptional sensory feedback mechanisms would allow for actions such as eating and writing, which require fine motor precision (Antfolk et al., 2010). Since the pressure sensations allow an amputee to manipulate varying degrees of force using their prosthetic, the status of the SmartHand as an assistive device is superior to that of current technology. Furthermore, due to the nature of a prosthetic as a substitute for a body part, the SmartHand would also be able to transition into support for social activity. The presence of a functioning hand allows for both vocational and recreational provisions because regaining mobility undoubtedly allows for enhanced participation in society (Scherer et al., 2007). Using the competence-press model proposed by Lawton, this device would produce a positive effect on adaptive behaviour. Comparatively, less advanced prosthetics would demonstrate lower competence in an equal press environment, thereby placing it in a category of marginally adaptive behaviour (Scherer et al., 2007). Even in comparing basic motor function capabilities, Tutton (2009) states that TMR requires the activation of chest muscles to control arm function. The rate of learning new movements and harnessing these unused muscles depends on each individual's sensory motor reorganization post-amputation (Antfolk et al., 2010). In contrast, the neural interface proposed does not have this difficulty. If the anticipated neural system in the article comes to fruition, this also would also allow the device to lessen social stigma. One of the detriments of using an assistive device is that it reinforces a disabled status and adds a social pressure (Scherer et al., 2007). Although the SmartHand may not eliminate this stigmatization, it may serve to reduce it as the SmartHand represents a step towards affirming the status quo.

Conclusion

The development of the SmartHand has culminated in a powerful new technology that has the potential to become the next step in modern prosthetics. Given its strong basis in the present robotics of myoelectric prostheses, the SmartHand is able to build on existing functionality with the addition of sensations. As previously mentioned, the claims put forth by the news report regarding the state of affairs in the scientific field are justified. Theoretically, implementing a neural interface into an individual's arm would overcome the sensory problems encountered by the TMR prosthetic. Notably, however, Tutton's emphasis on phantom limb experiences may not be plausible in all amputees (Tutton, 2009). Still, the science and efficacy behind the SmartHand can be deemed valid as the inferences of both sensory feedback and multifunction control result in an improved assistive living device. The greatest problem with the SmartHand, as claimed in the news report, was the issue of biocompatibility. The resulting risks are shown to be quite significant as a biological barrier to integrating the device inside a human arm. The news story problematically omits the possible cost implications of this neural interface. Additional research has demonstrated the disproportion in usage this would likely create within the target population, which would prove to be damaging in the long term. As Tutton (2009) proposes, the main research priority is to overcome rejection of the device by the body. Although progress has been made through successful transplantation in animal experiments, research efforts must be extended to include human models. Most importantly, because the neural interface remains largely theoretical until it can be implemented in human patients, the claims regarding the model have yet to be validated. Additionally, information pertaining to costs should be substantiated to determine whether or not the price will become an insurmountable leap for the majority of patients to make. Implementation of healthcare programs and subsidizations may help control for this limitation and promote the growth of this technology (Scherer et al., 2007). In spite of these challenges, the SmartHand is a remarkable device

that will provide essential information for the advancement of bioengineering in prosthetics.

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Section de Résumés / Abstracts Section

Introduction à l'epidémiologie / Introduction to Epidemiology

Classe 2011 / Class 2011

From Womb to Doom: Effects of Maternal Health on Schizophrenic Offspring

Abdelal, N., Mezher, K., Taleb , Z.

Known as one of the most devastating mental illnesses to affect the human brain, schizophrenia has been constantly studied as a major disease entity over the past century. The annual incidence of schizophrenia averages 15 per 100,000, and the point prevalence averages 4.5 per population of 1000. Risk of disease development is 0.7%. Despite disease commonality, the causes and pathogenesis of schizophrenia remain obscure, indicating a clear need for research aimed at detecting risk factors for disease development. Previous studies have proven that gene-environment interactions significantly contribute to the risks associated with schizophrenia onset. However, less emphasis is directed toward risk factors related to maternal exposure. This study aims to determine whether a relationship exists between maternal exposures to stress, viruses, and obstetric complications and the risk for schizophrenia development in offspring. Evidence is based on a collection of systematic reviews, meta-analysis, cohort, and case control studies; each study has presented significant and insignificant results. Overall results indicate that a relationship between prenatal maternal exposure and risk for schizophrenia development in offspring seems to exist.

The Post-therapy Effects of Testicular Cancer Treatments – Surgery and Chemotherapy – on Male Reproductive Fertility

Adeyemo, O. D., Barua , S., Saforo-Appiah, R.

Background Information: Testicular cancer (TC) affects men mostly between ages 15 and 49 years. The incidence rate of TC in 1989 was 4.2/100000 compared to 10.2/100000 in 2004. TC is the most curable solid tumour, with 10-year survival rate of more than 95%. Yet, preserved fertility is an important concern. This systematic review was implemented to determine which form of TC treatment (surgery or chemotherapy) had the most severe impact on post treatment fertility.

Method: A computerized search of English peer-reviewed literature on Fertility and Testicular Cancer published from June, 1995 through June, 2010 was conducted using the Pubmed Database. Pooled estimates were determined from the incidence of TC in relation to reduced fertility rate after treatment from 6 studies.

Result: It was observed that fertility rate was reduced in men after treatment for TC. In a self-reported survey of 297 patients treated for TC, 82.4% (98/119) of patients who tried to have children before treatment succeeded, and only 49.3% (74/150) were successful after treatment ($p<0.001$). The fertility rate of patients treated with surgery was markedly reduced to 56%. In another follow-up survey of 1462 patients diagnosed with TC from 1980 to 1994, it was observed that 85% (85 of 106, CI 95%) sustained fertility after treatment with two to four cycles of cisplastin-based chemotherapy.

Conclusion: This study suggests that overall fertility in men diagnosed with TC is reduced after treatment. Fertility is severely reduced after surgery; however, it is significantly preserved even after two to four cycles of chemotherapy.

Maternal Obesity During Prepregnancy and Neural Tube Defects

Bujak, A., Martin, C.

Research Question: Does maternal obesity during prepregnancy modulate a higher risk of neural tube defects in offspring? Introduction: Past trends indicate prevalence of obesity will continue to rise in the future. Maternal obesity during prepregnancy has been shown to heighten risk of NTD in recent studies. Association means impact of NTD on healthcare and individuals will increase as rates rise in accordance with obesity prevalence.

Methodology: Four studies concerning obesity and NTD were retrieved from PubMed and Medline. From these studies, attack rate, relative risk and risk were calculated.

Results: Risk of NTD in pregnant women increases with both BMI groups and weight. The attack rate of NTD in obese women (0.24, 0.61, 0.56) was higher than the attack rate in non-obese women (0.11, 0.46, 0.42) in 3 of the 4 studies. The risk ratio of NTD is significant for 3 of the 4 studies.

Discussion: Major known confounding variables such as folate status were controlled in each of the studies. Results showing that prepregnancy obesity heightens NTD risk remained significant despite statistical controls in 3 of the 4 studies. 1 of the 4 studies found NTD rate to be significantly higher when mothers were both obese and diabetic during prepregnancy.

Conclusions: In accordance with our hypothesis, maternal obesity during prepregnancy does increase the risk of NTD in offspring. Reducing the prevalence of obesity among women of reproductive age should result in fewer NTD amongst neonates.

Risk Factors Associated with Fractures in Postmenopausal Women with Osteoporosis

Carmanico, L., Duncan, H.

Fractures are a major health concern since they decrease quality of life, have high morbidity and mortality as well as economic impact on the health care system. Postmenopausal women with osteoporosis are highly susceptible to fractures. The principle risk factors expected to be associated with increased fracture occurrence are vitamin D insufficiency, smoking and low body mass index (BMI). Other risk factors include social and cultural variables, medical history, substance use, hormonal profile and nutritional as well as body composition factors. The majority of the risk factors are interdependent or demonstrate correlation in occurrence, readily confounding individual analysis of relative risk. Although some factors are genetic, most are under an individual's control. Understanding the risk factors associated with fractures in postmenopausal women with osteoporosis will help direct preventative care and allow risk reduction. Further research is warranted as a literature review revealed statistically insignificant findings and contradictions between studies.

Methods for Improving Adherence to Highly Active Antiretroviral Therapy (HAART) in Uganda

Kotb, A., Daoud, R., Ghavamzadeh, S., Chacon, S.

Background: In Uganda, a total of 293,000 life years have been gained as a result of the use of highly active antiretroviral therapy (HAART) since 1996. This can only be achieved when patients adhere to their prescribed treatments. Poor adherence to HAART is the major cause of treatment failure, development of drug resistance, HIV disease progression and premature death.

Objective: To determine the innovative methods for improving adherence to HAART in Uganda and the limitations of applying these methods elsewhere.

Methods: A systematic review of peer-reviewed articles related to innovative methods of improving adherence to HAART in Uganda was carried out. Articles were found using PubMed and SCOPUS databases with the following keywords: HIV, adherence, antiretroviral, compliance, and Uganda.

Results: Four innovative methods were found that increased the rate of adherence to HAART: (1) the use of mobile phones to remind patients to take medications, (2) home or community based treatment programs in rural communities, (3) the use of mobile team on motorcycles to track patients, and (4) task shifting. Based on our criteria, mobile phone reminders was found to be the most transferable method.

Conclusion: In Uganda, adherence levels are as high as, if not even higher than the levels in North America. Their high level of adherence is in part due to the previously described innovative methods. Mobile phone reminders have been employed in Kenya and found to increase adherence to HAART. Future research should focus on assessing the potential success of these methods in North America

Increased Risk of Suicide in Canadians with Bipolar Disorder

Dresch, A., Liang, R., Thomas, S., Tonkin, K.

Background: Bipolar disorder is a major psychiatric disorder that affects over 500 000 Canadians, however little is known about its prevalence in relation to attempted suicide.

Objective: To determine a link between increased suicide rates and Bipolar disorder among the Canadian adult population when compared to other mental illnesses.

Methods: A search was conducted across multiple databases to find peer reviewed articles containing data related to prevalence and suicide rates of various mental disorders. In total 14 articles were chosen and included in the review for data abstraction.

Results; The prevalence of Bipolar disorder in Canada is 2.2% with the highest rate of attempted suicide at least once in their lifetime falling between 25-60%. Depression, anxiety disorders, and schizophrenia had attempted suicide rates of 15%, 28%, and 31% respectively.

Conclusion: These findings indicate that Bipolar disorder has the highest risk for attempted and completed suicide among other psychiatric disorders.

The Effect of Vitamin A Micronutrient Intervention on Xerophthalmia Prevalence in Vulnerable Populations

Gedeon, J., Rahman, T., Riddoch, H., Yan, H.

Vitamin A is an essential nutrient in maintaining healthy eyes, vision, growth and development. Vitamin A deficiency (VAD), which affects over 250 million preschool-aged children worldwide, is characterized primarily by the prevalence of xerophthalmia. A literature review was used to determine the effectiveness of vitamin A supplementation programs in reducing xerophthalmia and its associated symptoms in vulnerable populations – namely in infants and pre-school aged children using Bitot's spots and night blindness as indicators. Vulnerable populations for this study are defined as being vitamin A deficient as determined by serum-retinol levels. 8 studies were selected based on availability of comparisons between pre- and post-intervention data or experimental group and control group data- 4 of which were statistically significant. There has been a decrease of xerophthalmia prevalence after vitamin A supplementation in the experimental or post-intervention group from 1.9 to 0.3% ($P<0.05$), 2.31 to 0.64% (95% CI, 0.17-0.79), 24.6 to 11.2% ($P<0.001$), and from 6.9 to 3.3% ($P<0.0001$) in an RCT in Indonesia (n = 12591), an RCT in Nepal (n= 1871), a pre/post evaluation in India (n= 818, a pre/post evaluation in Mali (n=1524), respectively. Vitamin A supplementation greatly reduces xerophthalmia prevalence in infants under 65 months, while effects are reduced in children older than 65 months. Therefore, results are primarily applicable to vulnerable populations which fall within the 0-5 year age-range. Based on the results of the study, vitamin A supplementation is a key intervention in reducing prevalence of xerophthalmia in vulnerable populations.

Breast Cancer Risk After First Full-Term Pregnancy Among Canadian Women

Gordon, T., Maschi, N.

Background: While there is no single cause of breast cancer, a number of risk factors have been identified. Pregnancy has been studied as a risk factor for its potential to increase the risk of breast cancer in terms of the effect of full-term pregnancy.

Methods: A computerized search was conducted using the PubMed database, using the following search strategies such as 'full-term pregnancy', 'breast cancer or breast neoplasms', 'risk' and 'Canada'.

Results: During pregnancy, there are many permanent changes to a woman's breast. It has been determined that Canadian women who have their first full-term pregnancy before the age of 30 are at a reduced risk of developing breast cancer. On the other hand, Canadian women who have their first full-term pregnancy after the age of 40 increase the risk of developing breast cancer. Also, Canadian woman who are predisposed to breast cancer in terms of carrying the BRCA1 or BRCA2 mutations do not benefit from early full-term pregnancy in the same ways as women without the mutations.

The Burden of TB in HIV-Positive South Africans

Gosain, S., Overhoff, N.

Background: HIV/TB co-infections rates in South Africa are among the highest in the world, and are climbing. Through knowledge of epidemiological information associated with HIV/TB co-morbidities, it is hopeful that policies will be created to reduce the incidence, prevalence and mortality rates associated with these infections.

Methods: A thorough literature review was employed to determine the burden of TB among HIV-positive individuals in South Africa. Various databases were consulted to retrieve data on to the incidence, prevalence, and mortality rates of HIV/TB co-infections in South Africa.

Results: It has been revealed that TB is the greatest killer of HIV-infected individuals in South Africa, where the incidence of co-morbidities is 563 per 100,000. As the prevalence of HIV increased in South Africa, the incidence of TB increased at a remarkable rate, resulting in the most dramatic rise in TB rates in Africa since the advent of antibiotics. The global burden of HIV/TB co-infections is greatest in Sub-Saharan Africa, and one third of all TB/HIV co-infections are isolated to South Africa; the highest rate of co-infections in the world.

Conclusions: Policies and interventions must focus on different perspectives; including HIV reduction to control co-infection rates. Additional research will be required to reduce the impact of concomitant HIV and TB infections in South Africa

Domino Effect of the Female Athlete Triad

Gregory, A., Smith, C.

Disordered eating, exercise-associated amenorrhea, and osteoporosis are the main constituents of the female athlete triad (FT) syndrome. Strenuous exercise and disordered eating act together synergistically to induce menstrual disorders and hypoestrogenism, leading to decreased bone mineral density and osteoporosis. Risk factors of the FT include being an elite or highly competitive level female athlete, age of adolescence and young adulthood, a family history of disordered eating, physiologic factors, higher socioeconomic status and athletic disciplines that emphasize low body weight and thinness. The true prevalence of FT is difficult to determine due to the secretive nature and denial of disordered eating. Consequences of the FT include impairment of athletic performance and increased risk of injury – primarily stress fractures. Prevention and early detection are crucial to decrease the risk of the FT. The ideal time to screen for the FT is during the pre-participation physical examination or during evaluations for other problems that may be suggestive of an underlying eating disorder, menstrual dysfunction or low bone density. Treatment of the FT focuses on recognition of the problem, identification and resolution of psychosocial issues, stabilization of medical and nutritional conditions and re-establishment of healthy eating patterns. Most importantly, coaches and parents need to be educated on prevention of disordered eating and awareness of the signs and symptoms.

La dépression Postpartum

Guilbault, E., Guidon, K.

La dépression postpartum est un trouble qui touche environ 13% des nouvelles mères au Canada. Celle-ci cause des problèmes propres à la dépression majeure, tels que des troubles d'anxiétés, une fatigue excessive, un état de confusion pouvant mené jusqu'au suicide. Aussi, l'enfant n'est pas épargné par cette maladie puisque l'état de la mère influe directement l'interaction qu'elle aura avec lui. La prévention tertiaire présentement en place pour contrer le problème de dépression chez les mères est inefficace. La prévention primaire et secondaire ont le potentiel de réduire la morbidité en s'attaquant au problème avant qu'il se manifeste. Présentement, en prévention primaire, rien n'est offert a toutes les femmes canadiennes pour cibler les femmes à risque. Des tests de dépistage tels que le Questionnaire des risques de grossesses devraient être implantés et des campagnes de sensibilisation touchant la population expliquant les risques de cette maladie devrait être créées. En prévention secondaire, la détection, effectuée grâce à l'évaluation par un professionnel de la sante, est la méthode la plus efficace. Celle-ci surpasse même l'échelle de dépression postpartum d'Edinbourg qui possède un sensibilité de 86% et une spécificité de 87%. En terme d'intervention, les approches personnalisées sont beaucoup plus efficaces que celles de groupe. De plus, les interventions s'échelonnant sur une période d'au moins un an après l'accouchement sont plus efficaces que celles seulement administrées quelques fois. Finalement, la recherche sur la prévention de la dépression postpartum doit être plus poussée et standardisée afin de pouvoir comparer sans équivoques1 les conclusions des articles.

Differences in HDL, LDL, and Total Cholesterol between Metabolically Healthy Obesity and Metabolically Abnormal Obesity

Bu, S., Duong, P., Ha, B., Lee, P.

Objective: to determine the differences in blood lipid cholesterol levels between the subgroups of metabolically healthy obese (MHO) and metabolically abnormal obese (MAO) individuals within the obese population.

Methods: a literature review for studies reporting MHO and MAO cholesterol measures was conducted. Mean total, HDL, and LDL cholesterol of MHO and MAO subjects were extracted and synthesized into a table.

Results: MHO individuals were seen to have significantly higher HDL cholesterol in seven out of ten studies, with mean differences ranging from +0.16 to 0.37 mmol/L. In addition, MHO individuals were seen to have significantly lower LDL cholesterol in two out of five studies, and significantly lower total cholesterol in two out of six studies, with mean differences ranging from -0.80 to 0.89 mmol/L and -0.94 to 1.10 mmol/L, respectively.

Conclusion: Our findings support the use of elevated HDL cholesterol as a characteristic differentiating MHO and MAO. Further research is needed to verify whether lower levels of LDL cholesterol and total cholesterol can be reliable indicators of the MHO phenotype.

The Repercussions of Professional Sports - Recurrent Concussions and Dementia

Harris, S., Boyer, J.

Objectives: To examine recurrent concussions as a risk factor for reduced cognitive functioning leading to dementia. Also, to discuss methods for reducing recurrent concussions as a risk factor as well as appropriate guidelines for "returning to play" after a concussion.

Methods: A computerized search of English language literature, with the key words "concussions", "Dementia", "Chronic traumatic encephalopathy", and "Traumatic Brain Injury" using the PubMed, Medline and Ovid Healthstar databases. Evidence related to the objectives was extracted using only articles between the years 1999 and 2011.

Discussion: Currently millions of Canadians participate in sports and the economic burden of sports-related injuries is stagnant. Concussions and traumatic head injuries are common within professional sports such as football, hockey, boxing, wrestling, rugby, lacrosse, soccer and skiing. With higher incidences of dementia, high prevalence of concussions an Traumatic Brain Injuries (TBIs), as well as a decrease in life expectancy and mental function, it is apparent that this fairly new realization needs further longitudinal research.

Conclusion: CTE research is in its infancy and the relevant merit of this research is an important start to the evident prospective longitudinal cohort studies that are necessary. Interventions are needed that both delay disease onset and delay progression in order to significantly reduce the global burden of the disease. It is clear that the repetitiveness of head injuries creates compounding neurological damage. This research shows that recurrent concussions are a risk factor for dementia in athletes and that this is something that needs further attention.

Red Wine Consumption Level and Prostate Cancer Risk

Kartolo, A. , Abimbola, A.

Background: Prostate cancer has the highest incidence rates in North American males. Despite its less-pervasive lethality, high incidence rates accounts for the fifth leading cause of cancer death in males due to increased mortality cases. Studies indicate that red wine contains high amount of resveratrol, a chemopreventive agent that may reduce carcinogen growth by modulating enzymatic activities. This paper aims to identify the relationship between various red wine consumption and prostate cancer risk among North American males.

Method: A literature review was conducted by using Medline and Scopus databases to search for related English language studies within the past 11 years in North America. Age adjusted data from 4 studies were standardized and categorized into low- (<6 oz/wk), medium- (6- 28 oz/wk), and high- (>28 oz/wk) consumption level groups (LCLG, MCLG, HCLG respectively). Meta analysis of fixed effect model was conducted to analyze the association between MCLG/ HCLG and prostate cancer risk. Analysis of the LCLG was conducted by calculating RR (95% CI) because there were only 2 studies with relevant data.

Results & Conclusions: Inconsistent association was shown in the LCLG (RR 0.88, 95% CI 0.75-1.03; RR 0.79, 95% CI 0.73-0.85). Result of the meta analysis of MCLG and HCLG revealed no significant association (RR 1.01, 95% CI 0.94-1.08; RR 1.01, 95% CI 0.87-1.18) and high heterogeneity levels of i2 = 78.5% and i2 = 59.1% respectively.

Implications: Futures studies need to consider the possibility of other components in the red wine that may interact with the protective effect of resveratrol.

Running Away from Depression: The Effects of Physical Activity on Depression

Lavoy, A., Cloutier, M.

Background: Students face many changes in their transition to university. Depression is common in this age group, affecting 1 in 4 students.

Objective: We explored associations among physical activity and depressive symptoms in university students.

Methods: We conducted a literature review examining studies that investigated the levels of exercise and self-reports of feelings of depression.

Results: Overall, males and females who engaged in physical activity demonstrated reduced levels of depressive symptoms.

Conclusion: There is an established association between increased physical activity and reduced depression which demonstrates that adding an exercise component to current treatment interventions would be beneficial.

Men and HPV: To Vaccinate or not to Vaccinate

Leclair, E., Salemi, P.

Background: HPV is the most common sexually transmitted disease. There is a great amount of data on HPV in females, however emerging research is showing that HPV is a concern in males also.

Objectives: To determine if males should be vaccinated against HPV, and if vaccinating men will decrease the incidence and prevalence of HPV.

Methods: Various government websites and computerized databases were searched for key terms such as “HPV”, “males”, “vaccination”, “disease burden”, “incidence”, “prevalence”, and “cancer”.

Results: HPV has the potential to cause cancers in men, more specifically penile, anal, and oropharyngeal. The Gardasil vaccine was recently approved for use in males, and was shown to be almost 90% effective in preventing HPV. Conclusion: Males should also be included in vaccination efforts, as this will impact both males and females.

Weighing in: How Public Perception of the Causes of Obesity is Keeping North Americans Overweight

Loncar, M., Pontone, A.

The prevalence of obesity has increased substantially over the past several decades both in Canada and the United States. Despite efforts to reduce the rising levels of obesity, existing preventative strategies have had very limited success. We examine evidence surrounding public perceptions of the causes of obesity and their impact on support for public policy solutions to reduce obesity rates seeing as public perception of risk is an important consideration in public health policies. Through a comprehensive literature review of English-language publications within the last 10 years, several obesity-related metaphors have been recognized to play a significant role in shaping public attitudes about the causes of obesity and promoting stigmatization of obese individuals. The public uses metaphors to help explain why North Americans have become overweight. These metaphors are also powerful indicators of support for public policy interventions, with varying influence across different types of obesity-related policies. Participants commonly blamed the individual for being obese. Those who blamed the individual hesitated to support obesity-related health policies. Current evidence concludes that obesity-related metaphors are not beneficial health. Lack of support results to serious risks of physiological and physical health, generates health disparities and interferes with implementation of effective obesity prevention efforts. Public support is key for sustained implementation of preventative measures to identify potential starting points for enhancing support of obesity reduction initiatives. Increased support for policies aimed at reducing obesity rates may be achieved if the public embraces low-blame metaphors, thereby agreeing that obesity is caused by both genetic and environmental factors.

Pregnancy as a Risk Factor for Mortality in Breast Cancer

Maurice, G., Caley, R.

Background: Pregnancy-associated breast cancer is an uncommon, yet serious occurrence (1 in 1,500 to 4,000 pregnancies in Canada). Studies have been conducted to understand the prevalence and prognosis of women diagnosed with pregnancy-associated breast cancer (PABC). To further the understanding of the above relationship, a meta-analysis was conducted of several cohort retrospective studies as well as case-control studies.

Methodology: A computerized search of English language literature was conducted using the PUBMEDR and Google Scholar database. This search was limited to original articles only, and only studies published from 1992 until 2011. Shared information examining this issue was derived from 10 studies.

Results: Statistically, a synthesis of six studies has demonstrated that cases with PABC had a lower 5-year survival rate than non-PABC cases; 51.9% compared with 75.2% respectively.

Discussion: Generally, these studies submit that the higher death rate of PABC cases has been attributed to three factors: (1) diagnosis delays, (2) possible pathology, and (3) maternal age. A review of this literature suggests that the data relating to risk factors of PABC are limited and require further investigation.

Conclusion: Pregnancy can be a risk factor for mortality in breast cancer. As such, health care professionals play an important role in the early detection of PABC and in promoting breast cancer awareness specifically during pregnancy.

The Spread Trees, Not AIDS Programme in KwaZulu-Natal, South Africa

Mohamed, S.

Background: South Africa's HIV epidemic remains the largest in the world, where young women represent half of all HIV infections in the country [1]. The province of KwaZulu-Natal has the highest HIV prevalence rate (39.5%) in the country [2]. There is a definite need for HIV prevention/education programmes.

Objective: To investigate community interest and acceptance of a peer education programme (Spread Trees, Not AIDS) that focuses on the issues of both HIV prevention and environmental degradation among youth aged 10-19 in the Amajuba, eThekwini, uThukela and uThungulu districts in KwaZulu-Natal, South Africa.

Methods: A prospective cohort study was conducted from mid-June to late-July 2008. Participating sites (i.e. Rural Partner Organizations) were selected by the AIDS Foundation of South Africa where each was then responsible for recruiting thirty youth within the target age range. Youth were selected to participate in two subsequent peer education workshops focusing on HIV, the environment and leadership. Age, gender and attendance to workshops were collected by our team.

Results: The combined mean age of all participants was 14.61 years old. The cumulative attendance at all workshops per community was: Amajuba (93.33%), eThekwini (100%), uThukela (96.15%) and uThungulu (60.00%).

Conclusion: There is an interest for HIV education/prevention programmes such as Spread Trees, Not AIDS in each Rural Partner Organization community.

Genetic Indicators: Examining the Internal Time Bomb that is Huntington's Disease

Persic, C., Vrbanach, H., Edwards, A.

The age of onset (AOO) of Huntington's Disease (HD) is inversely related to the CAG-expansion length in the short arm of chromosome 4. CAG-expansion length is only one of the factors that influences AOO; environmental factors and other candidate gene modifiers have the potential to impact AOO as well. A review of published statistical models was conducted to assess the accuracy in predicting the AOO of HD from the CAG-repeat length. A comparison longitudinal observational study, PREDICT-HD, was used to assess accuracy. Earlier detection of HD can lead to faster targeted treatments and therefore slow progression.

Obsessive-Compulsive Personality Disorder: What is its Relationship with Anorexia Nervosa in a Female Athlete Population?

Prentice, M.

In recent years, Obsessive Compulsive Personality Disorder (OCPD) has been implicated in the development of Anorexia Nervosa (AN) – an often chronic and life-threatening eating disorder. The personality traits shared across both OCPD and AN, which include a high degree of perfectionism, a preoccupation with details, and a need for order and control, are particularly manifest in female athletes – a population with a markedly elevated risk for AN. A systematic review of the literature was thus undertaken to elucidate the influence of OCPD on the development of AN in the female athlete population. Results suggest that the author is the first to explore this relationship: no epidemiological studies have established the prevalence of OCPD in female athletes, let alone its relationship to AN. This review has thus uncovered a new focus for women's mental health research, with important implications for prevention and treatment of AN in the growing population of female athletes.

Targeting Parkinson's Disease: A Systematic Review of the Association of Parkinson's and Coffee Drinking

Rashid, M., Watson, M., Alturki, H.

Introduction: About 1 in 100 Canadians over the age of 60 are diagnosed with Parkinson's disease (PD) (Parkinson's Disease Foundation, 2011). Risk factors need to be explored to help develop effective prevention methods. Studies have shown that caffeine intake may have a relationship with the risk of developing PD. Coffee represents a major source of caffeine for Canadians and coffee consumption increased by 3.6% to 90 Liters/person in 2009 (Statistics Canada, 2010).

Objective: To determine whether increased coffee intake reduces the risk of PD.

Methods: A systematic review was performed through searching the MeSH terms "Parkinson's disease", "coffee", and "risk factor" using MEDLINER database. Inclusion criteria incorporated articles in the English language, conducted within the past 20 years, and that reported risk of association between coffee and PD. Through analysis of titles and abstracts, followed by full texts, 7 articles were obtained. Associations between PD and other caffeinated beverages were excluded. Critical appraisal for each study was done and results were obtained.

Results: Overall, studies showed decreased risk of PD as coffee dose increases. Risk ratio for highest exposure ranged 0.18-2.0 compared to 0.50-2.7 for lowest exposure. Only one dependable study showed increased risk (for specific results refer to table 1 in the full study).

Conclusion: There is an overall decreased risk of developing PD as intake of coffee increases, however, further research needs to be done to account for confounders, standardize dose and conduct meta-analysis to determine heterogeneity of the studies.

Chloroform Carcinogenesis: A Review of Literature Regarding The Carcinogenic Effects of a Highly Prevalent Chlorination Disinfection By-product

Remillard, L., Vaid, S.

Context: Chlorinated by products have detrimental health effects in high consumptions. Specifically, evidence has shown a correlation between Trihalomethanes (THM) and bladder cancer. Chloroform, the most abundant THM, has been listed by numerous health agencies as a probable carcinogen. The purpose of this presentation is to gather evidence, summarize results, and draw a conclusion determining the relationship between chloroform and bladder cancer.

Methods: A thorough literature review was established using government and peer reviewed resources relevant to chloroform and bladder cancer. Regions concentrated with high and low rates of chloroform and bladder cancer were examined to determine whether there is a correlation between the two.

Conclusion: After reviewing current literature about the concentrations of chloroform and its contributing factors towards the incidence and prevalence of bladder cancer, conclusions were drawn. There is a correlation between bladder cancer and the consumption of chlorinated water. However, there is no definitive correlation between bladder cancer and chloroform. Nevertheless, chloroform is the most abundant THM leading to belief that an association between the two can be drawn. In brief, more research is needed to clarify chloroform's role in the development of bladder cancer.

Examining the Efficacy of Anti-Depressant Medication in the Treatment of Severe Major Depression: A Meta-Analysis

Rowed, C., Winterbottom, R.

Introduction: Approximately 8% of Canada's adult population is affected by Major Depressive Disorder (MDD). The most commonly prescribed forms of pharmacotherapy are selective serotonin reuptake inhibitors (SSRI) and tricyclic antidepressants (TCA). There is a lack of comprehensive analysis of the full efficacy of these drugs in placebo-controlled clinical trials despite their widespread usage.

Objectives: Examine the efficacy of SSRIs and TCAs in patient's with severe major depression.

Methodology: 8 placebo-controlled clinical trials were selected and included in this meta-analysis (n=1696). The primary measure of outcome was the Hamilton Rating Score for Depression (HRSD). From these results relative risks were calculated (CI 95%) and grouped according to medication.

Results: RR TCA= 1.52, NNT=6 (weighted mean of 4 studies) and RR SSRI 1.36, NNT=6 (weighted mean of 4 studies).

Discussion: Based on these results we can conclude that SSRIs and TCAs are both significantly effective in the treatment of severe melancholic major depressive disorder.

Does Prostate Cancer Discriminate? – Analyzing the Prevalence of Prostate Cancer Among Different Ethnicities

Seabrook, C., Weichert, E.

Prostate cancer is the most common type of male reproductive cancer. Several risk factors that contribute to its development have been established, with racial background being cited as one of the most influential. This literature review aimed to assess the discrepancies in prevalence of prostate cancer among African-American men, as compared to Caucasian men in the United States. Other potential risk factors contributing to prostate cancer development were controlled for, to see if this difference was attributable to racial background alone. The review assessed peer-reviewed articles published after the year 2000, and all were subject to a very specific set of inclusion/exclusion criteria, including controls for SES, age, treatment/ assessment techniques, and consistency in defining African-American and Caucasian populations. Insufficient literature exists on the exact prevalence of the two racial groups, therefore incidence rates and survival rates were analyzed to extrapolate a theoretical prevalence. The results yielded a consistently higher incidence rate for the African-American population in each of the studies reviewed, as well as a consistently indifferent survival rate between the two populations. From these results, it was concluded that African-American men are being afflicted by prostate cancer at a higher rate, yet both African-Americans and Caucasians are dying or surviving the disease at the same rate. This would leave a net effect of more African-Americans having prostate cancer. Since the exact prevalence values could not be identified, it is uncertain if this discrepancy exists currently; however, should these trends persist, the African-American prevalence will surpass that of the Caucasians.

Examining the Effects of Physical Activity as a Post-Cancer Intervention Treatment

Tennant, J.

Background: There are currently over 600,000 cancer survivors in Canada, and this number is expected to grow steadily with continual advances in treatment, early detection, and screening. Cancer treatments often produce debilitating side effects, negatively affecting physical functioning and quality of life. In the past, cancer patients were strongly advised to rest and to avoid physical activity. However, emerging research on exercise and physical activity during, and post-cancer treatment, has challenged this long-held belief. The objective of this research paper is to examine the effects of physical activity as a post-cancer intervention treatment. I hypothesize that all cancer survivors would benefit from physical activity.

Methods: Literature for this review was obtained through a PubMed database search from 2006-2011, using the following MeSH terms: “effects”, “physical activity”, “cancer”, “treatment” and “Canada”.

Results & Conclusion: Not surprisingly, research strongly indicates that exercise is both safe and beneficial during cancer treatment. Its effects included improved physical functioning on many different levels as well as improved aspects of quality of life, such as fatigue, anxiety and depression. However, due to the distinguishing symptoms and unique challenges of different cancers and their treatments, it is imperative that exercise regimens be carefully modified to individual patients, to ensure safety and efficacy. With the growing prevalence of cancer survivors in Canada, future initiatives encouraging physical activity as a post-cancer intervention treatment are essential. Further randomized clinical trials are justified and necessary.

Evaluating the Relationship Between Reproductive Outcomes and Ovarian Cancer: A Systematic Review

Van Beinum, A., Ingimundson, S., Wong, Z.

Background & Rationale: Ovarian cancer has one of the highest mortality rates of all reproductive cancers. Nonspecific symptoms and a lack of knowledge about etiology make effective screening and early diagnosis difficult. Current theories of ovarian cancer causes include excessive ovulation, hormone exposure, and exposure to carcinogens. Some pregnancy outcomes suppress ovulation and may reduce the risk of cancer. A recent database search revealed no recent literature reviews on the effects of pregnancy outcomes on ovarian cancer risk exists.

Research Question: How does the current literature surrounding ovarian cancer and pregnancy outcomes support theories of etiology of ovarian cancer?

Methods: Databases MEDLINE, Scopus, and PubMed were systematically searched for peer-reviewed journals published since 2000 using relevant MeSH terms. Articles were reviewed for validity, effect size, and potential bias using a data abstraction tool.

Results: Searches produced a total of 2581 articles. 289 articles were deemed relevant after reviewing titles and abstracts; 79 remained after deletion of duplicates. After review of full papers, 40 remained for data abstraction. Resulting ORs and RRs were compared for breastfeeding, pregnancy, abortion, number and sex of children. No strong trends were found. The heterogeneity of studies included meant that no pooled statistic could be calculated.

Conclusion: Outcomes that suppressed ovulation showed a protective effect though this was not consistent across studies. Neither abortion nor sex of child showed any trend across studies. More research is needed into the specific role ovulation plays in the etiology of ovarian cancer.

Making an Informed Decision on Taking the Pill: A Systematic Review of Evidence Regarding the Association Between Oral Contraceptive Use and Female Reproductive Cancers

Sabarre, K.A., Young, A.

Objective: To assess the association between the duration of oral contraceptive (OC) use and reproductive cancers.

Background: OCs are a common and effective method of contraception. OCs acts as an ovulation suppresser by inhibiting hormone synthesis and excretion. In Canada, 66.6% of sexually active females ages 15-19 and 58.3% of sexually active females ages 20-29 used oral contraceptives. Dated studies have shown an association between OC use and cancer. Here, a review of recent literature (2006-2011) was conducted to assess the relationship between duration of OC use and reproductive cancers.

Research Question: For females using oral contraceptives, what does evidence suggest regarding the association between the duration of oral contraceptive use and reproductive cancers?

Methods: Literature review of English peer-reviewed cohort and case-control studies regarding OC use, cervical, ovarian, uterine and breast cancer. Studies were assessed by reproductive cancers, duration of OC use, relative risk (RR), odds ratio (OR) and statistical significance of results.

Results: Cervical cancer: RR=1.11-6.10(95%CI); Ovarian cancer: RR=0.30-1.12(95%CI), OR=0.30-0.74(95%CI); Uterine cancer: RR=0.10-0.60(95%CI), OR=0.50-0.94(95%CI); Breast cancer: RR=0.90-1.22(95%CI), OR=1.30-2.40(95% CI).

Conclusion: Statistically significant associations included: increased risk of cervical cancer and decreased risk of ovarian cancer (OC use > 96 months); a reduced risk of uterine cancer (OC use > 48 months); increased risk of breast cancer (OC use > 12 months).

APPEL À CONTRIBUTIONS

Les critères de soumission se basent sur les douze déterminants de la santé, tels que définis par Santé Canada et l'Agence de santé publique du Canada. Idéalement, toute personne qui souhaite soumettre un manuscrit à la RISS devrait clairement identifier quel déterminant de la santé est associé à sa recherche, ainsi que la nature de cette relation : *de quelle façon le sujet à l'étude est-il relié à la santé humaine, à travers le déterminant de la santé choisi ?*

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