Revue interdisciplinaire des sciences de la santé
Interdisciplinary Journal of Health Sciences

RISS | IJHS

Volume 1, Numéro 1 | Issue 1

Inaugural Issue

La revue interdisciplinaire des sciences de la santé
The Interdisciplinary Journal of Health Sciences

Une revue académique libre d'accès | An Open-Access Academic Journal

Université d'Ottawa | University of Ottawa

ISSN : 1920-7433

www.riss-ijhs.ca

Table des matières | Table of Contents

Avant-propos

Premal PATEL Rédacteur en chef

En Juin 2009, après avoir été élu président de l'Association étudiante des sciences de la santé, j'ai été contacté par Dr. Raywat Deonandan concernant la perspective de la mise en oeuvre d'un journal dirigé par des étudiants au sein de l'École interdisciplinaire des sciences de la santé. Avec l'aide du vice-président aux affaires universitaires, Brendan McCullough, et une équipe d'étudiants dévouée, cette idée a rapidement porté fruits.

La Revue interdisciplinaire des sciences de la santé (RISS), dirigée par les étudiants et évaluée par des pairs est produite au sein de l'Université d'Ottawa. La revue vise à inclure toutes les facettes des sciences de la santé et est donc ouverte aux étudiants de l'École interdisciplinaire des sciences de la santé.

La RISS vise à promouvoir la recherche, de nouvelles normes d'éducation et la facilitation de la discussion scientifique. Notre mandat est de mettre la recherche en sciences de la santé à l'avant-garde de la communauté Université d'Ottawa. En soumettant des articles à la RISS, les étudiants auront la possibilité d'avoir leurs travaux examinés par des experts dans le domaine et de recevoir des commentaires sur les méthodes d'amélioration de leurs projets.

Après avoir été choisi comme récipiendaire de la 'Faculty of Health Sciences Mission Satisfaction Grant' nous espérons étendre au-delà de la revue de l'École des sciences de la santé interdisciplinaire et de l'intégrer au sein de la Faculté des sciences de la santé. Nous nous efforçons de fournir aux étudiants l'occasion de publier leurs propres travaux et de jouer un rôle actif dans la discussion scientifique qui est souvent largement sous-estimée dans l'enseignement de premier cycle.

J'ai apprécié mon poste de premier rédacteur en chef de la RISS. Je me réjouis de l'avenir de cette revue et continuerai d'offrir des conseils et du soutien au besoin.

Robyn WINTERBOTTOM Rédactrice en chef

Je suis honoré d'être le nouveau rédacteur en chef de Revue étudiante interdisciplinaire des sciences de la santé (RISS). Premal Patel, Dr. Raywat Deonandan et les derniers éditeurs, ont investi beaucoup de travail pour faire de ce journal une réalité. J'ai eu le plaisir de publier le premier numéro de la RISS, et je suis heureux de féliciter tous les auteurs qui ont consacré leur temps à la production de manuscrits admirables.

J'espère aider à la croissance et au succès de la RISS cette année, et travailler à son extension à toute la Faculté des sciences de la santé. Mes principaux objectifs consistent à produire un deuxième numéro avec une représentation égale des articles en français et en anglais, et d'augmenter l'inclusion des travaux produits au cours des projets originaux de recherche des étudiants.

J'ai hâte de travailler avec la nouvelle équipe de rédacteurs étudiants, avec les professeurs et les professionnels au sein de la Faculté des sciences de la santé à l'Université d'Ottawa. Un grand merci aux personnes qui ont participé au processus de révision des articles publiés dans le numéro actuel de la RISS. En outre, je remercie Premal Patel et M. Deonandan pour leur engagement dans cet effort, et pour les conseils qu'ils m'ont prodigué lorsque j'ai commencé mon rôle de rédacteur en

Foreword

Premal PATEL Editor in Chief

In June 2009, after being elected as President of the Health Sciences Student Association, I was approached by Dr. Raywat Deonandan concerning the prospect of implementing a student-run journal within the Interdisciplinary School of Health Sciences. With the aid of Vice-President of University Affairs, Brendan McCullough, as well as a team of dedicated students, this idea quickly grew to fruition.

The Interdisciplinary Student Journal of Health Sciences is a student-run, peer reviewed journal which currently operates at the University of Ottawa. The journal seeks to include all facets of health sciences and is therefore open to students within the Interdisciplinary School of Health Sciences.

The IJHS aims to promote research, further educational standards and facilitate scientific discussion, and our mandate is to bring health science research to the forefront of the University of Ottawa community. By submitting to the IJHS, students will have the opportunity to have their work reviewed by experts in the field and will receive feedback letting them know how their personal projects can be improved.

Having been selected as a recipient of the Faculty of Health Science Mission Satisfaction Grant we hope to expand the journal beyond the School of Interdisciplinary Health Sciences and to integrate it within the Faculty of Health Science. We strive to allow students the opportunity to not only publish their own work but to take an active role within scientific discussion which is often highly under-looked in undergraduate education.

I have enjoyed my position as the inaugural Editor-in-Chief of the IJHS. I look forward to the future of this journal and will continue to offer guidance and support as needed.

Robyn WINTERBOTTOM Editor in Chief

I am honoured to be the new Editor-in-Chief of the Interdisciplinary Student Journal of Health Sciences. A lot of hard work on the part of Premal Patel, Dr. Raywat Deonandan, and last years' editors, has gone into making this journal a reality. I had the pleasure of publishing the inaugural issue of the IJHS, and I am glad to say congratulations to all of the authors who dedicated their time to producing the admirable manuscripts within.

I hope to aid in the continued growth and success of the IJHS this year, and will work toward its extension to the entire Faculty of Health Sciences. My primary goals include producing a second issue with equal representation of both French and English articles, and increasing the inclusion of work produced by original student research projects.

I look forward to working with the new team of student editors and with the professors and professionals within the Faculty of Health Science at the University of Ottawa. My great thanks goes out the individuals who participated in the peer-review process of the articles in the current issue of the IJHS. Furthermore, I thank Premal Patel and Dr. Deonandan for their commitment to this endeavor, and for their guidance as I've commenced the role of Editor-in-Chief.

Les Risques Associés à l'Utilisation Inappropriée des Stéroïdes Anabolisants

Marie-Claude BORGEAT* [1], James GOMES [2]

[1] Étudiante, Université d'Ottawa, Canada

[2] Professeur, Université d'Ottawa, Canada

* *Auteur(e) correspondant | Corresponding author:* N/A

Résumé :

(traduction)

Notre société met une emphase énorme sur la beauté et la performance physique. Il n'est donc pas surprenant qu'une tranche importante de celle-ci prenne recourt à des méthodes drastiques qui lui permettront de s'approcher ou d'atteindre ces objectifs. Une des méthodes devenue populaire est l'utilisation inappropriée de stéroïdes anabolisants. Plusieurs études ont évalué les effets néfastes et indésirables de ces composés à des doses supra-physiologiques. Nous présentons donc une révision et synthèse de ces effets dans le but de mieux comprendre les effets néfastes de ce composé lorsqu'il est utilisé de façon inappropriée.

Mots-clés : N/A

Introduction

Malgré leur présence et synthèse endogène dans les mammifères et plusieurs autres espèces animales, la synthèse d'hormones stéroïdes dans le domaine pharmaceutique existe principalement pour des buts thérapeutiques, tel que des thérapies de remplacement d'hormones chez les femmes et les hommes souffrant d'une insuffisance ainsi que pour le traitement de problèmes gynécologiques féminins (Mottram & George, 2000).

La testostérone a été isolée pour la première fois en 1935 par David *et al.* (Kanayama, Hudson, Harrison, & Popeet, 2008). L'utilisation de dérivés de testostérone pour des fins d'amélioration d'une performance physique semble avoir débuté en 1954 lors d'une compétition d'haltérophiles Russes à Vienne (Kanayama et al., 2008; Mottram & George, 2000). La prise de stéroïdes est ensuite devenue une pratique chez les haltérophiles américains et par la suite ceux-ci ont été introduits dans d'autres sports (Kanayama et al., 2008; Mottram & George, 2000).

Il ne date que dans les années 1970 que nous pouvons détecter ces composés synthétiques. L'interdiction de la prise de stéroïdes chez les athlètes par le Comité International Olympique (CIO) s'est fait en 1975 et les premiers dépistages lors des Jeux Olympiques de 1976 à Montréal (Mottram & George, 2000). Lors des tests de dépistage effectués entre 1993 et 1997 par le CIO il y a eu moins de 2% de résultats positifs, et ce pour n'importe quel drogues. Par contre, les stéroïdes anaboliques sont les composés chimiques les plus identifiés parmi la liste des substances interdites du CIO (Mottram & George, 2000). Même si ces donnés concernant la prévalence de ces produits sont assez basses, nous avons plusieurs raisons de croire que la vraie valeur serait plus élevée. Par exemple, les athlètes ont adapté leurs régimes de stéroïdes pour qu'il n'y ait pas de détection, puisque ceux-ci sont effectués lors des compétitions (Mottram & George, 2000). L'utilisation inappropriée des stéroïdes s'est propagée des sportifs professionnels aux amateurs, y inclue ceux provenant des écoles secondaires et des collèges (Kanayama et al., 2008, Kutscher, Lund, & Perry, 2002; Mottram & George, 2000). Il est estimé qu'environ 50% des culturistes prennent des stéroïdes malgré que ces substances ne sont pas permises en compétition; peu de tests de dépistage sont fait, ce qui ne dissuade donc pas les utilisateurs (Kutscher et al., 2002).

Le phénomène de beauté musclée s'est aussi propagé par les médias ce qui a aussi incité la prise de stéroïdes par la population au large (Kanayama et al., 2008). Plusieurs guides de références secrets ont été écrits pour les utilisateurs de stéroïdes illicites dont : « *Original Underground Steroid Handbook* » par Daniel Duchaine et « *Anabolic Reference Guide* » par W. Phillips (Kanayama et al., 2008). Il se trouve que présentement, la majorité des utilisateurs de ces drogues ne sont pas des athlètes compétitifs, mais plutôt des gens qui s'entraîne comme passe-temps et qui veulent développer leur muscles davantage (Kanayama et al., 2008). Jusqu'à 6.6% des adolescents sont estimés d'utiliser des stéroïdes anabolisants pour des fins inappropriées (Buckley, Yesalis III, Friedl, Anderson, Streit, & Wright, 1988) tandis que l'utilisation chez les adultes se retrouve entre 5 et 15%, l'incidence étant plus élevée chez les hommes (Kutscher et al., 2002; Mottram & George, 2000; Petrocelli, Oberweis, & Petrocelliet, 2008). Les stéroïdes anabolisants représentent la substance la plus consommée pour augmenter la performance athlétique, suite seulement à la créatine (Kutscher et al., 2002).

Les stéroïdes anabolisants sont des dérivés synthétiques de la testostérone, une hormone endogène synthétisée à partir du cholestérol. D'une part, celle-ci est importante à la masculinisation, c'est-à-dire au développement des caractèristiques sexuelles primaires et secondaires chez les mâles et d'une autre part, à l'augmentation de la masse musculaire par la synthèse accrue de protéine, soit son effet anabolisant (Kanayama et al., 2008; Mottram & George, 2000). Les stéroïdes anabolisants synthétiques ont été créés avec l'intention d'augmenter leur effet anabolisant malgré qu'il soit impossible d'éliminer tous les autres effets androgéniques (Mottram & George, 2000). La testostérone a été modifiée de trois manières différentes, ce qui a donné trois classes de stéroïdes anabolisants. La première classe peut être injecté à l'aide d'une aiguille, la deuxième classe et la troisième classe sont des composés qui peuvent être pris oralement, par contre, la dernière possède une puissance élevée et un métabolisme plus lent (Mottram & George, 2000). Les stéroïdes anabolisants font partie de la classe plus large d'agents anabolisants y inclu les bêta-agonistes, tel que le salbutamol, le clenbutérol et le terbutaline, qui sont des agents utilisés à d'autres fins qui n'ont pas une structure stéroïdienne mais qui possèdent tout de même des propriétés anabolisantes (Mottram & George, 2000) et ne seront donc pas abordé d'avantage dans ce projet. Les stéroïdes anaboliques exogènes seront le sujet de cette revue de la littérature et plus principalement, ceux pris de façon inappropriée, donc qui ne sont pas consommé médicalement. Voici quelques exemples de stéroïdes anaboliques; testostérone énanthate, nandrolone, oxandrolone,

androsténédiol, méthénolone, et ce parmi tant d'autres (Mottram & George, 2000).

Les effets secondaires et indésirables associés à la prise de stéroïdes anabolisants sont causés par leur action au niveau des systèmes cardiovasculaire et reproducteur, l'axe neuroendocrinien et le foie, parmi d'autres. Notre but est donc d'élaborer au sujet de leur fréquence d'apparition à travers la population à risque ainsi que les effets les plus communs chez les abuseurs de ces stéroïdes. Nous cherchons aussi de mieux comprendre les risques reliés à l'utilisation des stéroïdes anabolisants, et ce chez les athlètes, les sportifs, mais également dans la population générale qui utilisent ces composés de manière inappropriée.

Méthodologie

Nous avons utilisé trois classes de mots clés pour faire notre recherche. La première regroupe les mots pour identifier nos composés (ex : anabolic steroids OR doping in sport), la deuxième classe de mots concerne la population voulu (ex : athletes OR bodybuilding) et la dernière classe vise les effets sur la santé (ex : adverse effect OR medical effect). Ces trois classes de mots ont été regroupées ensemble par «AND». Voici les divers bases de donnés qui ont été utilisées; Ovid MEDLINE (R) In-process & Other Non-Indexed Citations and Ovid MEDLINE (R), Ovid MEDLINE (R) Embase et Web of Science. Avec une année de publication des dix dernières années et des sujets de recherche qui se limite aux humains, nous avons trouvé 1440 articles (respectivement 438, 517 et 485 articles). Après avoir enlevé les copies en doubles et avoir trié les articles avec les critères d'inclusion et d'exclusion, nous avons 88 articles.

Les critères d'inclusions étaient : les articles doivent 1) avoir été publiés entre les années 2000 à 2010, 2) avoir été publiés en anglais ou en français, 3) présenter des données sur les stéroïdes anabolisants seulement et non sur un autre agent anabolisant, et 4) les sujets de recherche doivent être soit des sportifs, des athlètes ou des utilisateurs dans la population générale. Les critères pour lesquels nous avons exclus des articles : 1) utilisation de sujet animal ou d'humain traité médicalement.

Résultats

L'abus des stéroïdes anabolisants peut amener plusieurs problèmes de santé chez les humains. Certains de ces effets disparaissent lorsque l'utilisation des stéroïdes est arrêtée mais d'autres persistent. Selon quatre revues de la littérature sur les stéroïdes anaboliques, voici quelques uns des effets néfastes, mais tous ne sont pas encore prouvé scientifiquement ou a été observé dans de rare cas et d'autres recherches devraient être entreprises (Kanayama et al., 2008; Kutscher et al., 2002; Mottram & George, 2000) :

- Problèmes cardiovasculaires : Hypertension, athérosclérose, cardiomyopathie, hypertrophie du ventricule gauche, dyslipidémie, ischémie du myocarde, augmentation de la coagulation du sang, agrégation des plaquettes, arythmie, mort causée par des problèmes cardiaques, diminution des HDL et augmentation des LDL, thrombose, vasospasme de l'artère coronaire, augmentation de la pression sanguine (Kanayama et al., 2008; Kutscher et al., 2002; Mottram & George, 2000; Petrocelli et al., 2008)
- Problèmes neuroendocriniens : suppression de l'axe hypothalamique-pituitaire-testiculaire, hypogonadisme qui peut amener l'infertilité et une dépression majeure, hypertrophie de la prostate, diminution des hormones LH et FSH (Kanayama et al., 2008; Kutscher et al., 2002; Mottram & George, 2000)
- Problèmes du foie : jaunisse, carcinome hépatique, péliose hépatique, cholestase intra-hépatique, adénomes ou carcinomes hépatocellulaires, angiosarcome hépatique, rupture hépatique spontanée, test de la fonction hépatique élevé, cancer de la prostate (Kanayama et al., 2008; Kutscher et al., 2002; Mottram & George, 2000; Petrocelli et al., 2008)
- Problèmes sexuels : diminution des spermatozoïdes, azoospermie, augmentation des spermatozoïdes immobiles et diminution de la motilité des spermatozoïdes (Kutscher et al., 2002; Mottram & George, 2000; Petrocelli et al., 2008)
- Régulation de la glycémie : résistance à l'insuline, diminution de la tolérance du glucose et diabète de type 2 (Mottram & George, 2000)
- Problèmes psychiatriques et comportementales : manie, trouble bipolaire, dépression, dépendance, augmentation de l'hostilité et de l'agression, suicide, utilisation plus fréquente de drogues différentes (Kanayama et al., 2008; Kutscher et al., 2002; Mot-

tram & George, 2000; Petrocelli et al., 2008)

- Autres : Apoptose cellulaire, diminution de la libido, gynécomastie, dommage aux tendons, acné et autres changements dans la peau (Kanayama et al., 2008; Kutscher et al., 2002; Mottram & George, 2000; Petrocelli et al., 2008)

- Chez les femmes : hirsutisme, acné, aggravation de la voie, hypertrophie du clitoris, diminution de la masse des seins, diminution de la menstruation, augmentation de l'appétit, calvitie (Kutscher et al., 2002)

Notre revue de la littérature nous a informée sur ces différents effets néfastes sur la santé :

Problèmes cardiovasculaires

Les effets néfastes les plus souvents associés avec la prise de stéroïdes anabolisants semblent être les problèmes cardiovasculaires. Plusieurs de ces effets sont présentés dans le Tableau 1. Nous retrouvons dans la littérature plusieurs études de cas indépendantes de gens qui se présentent chez un praticien de la santé avec des symptômes, sans soupçonner que ceux-ci peuvent être reliés aux stéroïdes. Un de ces cas décrit des douleurs thoraciques causées par un infarctus aigu du myocarde chez un culturiste professionnel de 31 ans ayant une historique de 10 ans d'abus de stéroïdes anabolisants dont, l'énanthate, le décanoate, et le sipanate (Wysoczanski, Rachko, & Bergmann, 2008). Le diagnostic, une lésion obstructive à l'athérothrombose de l'artère coronaire droite qui aurait été favorisée par l'abus des stéroïdes. Un deuxième cas est celui d'un culturiste de 40 ans qui se présente à l'urgence suite à plusieurs symptômes qui persistent et s'engravent depuis un mois. Cet athlète recevait depuis un certain temps des injections, en doses progressivement élevées, d'éthandrosténolone, de nandrolone décanoate, d'éphédra et de g-hydroxybutyrate. Une apparition récente d'insuffisance cardiaque congestive due à une cardiomyopathie dilatée non ischémique à été diagnostiquée ainsi qu'une hépatite aiguë avec une insuffisance rénale précoce (Clark et Schofield, 2005). Finalement, un ex-culturiste au début de la quarantaine arrive à l'hôpital souffrant d'une insuffisance cardiaque reliée à une cardiomyopathie dilatée. Il admet avoir pris deux régimes de testostérone énanthate quatre ans auparavant, ainsi que de se servir du furosémide, du spironolactone et du hydrochlorothiazide pour sa perte de poids avant ces compétitions. L'entrevue avec ces parents révèle qu'il prenait probablement aussi des hormones de croissance. Les spécialistes ont concluent que son insuffisance cardiaque est due à l'utilisation inappropriée de ces stéroïdes (Ahlgrim & Guglin, 2009).

Il existe aussi des études empiriques où la santé cardiovasculaire est comparée chez des groupes prenant des stéroïdes, ayant pris des stéroïdes ou groupe témoin, c'est-à-dire n'ayant jamais pris de stéroïdes anabolisants. Climstein *et al* (2003) ont démontré des mouvements anormaux de la paroi du ventricule gauche du cœur chez un groupe de 23 athlètes ayant consommé une dose physiologique minimale de stéroïdes anabolisants pour un minimum de 2 ans, comparés à un groupe d'athlètes n'ayant jamais utilisé de stéroïdes. Une étude par échocardiogramme démontre une restructuration concentrique marqué du ventricule gauche chez des athlètes qui utilisent des stéroïdes comparés à des hommes sédentaires non utilisateur (Karila et al, 2003) tandis qu'une dysfonction précoce du myocarde du ventricule gauche a été démontrée par échocardiogramme de 20 culturistes utilisant des stéroïdes anabolisants depuis plus de cinq ans (D'Andrea et al 2007). Le rapport démontre que les 20 athlètes consommaient des stéroïdes anabolisants ainsi que des hormones de croissance (Karila et al 2003), tandis que les culturistes s'administraient une variété de stéroïdes soit par injections intramusculaires (méténolone, nandrolone ou testostérone estérifiée) et/ou par ingestion orale (fluoxymestérone, mestérolone, méténolone, métandienone, oxandrolone et oxymétholone (D'Andrea et al 2007).

Une quatrième étude a comparé des culturistes n'utilisant pas de stéroïdes ainsi que des personnes sédentaires démontrant aucune utilisation à des culturistes ayant pris des stéroïdes anabolisants par voie orale (stanozolol, méténolone, nandrolone, testostérone, oxymétholone, méthandrosténolone et/ou drostanolone) en diverses combinaisons et cycles (Kasikcioglu, Oflaz, Umman, & Bugra, 2008). Les résultats d'analyse tissulaire par Doppler et de la vélocité de l'afflux trans-mitral mesuré par échocardiogramme Doppler à impulsions dévoilent une dépression diastolique des deux ventricules, mais surtout du ventricule droit chez les culturistes traités aux stéroïdes (Kasikcioglu, Oflaz, Umman, & Bugra, 2008). Une autre étude chez les culturistes utilisant de façon cyclique des stéroïdes anabolisants, tels la nandrolone ou testostérone estérifiée (nandrolone phénylpropionate, nandrolone décanoate, testostérone propionate, testostérone cypionate, testostérone énanthate), ou la winobanin, mestérolone ou

testostérone undécanoate, révèle une réduction de la vasodilatation médiée par le débit (FMD – Flow-mediated vasodilation) chez ces culturistes, peut importe la phase du cycle dans lequel l'évaluation se fait. Ces données suggèrent un effet de durée prolongée sur la fonction endothéliale par les stéroïdes anabolisants (Ebenbichler et al., 2001). De plus, le groupe de Urhausen, Albers & Kindermann (2004) a démontré une légère hypertrophie concentrique du ventricule gauche, avec une certaine indication de diminution de la fonction diastolique chez des athlètes qui utilisaient des stéroïdes depuis 1 à 8 ans mais aussi chez ceux ayant discontinué l'utilisation de stéroïdes au moins un an avant le début de l'étude. Ces données démontrent que malgré l'arrêt de la prise des stéroïdes, plusieurs de leurs effets sur système cardiovasculaire persistent et semblent irréversibles.

Finalement, les résultats d'une étude par Graham et al (2006) démontrent que l'utilisation à long terme de stéroïdes anabolisants à des doses supraphysiologiques est associée à une hyperhomocystéinémie et une hausse dramatique de la concentration des hématocrites, ce qui est désavantageux pour la santé du cœur et peut aboutir en une mortalité cardiovasculaire. En effet les résultats d'autopsies de quatres athlètes décédés subitement démontrent qu'ils souffraient tous de la maladie des petits vaisseaux artériolaires, dont une augmentation de l'épaisseur des vaisseaux et une hyperplasie de l'intima (Di Paoloa et al., 2007). Des analyses supplémentaires ont confirmé que ces quatres individus consommaient du stanozolol et de la testostérone.

Problèmes hépatiques et rénaux

Des études de cas indépendantes démontrent aussi plusieurs problèmes du système hépatique et du système rénal reliés à la prise de stéroïdes anabolisants chez des culturistes. Le premier, un culturiste de 31 ans s'est présenté pour des soins médicaux suite à des nausées et des douleurs abdominales supérieures sévères. Le patient est diagnostiqué avec une adénomatose hépatique et des saignements. (Bagia, Hewitt & Morris, 2000). Nous retrouvons aussi deux cas de culturistes de 40 ans ayant rapportés l'utilisation de stéroïdes anabolisants depuis plusieurs années, tel la méthandrosténolone, stanozolol, oxymétholone, nandrolone décanoate, testostérone énanthate et trenbolone énanthate, par exemple (pour 10 ans dans un des cas). Suite à des malaises sévères, les deux sont diagnostiqués avec une cardiomyopathie qui semble être reliée à une insuffisance hépatique aiguë (Bispo et al., 2009 ; Clark & Schofield, 2005) et une insuffisance rénale précoce dans un des cas (Clark & Schofield, 2005). De plus, un culturiste de 27 ans est diagnostiqué avec une insuffisance rénale en stage terminal, qui semble être causée par la prise de doses élevées de stéroïdes anabolisants, testostérone et clenbutérol, dans ce cas (Hartung, Gerth, Fünfstück, Gröne, & Stein, 2001) tandis qu'un autre âgé de 21 ans qui supplémentait sa consommation de stéroïdes avec des vitamines (A, D et E) a été diagnostiqué avec une blessure rénale aiguë (Daher et al., 2009).

Problèmes endocriniens

Les problèmes endocriniens rencontrés le plus fréquemment chez les gens qui consomment des stéroïdes anabolisants sont ceux qui affectent le trajectoire neuroendocrinien ainsi que le système de reproduction. Daly et al (2003) ont démontré qu'un régime de méthyltestostérone pour trois jours à une dose de 40 mg/jour et suivi de trois jours à une dose de 240 mg/jour, encadré par trois jours de placebo avant et après, affecte l'homéostasie hormonale de l'axe hypothalamo-hypophyso-gonadique avec un impact minime sur l'axe hypothalamo-hypophyso-surrénalien. Un changement dans les taux physiologiques de la testostérone et de la FT4 (paramètre thyroïdien) a été associé au développement de symptômes cognitifs et agressifs (Daly et al., 2003).

L'analyse de résultats d'une étude empirique, révèle que la consommation de stéroïdes anabolisants de façon excessive est reliée à une modification athérogène du profil lipidique chez 80% des sujets et que celle-ci est asymptomatique. Ils ont aussi remarqué plusieurs changements au système reproducteur, soit une hypogonadisme associée à l'atrophie des testicules, une production diminuée de spermatozoïdes ainsi qu'une gynécomastie (Bonetti et al., 2008). Par conter, ces effets semblent réversibles. Un culturiste âgé de 20 ans qui consomme des stéroïdes anabolisants depuis dix mois démontre une azoospermie à son admission hospitalière, un profil d'oligospermie cinq mois après l'arrêt des stéroïdes, et un compte normal de spermatozoïdes dix mois après l'arrêt. (Boyadjiev, Georgieva, Massaldjieva, & Gueorguiev, 2000). Pour contrer des problèmes d'oligozoospermie certains utilisateurs de stéroïdes anabolisants consomment également des gonadotrophines chorioniques humaines. Karila, Hovatta, & Seppälä (2004)

démontrent que l'addition des gonadotrophines chorioniques maintient la production de spermatozoïdes chez 18 athlètes qui utilisent de grandes quantités de stéroïdes anabolisants mais que la qualité du sperme est altérée.

Autres problèmes

Malgré que les problèmes cardiovasculaires, hépatiques, rénaux et endocriniens semblent être les plus répandus, la consommation de stéroïdes anabolisants est aussi associée à d'autres symptômes moins communs. Ceux-ci inclus des comportements agressifs, dépressifs ou même des idées suicidaires (Bolding, Sherr, & Elford, 2002). Nous retrouvons aussi des problèmes au site d'injection dans le cas d'administration de stéroïdes anabolisants par ce mode. Ces complications incluent une infection locale de bacilles acido-résistants chez un patient qui s'injectait de façon chronique dans le muscle du fessier (Al-Ismail, Torreggiani, Munk, & Nicolaou, 2002). Par contre, la prévalence d'infection au virus de l'hépatite C est plus basse chez ceux qui s'auto-administrent les stéroïdes anabolisants par injection que chez les gens qui s'injectent d'autres drogues (Aitkena, Delalandeb, & Stanton, 2002). Il existe aussi au moins un cas de rhabdomyolyse localisé au site d'injection répétée (4 x par semaine/7 ans) de stéroïdes (Farkash, Shabshin, & Pritsch, 2009) mais aussi dans le cas douteux d'un patient qui se dosait oralement que depuis deux semaines (Braseth, Allison, & Gough, 2001).

Il existe aussi une étude de cas qui relie un hochet persistant à la prise chronique et à doses élevées de stéroïdes anabolisants par injection intramusculaire (Dickerman, & Jaikumar, 2001); nous pouvons supposer qu'il y avait un effet des stéroïdes au fonctionnement du diaphragme chez ce dynamophile âgé de 35 ans. Nous retrouvons aussi les cas de deux patients sans traumatisme de l'encéphale qui se présentent à l'hôpital avec des maux de tête, des nausées, une vision flou et des épisodes de vomissement. Ceux-ci sont diagnostiqués avec un hématome sous-dural spontané (Alaraj, Chamoun, Dahdaleh, Haddad, & Comair, 2004). Les médecins spéculent que l'utilisation de stéroïdes anabolisants, d'hormones de croissance et de surplus de protéines soient à la source des hématomes. De plus, on soupçonne que l'augmentation et croissance musculaire associées à la prise de stéroïdes aurait rendu un jeune patient de 23 ans plus susceptible à un syndrome de compartiment suite à un accident de motocyclette (Bahia, Platt, Hart, & Baguley, 2000).

Jusqu'à présent, nous avons présenté plusieurs problèmes de santé reliés à l'utilisation de stéroïdes anabolisants. Dans certains cas, ces déficiences sont extrêmes et peuvent être mortelles. En effet, Pärssinen *et al.*, (2000) ont comparé les raisons de décès chez des dynamophiles lors des années 1977 à 1982. Ceux-ci étaient fortement soupçonnés de prendre des stéroïdes anabolisants, un comportement fréquent dans ce groupe. Les résultats de cette étude suggèrent que comparé à la population au large, l'utilisation de stéroïdes anabolisants est associée à plus de décès prématurés, et ce, par le suicide ou par une condition médicale (Pärssinen, Kujala, Vartiainen, Sarna, & Seppälä, 2000).

Discussion

D'après les résultats présentés, il semble que les effets secondaires des stéroïdes anabolisants soient très diversifiés, touchant plusieurs organes et étant souvent irréversibles (Kanayama et al., 2008, Kutscher et al., 2002; Mottram & George, 2000; Petrocelli et al., 2008). Le système cardiovasculaire est celui le plus souvent affecté et qui peut engendrer des effets à d'autres systèmes, tel le foie et les reins. Par contre, il est difficile de généraliser ces résultats à tous les athlètes et à la population générale qui consomment de façon illégale des doses supra-physiologiques de stéroïdes anabolisants. La première raison est le petit nombre d'études empiriques, une grande majorité des études qui existent sont des études de cas. Malgré que ces études nous démontrent des effets possibles associés à la prise de stéroïdes, les antécédents particuliers du cas à l'étude sont fort probable différents des antécédents de d'autres utilisateurs. Un deuxième raison est que si ces stéroïdes proviennent de source illégale, la consistance du produit est incertaine, donc les composées néfastes peuvent différerd'une personne à l'autre ou même de l'utilisation d'une fois à l'autre chez le même individu.

Il est aussi important de faire reconnaitre que la plupart des utilisateurs de stéroïdes anabolisants consomment d'autres produits conjointement ou 2 à 3 différents stéroïdes en même temps. Ceux-ci incluent les hormones de croissances, des suppléments de minéraux ou de vitamines, des drogues comme la marijuana ou autres médicaments quelconques. Les effets néfastes démontrés pourraient être causés soit par les autres substances ou par une interaction médicamenteuse avec les stéroïdes. Il y a donc deux types d'interactions soit: stéroïdes entre eux ou avec d'autres composés chimiques.

Conclusions

En conclusion, cette revue de la littérature démontre l'immensité des effets néfastes pouvant être causés par l'utilisation de stéroïdes anabolisants, soit au niveau des systèmes cardiovasculaire, hépatique, rénale, endocrinien ou autre. Par contre, pour mieux cerner l'ampleur et la fréquence des risques associés à la prise inappropriées à long terme ou à court terme de stéroïdes anabolisants, il est nécessaire de faire plus d'études dans ce domaine, et ce avec des groupes contrôles appropriés.

Références

Ahlgrim, C., & Guglin, M. (2009). Anabolics and Cardiomyopathy in a Bodybuilder: Case Report and Literature Review. *Journal of Cardiac Failure, 15*(6), 496-500. doi: 10.1016/j.cardfail.2008.12.014

Aitkena, C., Delalandeb, C., & Stanton, K. (2002). Pumping iron, risking infection? Exposure to hepatitis C, hepatitis B and HIV among anabolic–androgenic steroid injectors in Victoria, Australia. *Drug and Alcohol Dependence, 65*(3), 303-308. Retrieved from http://dx.doi.org/10.1016/S0376-8716(01)00174-0

Alaraj, A. M, Chamoun, R. B., Dahdaleh, N. S., Haddad, G. F., & Comair, Y. G. (2004). Case Report. Spontaneous subdural haematoma in anabolic steroids dependent weight lifters: reports of two cases and review of literature. *Acta Neurochir, 147*, 85–88. doi: 10.1007/s00701-004-0415-0

Al-Ismail, K., Torreggiani, W. C., Munk, P. L., & Nicolaou, S. (2002). Gluteal mass in a bodybuilder: radiological depiction of a complication of anabolic steroid use. *European Radiology, 12*(6), 1366-1369. doi: 10.1007/s00330-001-1169-1

Bagia, S., Hewitt, P. M., & Morris, D. L. (2000). Anabolic steroid-induced hepatic adenomas with spontaneous haemorrhage in a bodybuilder. *Australian & New Zealand Journal of Surgery, 70*(9), 686–687. doi: 10.1046/j.1440-1622.2000.01932.x

Bahia, H., Platt, A., Hart, N. B., & Baguley, P. (2000). Case Report. Anabolic steroid accelerated multicompartment syndrome following trauma. *British Journal of Sports Medicine, 34*(4), 308-309. doi: 10.1136/bjsm.34.4.308

Battista, V., Combs, J., & Warme, W. J. (2003). Asynchronous Bilateral Achilles Tendon Ruptures and Androstenediol Use. *The American Journal of Sports Medicine, 31*(6), 1007-1009.

Bhasin, S., Storer, T.W., Berman, N., Callegari, C., Clevenger, B. A., Phillips, J., ...Casaburi, R. (1996). The effects of supraphysiologic doses of testosterone on muscle size and strength in normal men. *New England Journal of Medicine, 335*, 1-7. doi: 10.1056/NEJM199607043350101

Bispo, M., Valente, A., Maldonado, R., Palma, R., Glória, H., Nóbrega, J., & Alexandrino, P. (2009). Anabolic steroid-induced cardiomyopathy underlying acute liver failure in a young bodybuilder. *World Journal of Gastroenterology, 15*(23), 2920-2922. doi: 10.3748/wjg.15.2920

Bolding, G., Sherr, L., & Elford, J. (2002). Use of anabolic steroids and associated health risks among gay men attending London gyms. *Addiction, 97*(2), 195-203. doi: 10.1046/j.1360-0443.2002.00031.x

Bonetti, A., Tirelli, F., Catapano, A., Dazzi, D., Dei Cas, A., Solito, F., ... Magnati, G. (2008). Side Effects of Anabolic Androgenic Steroids Abuse. *International Journal of Sports Medicine, 29*(8), 679-687. doi: 10.1055/s-2007-965808

Boyadjiev, N. P., Georgieva, K. N., Massaldjieva, R. I., & Gueorguiev, S. I. (2000). Reversible hypogonadism and azoospermia as a result of anabolic-androgenic steroid use in a body builder with personality disorder: A case report. *Journal of Sports Medicine and Physical Fitness, 40*(3), 271-275.

Braseth, N. R., Allison, E. J. Jr., & Gough, J. E. (2001). Exertional rhabdomyolysis in a body builder abusing anabolic androgenic steroids. *European Journal of Emergency Medicine, 8*(2), 155-157.

Buckley, W. E., Yesalis III, C. E., Friedl, K. E., Anderson, W. A., Streit, A. L., & Wright, J. E. (1988). Estimated prevalence of anabolic steroid use among male high school seniors. *JAMA, 260*, 3441-3445. doi: 10.1001/jama.1988.03410230059028

Clark, B. M., & Schofield, R. S. (2005). Dilated Cardiomyopathy and Acute Liver Injury Associated with Combined Use of Ephedra, g-Hydroxybutyrate, and Anabolic Steroids. *Pharmacotherapy, 25*(5), 756-761. doi: 10.1592/phco.25.5.756.63592

Climstein, M., O'Shea, P., Adams, K. J., & DeBeliso, M. (2003}. The effects of anabolic-androgenic steroids upon resting and peak exercise left ventricular heart wall motion

kinetics in male strength and power athletes. *Journal of Science and Medicine in Sport, 6*(4): 387-397.

Daher, E. F., Silva Júnior, G. B., Queiroz, A. L., Ramos, L. M. A., Santos, S. Q., Barreto, D. M. S.,...Patrocínio, R. M. S. V. (2009). Acute kidney injury due to anabolic steroid and vitamin supplement abuse: report of two cases and a literature review. *International Urology and Nephrology, 41*(3), 717-723. doi: 10.1007/s11255-009-9571-8

Daly, R. C., Su, T. P., Schmidt, P. J., Pagliaro, M., Pickar, D., & Rubinow, D. R. (2003). Neuroendocrine and behavioral effects of high-dose anabolic steroid administration in male normal volunteers. *Psychoneuroendocrinology, 28* (3), 317-331. doi: 10.1016/S0306-4530(02)00025-2

D'Andrea, A., Caso, P., Salerno, G., Scarafile, R., De Corato, G., Mita, C.,...Calabrò, R. (2007). Left ventricular early myocardial dysfunction after chronic misuse of anabolic androgenic steroids: a Doppler myocardial and strain imaging analysis. *British Journal of Sports Medicine, 41*(3), 149 -155. doi: bjsm.2006.030171v1

Dickerman, R. D., & Jaikumar, S. (2001). The Hiccup Reflex Arc and Persistent Hiccups with High-dose Anabolic Steroids: Is the Brainstem the Steroid-Responsive Locus? *Clinical Neuropharmacology, 24*(1), 62-64. doi: 10.1097/00002826-200101000-00011

Di Paoloa, M., Agozzinob, M., Tonia, C., Luciania, A. B., Molendinic, L., Scaglionec, M.,...Arbustini, E. (2007). Sudden anabolic steroid abuse-related death in athletes. *International Journal of Cardiology, 114*(1), 114-117. Retrieved from http://dx.doi.org/10.1016/j.ijcard.2005.11.033

Ebenbichler, C. F., Kaser, S., Bodner, J., Gander, R., Lechleitner, M. Herold, M., & J. Patsch, R. (2001). Hyperhomocysteinemia in bodybuilders taking anabolic steroids. *European Journal of Internal Medicine, 12*(1), 43-47. Retrieved from http://dx.doi.org/10.1016/S0953-6205(00) 00131-X

Ebenbichler, C. F., Sturma, W., Gänzera, H., Bodnerb, J., Mangwethb, B., Ritscha, A.,...Patscha, J. R. (2001). Flow-mediated, endothelium-dependent vasodilatation is impaired in male body builders taking anabolic-androgenic steroids. *Atherosclerosis, 158*(2), 483-490. Retrieved from http://dx.doi.org/10.1016/S0021-9150(01)00465-8

Farkash, U., Shabshin, N., & Pritsch, M. (2009). Rhabdomyolysis of the Deltoid Muscle in a Bodybuilder Using Anabolic-Androgenic Steroids: A Case Report. *Journal of Athletic Training, 44*(1), 98–100. Retrieved from 10.4085/1062-6050-44.1.98

Graham, M. R., Grace, F. M., Boobier, W., Hullin, D., Kicman, A., Cowan, D.,...Baker, J. S. (2006). Homocysteine induced cardiovascular events: a consequence of long term anabolic-androgenic steroid (AAS) abuse. *British Journal of Sports Medicine, 40*(7), 644-648. doi: 10.1136/ bjsm.2005.025668

Hartung, R., Gerth, J., Fünfstück, R., Gröne, H. J., & Stein, G. (2001). End-stage renal disease in a bodybuilder: a multifactorial process or simply doping? *Nephrol Dial Transplant, 16*(1), 163-165. doi: 10.1093/ndt/16.1.163

Kanayama, G., Hudson, J. I., Harrison, G., & Pope, Jr. (2008). Long-term psychiatric and medical consequences of anabolic-androgenic steroid abuse: A looming public health concern? *Drug and Alcohol Dependence, 98*(1-2), 1-12. doi: 10.1016/j.drugalcdep.2008.05.004

Karila, T. A. M., Karjalainen, J. E., Mäntysaari, M. J., Viitasalo, M. T. & Seppälä, T. A. (2003). Anabolic Androgenic Steroids Produce Dose-Dependent Increase in Left Ventricular Mass in Power Athletes, and this Effect is Potentiated by Concomitant Use of Growth Hormone. *International Journal of Sports Medicine, 24*(5), 337-343. doi: 10.1055/s-2003-40702

Karila, T., Hovatta, O., & Seppälä, T. (2004). Concomitant Abuse of Anabolic Androgenic Steroids and Human Chorionic Gonadotrophin Impairs Spermatogenesis in Power Athletes. *International Journal of Sports Medicine, 25*(4), 257-263. doi: 10.1055/s-2004-819936

Kasikcioglu, E., Oflaz, H., Umman, B., & Bugra, Z. (2008). Androgenic anabolic steroids also impair right ventricular function. *International journal of cardiology, 134*(1), 123-125. doi: 10.1016/j.ijcard.2007.12.027

Kutscher, E. C., Lund, B. C., & Perry, P.J. (2002). Anabolic steroids: A Review for the Clinician. *Sports Med, 32*(5), 285-296.

Mottram, D. R., & George, A. J. (2000). Anabolic steroids. *Baillière's Clinical Endocrinology and Metabolism, 14*(1), 55-69. Retrieved from http://dx.doi.org/10.1053/ beem.2000.0053

Pärssinen, M., Kujala, U., Vartiainen, E., Sarna, S., & Seppälä, T. (2000). Increased Premature Mortality of Competitive Powerlifters Suspected to Have Used Anabolic

Agents. *International Journal of Sports Medecine, 21*(3), 225-227. doi: 10.1055/s-2000-304

Petrocelli, M., Oberweis, T., & Petrocelli, J. (2008). Getting Huge, Getting Ripped: A Qualitative Exploration of Recreational Steroid Use. *Journal of Drug Issues, 38*(4), 1187-1205. doi: 10.1177/002204260803800412

Urhausen, A., Albers, T., & Kindermann, W. (2004). Are the cardiac effects of anabolic steroid abuse in strength athletes reversible? *Heart, 90*(5), 496–501. doi: 10.1136/hrt.2003.015719

Wysoczanski, M., Rachko, M., & Bergmann, S.R. (2008). Acute Myocardial Infarction in a Young Man Using Anabolic Steroids. *Angiology, 59*(3), 376-378. doi: 10.1177/0003319707304883

Safe Injection Sites and Needle Exchange Programs: An Important Part of Ensuring Health to Injection Drug Users

Stephanie AUBIN* [1]

[1] Student, University of Ottawa, Canada

* *Auteur(e) correspondant | Corresponding author*: N/A

Abstract: None provided

Keywords: N/A

Introduction

When one thinks of current epidemics, surely HIV/AIDS is one of the first to come to mind. Although one perhaps thinks of it as mostly an epidemic associated with developing countries and in particular Africa, it is a problem here in Canada as well. In the 1990's Vancouver had the highest infection rate of all developed nations (BC Partners for Mental Health). This infection rate was largely driven by addicts (Ball, 2007), as HIV/AIDS can be transmitted through sharing of injecting equipment (Tyndall et al., 2006). In fact, the spread of HIV/AIDS by injection drug use is reportedly responsible for a third of new infections outside of sub-Saharan Africa (Ball, 2007). To try and slow the spread of infection through sharing of injecting equipment, needle exchange programs (NEPs) were developed (BC partners for Mental Health). The idea behind these programs is to provide injection drug users with safe equipment for injecting, but they serve also to reduce drug associated litter in the community as one is required to exchange a used needle to obtain a clean one (BC Partners for Mental Health). Following the example of European countries, Canada's first needle exchange programs were opened in the 1980's – in Toronto unofficially in 1987 and in Vancouver officially in 1989 (BC Partners for Mental Health). More controversial are safe injection sites (SISs). On top of supplying safe injection equipment, these sites provide the user with a safe place to inject as well as access to medical care on the premises (Canadian Centre on Substance Abuse, 2009, Bayoumi & Zaric, 2008). SISs and NEPs both fall under the term harm reduction: programs with the goal of reducing harm associated with drug use (and other unhealthy behaviours) by means other than reducing the behaviour itself (Weatherburn, 2009). Harm reduction strategies are important when the costs of the behaviour are great, and eradicating the behaviour poses many challenges (Weatherburn, 2009)

In 2002 Larry Campbell ran for mayor of Vancouver and his platform called for the immediate opening of a safe injection site to help combat Vancouver's AIDS epidemic (Kerr, Oleson, & Wood, 2004). When he won, and no SIS was opened, local activists opened a user-run SIS (Kerr, Oleson & Wood, 2004). This site was opened for 181 days before being shut down and was the first SIS in operation in Canada (Kerr, Oleson & Wood, 2004). In 2003 the pilot safe injection site called "Insite" began in Vancouver (Garmaise, 2005). Since its opening there has been ongoing research to establish its costs and benefits, and whether it should stay open on legal and ethical grounds.

This paper argues that harm reduction strategies such as needle exchange programs and safe injection sites are an important part of ensuring that injection drug users are afforded health equity. Despite the inappropriateness of drug use, the harms associated, such as contracting HIV, are disproportionate to the fact that drug use is illegal (Kleinig, 2006). There are criticisms to this point of view. First, some believe that the primary aim of any program funded by the government should be treatment, as opposed to reducing harm (Collier, 2008). Second, there are concerns that needle exchange programs promote drug use, as opposed to recovery from addiction. Third, there are concerns that needle exchange programs and safe injections sites will increase drug use and therefore increase associated crime.

In fact, safe injection sites do promote treatment and recovery and are not associated with an increase in drug use or crime. Therefore, despite the controversy surrounding safe injection sites, needle exchange programs and harm reduction strategies in general, drug users have a right to the health equity that can be obtained through these programs.

Counterargument

There are many counterclaims to the argument that Safe Injection Sites are beneficial to the addict and the community. In an address to the Canadian Medical Association's 141st annual general council, Health minister Tony Clement summed up many of the criticisms. One point stated was that the money used to run this safe injection site, an estimated $3 million a year, should be used on programs with the primary aim of treatment (Collier, 2008). Clement implied safe injection sites were a so-called band-aid as opposed to a cure, using smoking as an example and saying, "doctors tell patients to quit, not smoke less" (Collier, 2008). The Journal of Global Drug Policy and Practice takes a similar stand, highlighting that the risk of infection rises with each subsequent injection; hence abstinence is preferable (Voth, 2008). In a paper on needle exchange programs and ethics, Kleinig (2006) states that some see needle exchange programs as a "counsel of despair". One other person who has aligned himself with those staunchly against harm reduction is former president of the United States George W. Bush, who was quoted as saying:

> I do not favour needle exchange programs and other so-called "harm reduction" strate-

> gies to combat drug use. I support a comprehensive mix of prevention, education, treatment, law enforcement, and supply [prohibition] to curb drug use and promote a healthy, drug-free America, not misguided efforts to weaken drug laws. [...] America needs a President who will aim not just for risk reduction, but for risk elimination that offers people hope and not a dead-end approach that offers despair and addiction (Kleinig, 2006, p. 818).

As Ball (2007) brings to our attention, a type of dichotomy has been set up: treatment versus harm reduction. Critics seem to believe it is all or nothing and that a focus on both cannot exist simultaneously.

A second point of concern for Clement was the extent to which recovery was promoted at the safe injection site, let alone that treatment was not the primary goal (Collier, 2008). More and more needles are being handed out by the needle exchange program in Vancouver; in fact there has been a tenfold increase in the last decade (BC Partners for Mental Health). Could this indicate that there is in fact no recovery by the injection drug users using the needle exchange program? It has even been hypothesized that safe injection sites may have a negative effect on recovery. The theory goes that with medical supervision a user may be more likely to inject higher doses of the drug, seeing as the medical personnel create a sense of security, a sense that if ill consequences do follow, the user need not worry as they will be attended to (Canadian Centre on Substance Abuse, 2009).

Lastly, of concern is the link between safe injection sites and crime. Clement put forth the question: is it ethical for doctors to be involved in the administration of illegal substances (Collier, 2008)? Critics have also noted that injection drug users often commit crimes to obtain drugs, and therefore the link is made that safe injection sites promote crime (Canadian Centre on Substance Abuse, 2009). This has been a particular concern to conservative religious groups (Wynia, 2005). They worry that, "harm-reduction efforts provide tacit social approval of risky, and 'immoral,' behaviours" (Wynia, 2005). Kleinig (2006) also notes that the effectiveness of a needle exchange program does not eliminate the need to meet ethical requirements. In a discussion forum on supervised injection sites it was noted that because of Insite's association with illegal substances and illegal practices, the site is being evaluated much more harshly than other public health initiatives (Canadian Centre on Substance Abuse, 2009).

Position argument

Although research is ongoing, so far studies have pointed to needle exchange programs and safe injection sites as having a positive influence on injection drug users individually and on the community collectively. Treatment would be ideal, as would full recovery of all substance abusers; however currently, with respect to certain drugs in certain countries, harm reduction is a much more realistic proposition (Ball, 2007). Meanwhile, unrecovered substance abusers are deserving of a life without AIDS or Hepatitis C. As Dr. Bonnie Cham, chair of the CMA's Committee on Ethics points out, "IV drug users have the right to compassion and access to care that has proven to be beneficial," (Collier, 2008). Kleinig (2006) notes:

> Even a minimally humane society does not leave by the roadside those whose reckless driving has resulted in an accident, and we cannot ignore the medical conditions of those whose drug use has resulted in their contraction of serious disease (p. 821).

In fact the Canadian Charter of Rights and Freedoms, and the Canadian Human Rights Act protect the rights of drug users as a group, giving them legal entitlement to "reasonable personal safety" (BC Partners for Mental Health). It would appear that harm reduction strategies have played a role in ensuring such safety. A study conducted in the U.S. highlighted that drug users with access to a needle exchange program are up to six times less likely to become infected with HIV/AIDS as compared with drug users who had no access (BC Partners for Mental Health). In a U.S. study conducted from 1994 to 2004, it was found that those using NEPs were less likely to share needles and therefore NEPs had an indirect effect on the reduction of Hepatitis C among injection drug users (Holtzman et al., 2009). In France, after the introduction of a needle exchange program in 1994, HIV prevalence decreased from 40% to 11% (Carrieri, 2008). This is not to say that treatment and recovery should be ignored. Needle exchange programs and safe injection sites are a useful way to come into contact with the drug using population and expose them to treatment options (Wynia, 2005). In fact, during twelve months of supervision of Vancouver's safe injection site, 2171 referrals were made, and 37% of these were for

addictions counselling (Tyndall et al., 2004). Despite this achievement, it must not be ignored that treatment and recovery are secondary aims of the safe injection site pilot project in Vancouver; the primary aim is reducing transmission of HIV/AIDS (Canadian Centre on Substance Abuse, 2009). In this respect the site would again seem to be successful: in the last five years incidence has decreased from 310 new cases to 163. And although there has been a tenfold increase in needles handed out, there has been a 110% return rate, indicating a decrease in needles disposed of inappropriately in the community (BC Partners for Mental Health). As for safe injection sites causing IV drug users to inject higher doses, to date there is no evidence to support this claim (Canadian Centre on Substance Abuse, 2009). To reinforce the utility of needle exchange programs and safe injection sites it must be noted that Clement and Voth are correct: harm reduction is not a cure and drug injection is dangerous; however SISs and NEPs help injection drug users on the road to recovery (although not its primary aim) and meanwhile reduce the danger of contracting AIDS and Hepatitis C through injection.

Another point the health minister brings up is the cost of Insite. Would this money be better spent elsewhere? The above paragraph argues that Insite is money well spent, however it should be noted that a case study of an unsanctioned user-run safe injection site suggests that the program could be run quite economically (Kerr, Oleson, & Wood, 2004). In 2003, a group of volunteers opened a safe injection site in Vancouver in response to a police crackdown on drugs as well as in response to the mayor's failure to fulfill his campaign promise to open a sanctioned safe injection site. Over 181 days the site was able to support 9000 visits and 3000 injections despite having limited financial support and being run by volunteers and users of the facility (Kerr, Oleson, & Wood, 2004). Another study estimated that if one looks only at the impact on health of using non-contaminated injection equipment, the health care system saves $14 million and 920 years of life lost over a ten year period (Bayoumi & Zaric, 2008). Another study found that by conservative estimates Insite prevents thirty-five new cases of HIV and three deaths each year (Andresen & Boyd, 2009). This is further proof that government funds used on safe injection sites are well spent.

Another concern voiced by critics is that needle exchange programs and safe injection sites appear to condone the use of illegal substances and therefore the use of illegal substances may increase, and we would subsequently see a rise in crime rates. To date, there is no evidence that safe injection sites increase drug use (Health Canada releases report, 2008). As for the implication that safe injection sites condone crime, NEPs convey no positive regard for non-dependent drug dealers (Kleinig, 2006).

Secondly it has been found that the opening of Insite had no visible effect on drug trafficking and assaults and robbery, whereas the breaking and entering of vehicles and vehicle theft diminished in the neighbourhood in which Insite operates (Wood, Tyndall, Lai, Montaner & Kerr, 2006). Similar results were also found upon evaluation of a safe injection site in Australia: there was no increase in theft, robbery, or drug-related loitering after the opening of the site (Freeman, Jones, Weatherburn, Rutter, Spooner, & Donnelly, 2005). In another study evaluating a SIS in Australia the public was surveyed. It was found that 90% of the public surveyed listed at least one benefit of the SIS, indicating their awareness of the necessity of the site. Also there was a significant reduction reported in the amount of public injections witnessed (Salmon, Thein, Kimber, Kaldor, & Maher, 2007).

The health minister was also concerned with the ethical implications of physicians and other medical personnel being involved with the administration of banned substances. A study printed in the Annals of Internal Medicine and conducted by Temple University School of Law found there were no ethical concerns with physicians prescribing safe injecting equipment (Burris, Lurie, Abrahamson, & Rich, 2000). There is a standard of care for patients who inject drugs, and it is in fact unethical not to meet this standard. Their study also notes:

> Prescribing sterile injection equipment is certainly appropriate from a clinical perspective. Many injection drug users cannot or will not abstain; others may be willing to try but cannot gain access to drug treatment services. Health care providers are well acquainted with the notion of setting intermediate goals in caring for patients. For example, a physician might suggest that a two-pack-a-day smoker reduce his or her daily tobacco consumption to a single pack because predictable benefits result from even a reduction in smoking (Burris, Lurie, Abrahamson & Rich, 2000, p. 219).

Furthermore, an analysis of the relevant laws in 50 states in the U.S. and in Puerto Rico found that physicians prac-

ticing in these states were well within the law to prescribe sterile injection equipment with the aim to reduce disease transmission (Burris, Lurie, Abrahamson, & Rich, 2000).

In response to the concerns of religious groups, Kleinig (2006) notes the dangers of public policy being directed by religious beliefs. He suggests that their idealistic principles for the drug user population should be proven as possible of effecting some change before being adopted. Another point Kleinig brings up is the belief that reducing NEPs and SISs will reduce drug use. As Kleinig put it, it is "a serious misunderstanding of the dynamics of drug use as well as the drug-injecting population." In essence there is little evidence that NEPs increase drug use or crime rates in the surrounding area in which they are established and in some cases may appear to diminish certain types of crime. Also, medical practitioners are not behaving unethically when working with safe injection sites. As for the place of religious beliefs in this debate, they do have a place, but the safety of the drug users must be put first.

Conclusion

Injection drug users are a part the Canadian population and therefore deserve health equity. This was taken into consideration when Justice Ian Pitfield of the BC Supreme Court ruled that the federal government could not close Insite (Vancouver Coastal Health, 2009). His decision was based on the fact that Insite is a public health initiative to which users have a constitutional right. There have been over 30 peer reviewed studies evaluating Insite in particular, and many more evaluating safe injection sites in general. According to Kerr, one of these researchers, the academic debate concerning the medical utility of Insite is over (O'Connor, 2009). Although the health minister has expressed many concerns, these concerns have been more political and moral in nature as opposed to viewing the matter from a strictly academic standpoint. The health minister wonders if government funds should be spent on harm reduction as opposed to strict treatment and detoxification programs, whether SISs promote recovery, and whether it is ethical for the government to fund a program associated with illegal substances and practices (Collier, 2008). In fact these questions have been answered in the literature. Treatment and recovery are promoted at safe injection sites, and if we look at the impact that these sites have on the user, we know the sites are an appropriate use of government funds. Further, safe injection sites and needle exchange programs are not associated with any increase in illegal activity, whether it is drug use or criminal acts to obtain such drugs. But the bottom line is this: the availability of safe injection equipment through safe injection sites and needle exchange programs reduces the rate of contraction of HIV and Hepatitis C among injection drug users. Public health initiatives such as Insite are important if all socio-economic segments of the population are to be afforded health equity.

References

Andresen, M. A., & Boyd, N. (2009). A cost-benefit and cost-effectiveness analysis of Vancouver's supervised injection facility. *Int J Drug Policy, 21(*1), 70-76.doi: 10.1016/j.drugpo.2009.03.004

Ball, A. L. (2007). HIV, injecting drug use and harm reduction: a public health response. *Addiction, 102*(5), 684-90

Bayoumi, A. M., & Zaric, G. S. (2008). The cost-effectiveness of Vancouver's supervised injection facility. *CMAJ, 179*(11), 1143-51. doi: 10.1503/cmaj.08080

Burris, S., Lurie, P., Abrahamson, D., & Rich, J. D. (2000). Canadian Medical Association's 141st annual general council - Physician Prescribing of Sterile Injection Equipment To Prevent HIV Infection: Time for Action. *Annals of Internal Medicine, 133*(3), 218-226. doi: 10.7326/0003-4819-133-3-200008010-00015

Carrieri, M. P., & Spire B. (2008). Harm reduction and control of HIV in IDUs in France. *Lancet, 372*(9637), 448. doi: 10.1016/S0140-6736(08)61195-2

Collier, R. (2008). Clement unleashes barrage at safe injection site supporters. *CMAJ*, [Epub ahead of print], PMID: 18713814, retrieved from PubMed doi: 10.1503/cmaj.081305

Discussion Forum: Supervised Injection Site Evaluative Research. (2009). Canadian Centre on Substance Abuse. Retrieved from http://www.ccsa.ca/2009%20CCSA%20Documents/ccsa0117852009_e.pdf

Freeman, K., Jones, C. G., Weatherburn, D. J., Rutter, S., Spooner, C. J., & Donnelly, N. (2005). The impact of the Sydney Medically Supervised Injecting Centre (MSIC) on crime. *Drug Alcohol Review, 24*(2), 173-84. doi: 10.1080/09595230500167460

Garmaise, D. (2005). Officials in two Canadian cities express support for safe injection sites. *HIV/AIDS policy & law review /Canadian HIV/AIDS Legal Network, 10*(2), 21-2.

Health Canada releases report on supervised injection facility. (2008). *HIV AIDS Policy Law Rev, 13*(1), 31-32.

Holtzman, D., Barry, V., Ouellet, L. J., Des Jarlais, D. C., Vlahov, D., Golub, E. T., ... Garfein, R. S. (2009). The influence of needle exchange programs on injection risk behaviors and infection with hepatitis C virus among young injection drug users in select cities in the United States, 1994 -2004. *Prev Med., 49*(1), 68-73. doi: 10.1016/j.ypmed.2009.04.014

Kerr, T., Oleson, M., & Wood, E. (2004). Harm-reduction activism: a case study of an unsanctioned user-run safe injection site. *Can HIV AIDS Policy Law Rev., 8*(3), 142-143.

Kleinig, J. (2006). Thinking ethically about needle and syringe programs. *Subst Use Misuse., 41*(6-7), 815-25. doi: 10.1080/10826080600668670

Legal Status of Insite. Vancouver Coastal Health. (2009).

O'Connor, E. (July 7, 2009). Insite drug-injection facility awaits fate amid controversy. The Province. Retrieved from http://www.theprovince.com/health/Insite+drug+injection+facility+awaits+fate+amid+controversy/1767204/story.html

Salmon, A. M., Thein, H. H., Kimber, J., Kaldor, J. M., & Maher, L. (2007). Five years on: what are the community perceptions of drug-related public amenity following the establishment of the Sydney Medically Supervised Injecting Centre? *National Int J Drug Policy, 18*(1), 46-53. Retrieved from http://dx.doi.org/10.1016/j.drugpo.2006.11.010

State of the Knowledge: Needle Exchange Programs. BC Partners for Mental Health and Addictions Information. Retrieved from www.upnbc.org/needleexchange.pdf

Tyndall, M. W., Kerr, T., Zhang, R., King, E., Montaner, J. G., & Wood, E. (2006). Attendance, drug use patterns, and referrals made from North America's first supervised injection facility. *Drug Alcohol Depend., 83*(3),193-8. Retrieved from http://dx.doi.org/10.1016/j.drugalcdep.2005.11.011

Tyndall, M. W., Currie, S., Spittal, P., Li, K., Wood, E., O'Shaughnessy, M. V., & Schechter, M. T. (2003) Intensive injection cocaine use as the primary risk factor in the Vancouver HIV-1 epidemic. *AIDS, 17*(6), 887-93. doi: 10.1097/01.aids.0000050859.71999.ae

Voth, E. A. (2008). Harm reduction drug policy. *Lancet Infect Dis., 8*(3), 142-3. Retrieved from http://dx.doi.org/10.1016/S1473-3099(08)70189-0

Wood, E., Tyndall, M. W., Lai, C., Montaner, J. S, & Kerr, T. (2006). Impact of a medically supervised safer injecting facility on drug dealing and other drug-related crime. *Subst Abuse Treat Prev Policy, 8*(1), 13. doi: 10.1186/1747-597X-1-13

Wynia, M. K. (2005). Science, Faith and AIDS: The Battle Over Harm Reduction. The *American Journal of Bioethics, 5*(2), 3-4. doi: 10.1080/15265160590961699

Weatherburn, D. (2009). Dilemmas in Harm Minimization. *Addiction, 104*(3), 335-339. doi: 10.1111/j.1360-0443.2008.02336.x

A Review of the Effects of Psychological Interventions on the Quality of Life for Children with Atopic Dermatitis

Maria A. CZERNIAKOW* [1]

[1] Student, University of Ottawa, Canada

* *Auteur(e) correspondant* | *Corresponding author*: N/A

Abstract:

Atopic Dermatitis (AD) is a psychologically debilitating disease due to its embarrassing skin lesions and pruritic nature which disturb the quality of life (QOL) of the patients. Even though children are primarily affected, caregivers can also be affected due to being the first line of care for others who are inflicted. This review focuses on randomized control trials which investigated the use of non-chemical forms of treatment to improve QOL and disease severity in children. A search of the PubMed database identified six studies that met the inclusion criteria. The studies were ranked from most rigorous trial to least. Various forms of education as an intervention were used. Conversely, the viewing of a humorous film was tested to examine if it had an impact on QOL. Education intervention versus no education at all showed that the intervention group had a larger decrease in disease severity than the control group. The form of education as a single consult with an AD educated nurse showed no difference between the control and the intervention group. Comparison of nurse-led clinics with the dermatologist-led clinics indicated that the nurse-led clinics were more successful. Viewing humorous films before bedtime was demonstrated as a successful means of reducing night-time awakenings. Also specific AD education versus routine education and consultations showed improvement in both groups. Finally, AD video-education versus direct parental teaching concluded that the video-education was more effective. Although the studies show that any form of education intervention is better than none, the methodological assessment of the studies showed that four of the studies were not rigorous enough or were not described at all. Further studies must be conducted in a more methodologically sound manner for the results to be considered replicable and valid.

Keywords: N/A

Introduction

Atopic Dermatitis (AD) is a chronic, relapsing, and intensely pruritic skin disorder that frequently affects infants, children and young adults, but has been known to affect people of all ages. Also called eczema, it is a highly unpredictable disease composed of skin lesions of varying severity which typically precedes the development of asthma or other allergic rhinitis (Boguniewicz & Beltrani, 2002, p.165). The most common treatment takes the form of a topical corticosteroid ointment or cream, tar preparations, oral corticosteroids, anti-infection medications, and antixiolytics for severe nocturnal pruritis (Boguniewicz & Beltrani, 2002, p. 166). It is reported that the prevalence in adults of the presence of eczema for at least one year is at 1 to 3% and that 90% of cases begin before age five, of which most terminate at some point during childhood (Jones, Buchanan, & Burks, 2007, p. 218). Over the past three decades the disease has more than doubled ; a notable trend with ever more prevalent asthma, and increasingly severe allergies.

Boguniewicz *et al.* states that there is 10 to 20% prevalence of atopic dermatitis in children in industrialized nations. Even though the majority of the research on this topic has been carried out in the United Kingdom (Ben-Gashir, Seed, Hay, 2004, p. 285), where the incidence has been shown to be very high, it remains a disorder that also inflicts a large number of Canadians. In Hamilton and Saskatoon respondents representing children aged six to seven years and thirteen to fourteen years reported the prevalence of AD at 21.3% and 15.6%, respectively (Williams et al., 1999, p. 127). While AD is a rather common disease appearing in many forms with many available treatments, yet the disease has no cure.

Despite the numerous years of research; AD has no unique skin lesions, or laboratory tests available to make a definite diagnosis. The disease is generally characterized by the features presented in Table I. Patients with AD have also shown an increased susceptibility to bacterial infections, thus further complicating their condition. Note that none of the above-mentioned descriptors can accurately describe what it feels to be a patient with AD. The psychological consequences of living with a skin disease are often undervalued. Moderate-to-severe AD can have a profound effect on the quality of life for both sufferers and their families. In addition to the effects of intractable itching, skin damage, soreness, sleep loss and the social stigma of a visible skin disease, other factors such as frequent visits to doctors, special clothing and the constant application of messy topical ointments all add to the burden of disease (Hoare et al., 2000, p. 5).

All this demonstrates that AD has a significant impact on children. The severe symptoms of AD put children into a state of psychological dysfunction where they experience feelings of loss of control, guilt and stigmatization or bullying, distorted body-image and self-esteem (Ben-Gashir, Seed, Hay, 2004, p. 284). This review addresses the question: how well do non-topical or non-oral treatments improve quality of life, and reduce disease severity in children with atopic dermatitis? The categories of non-oral or non-topical treatments included care-giver and patient education through various forms of media, and watching humorous films before bedtime.

Methods and Materials

A search of the literature was conducted to locate research related to atopic dermatitis and eczema. Beginning with search terms such as *atopic dermatitis*, the search further specified into search terms such as: *infants, children, and adolescents with atopic dermatitis*. The population of interest was between ages 0 and 18 years and had to have a diagnosis of atopic dermatitis. The focus of this search was the limited to how quality of life is improved in children with AD through non-medicinal practices. Search strategy used was: *how does treatment improve quality of life for children with atopic dermatitis, SCORAD index, atopic eczema, child, nurse intervention, primary care, quality of life, randomized control trial, eczema severity, nurse-led clinics, and education intervention*. Most studies were found by using references from various articles which defined how quality of life was affected. Many types of study designs and methods were considered including randomized control trials, nonrandomized study designs, systematic reviews and meta-analyses.

The following databases were searched: Pub Med (MEDLINE), Scopus, Nursing and Allied Health Source, Psych Info, University of Ottawa Library Catalogue, and Google Scholar where links to articles were found which were then accessed through E-journals at the University of Ottawa website.

Studies that used non-conventional topical treatments such as aroma-therapy massage were excluded because they were involved in the relief of stress by chemical means

not through psychological or educational interventions. The study by Staab *et al.* (2002) was also excluded given that a more recent comprehensive study was explored instead.

Criteria for Inclusion

The study had to be published in an internationally peer-reviewed journal and had to be described as randomized control trials. It had to be published within the last 10 years, 1999-2009, and had to be available in English, or a detailed review of it had to be available in English. Studies had to demonstrate how a non-topical and non-oral form of treatment, such as education through various forms of media improved quality of life in children with AD. They had to demonstrate how the treatment had an effect on the quality of life and/or disease severity in children aged from 0-18 years diagnosed with atopic dermatitis. Also the minimum number of participants in both the experimental group and the control group had to be 40. The studies were arranged from most number of participants, and therefore most robust and valid, to least number of participants. All studies were based on a care-giver and patient education approach. Although one study did not use a QOL index as listed, it did report improvement in reducing sleep disturbances which would have resulted in an increased QOL. Only randomized control trials could be considered the most rigorous form of assessment and were therefore included in this review.

Each study was assessed using a modified 0–5 scale (Jadad et al., 1996, p. 7) which gave a point if the answer was yes to the study containing descriptions of randomization, withdrawals, and the method of blinding, up to a maximum score of 5. One point was deducted if methods for randomization or blinding were inappropriate. Modification of this scale was essential because, due to the nature of the psychological interventions it would be difficult to conduct double-blinded trials; therefore, in steps 2 and 5 above 'double-blind' was changed to 'blind' (Jadad et al., 1996, p. 9).

Results

In total fifteen studies met the search criteria. Six of these were chosen for review because they were the articles referenced by relevant review articles and also because they met the inclusion criteria. The results of the studies that fit the inclusion criteria and how they rated on the scale may be viewed in Table II. Four of the studies observed education as an intervention, one of the studies investigated consultations with a primary care nurse, and the last study explored how watching humorous films improved night time awakenings.

Staab *et al.,* (2006) was the most rigorous study investigated; fulfilling all the criteria on the scale, especially adequate blinding and randomization. It aimed to determine the effects of age related structured educational programs on the management of moderate to severe atopic dermatitis in children and adolescent. The three participating groups were parents of children with AD aged 3 months to 7 years and 8-12 years and adolescents with AD aged 13-18 years and corresponding controls. Participants were recruited from seven centers in Germany. The inclusion criteria were: diagnosis of atopic dermatitis according to criteria as described in the study. 823 participants could be reached for evaluation: dropout rate of 17%. The study was designed as a randomized, controlled intervention study. The treatment program consisted of six, weekly group sessions. The primary end points were the differences in severity of eczema and parents' quality of life between the start of the study (baseline) and follow-up at 12 months. In this study the subjective severity score for eczema decreased significantly in the intervention groups, demonstrating that education as an intervention was effective.

In Chinn *et al.* (2002) children with eczema were recruited from two general practices into a randomized control trial over a twelve month period from Stockton-on-Tees, UK. The inclusion criteria were: 6 months to16 years, and a diagnosis of atopic eczema. After filling out questionnaires that evaluated QOL, severity of AD, each child was randomized into the control or intervention group. The intervention involved demonstration of techniques for applying medication together with advice and education, delivered in a single session of 30 minutes by a trained dermatology nurse. A total of 119 intervention and 116 control children were recruited and followed up. There was an issue with obtaining complete data from all the children participating, and the description of withdrawals and drop-outs is rather poorly organized, as well there was no attempt at blinding. The data obtained for children who completed the whole process revealed no statistically significant improvements at 4 weeks or 12 weeks in the QOL of children with eczema as the result of the 30-min intervention.

The Moore *et al.* (2009) study was conducted in Melbourne, Australia with good blinding and randomization techniques. A total of 182 new referrals for the management of eczema were received and randomized to attend either the eczema workshop or the dermatologist-led clinic. A comprehensive diagram of participant flow is included in the study. Patients in the workshop had 90 minutes of contact time each with the nurse compared with an average of 40 minutes with the doctor in the dermatologist-led clinic. The criteria for inclusion in the study were infants, children and adolescents, aged 16 years or less, who were referrals from various professionals. The primary outcome was the severity of eczema of infants, children and adolescents, as measured using the SCORAD index 4 weeks after attending an eczema workshop or a dermatologist-led clinic for the management of eczema. A total of 99 patients participated in the study. At the 4-week review there was a significantly greater improvement in SCORAD in the patients of the eczema workshop.73% of children improved to mild eczema after attending the eczema workshop compared with only 40% of children attending the dermatologist-led clinic.

Kimata (2007) presents a significantly different study design. In this study ghrelin levels associated with night-time awakening and stress measured during the night in AD patients, who tend to suffer from night-time awakenings due to pruritis. Ghrelin is involved in growth hormone secretion, regulation of appetite, anxiety, and night-time wakening (Kimata, 2007, p. 282). Salivary levels of ghrelin also correlate with plasma levels of ghrelin; therefore measuring salivary ghrelin levels is a useful non-invasive technique (Kimata, 2007, p. 282). After obtaining consent from parents, 40 male healthy children without AD and 40 male patients with moderate AD, graded on the SCORAD index, were studied. Since nocturnal ghrelin secretion is different between males and females the study was conducted separately for female children. All of the AD patients complained of night-time wakening prior to beginning of the study. The baseline study consisted of all participants viewing no film, and sleeping at the sleep laboratory in the hospital, and saliva was collected without stimulation periodically during the night. Randomly assigned 20 healthy children and 20 AD patients first viewed a humorous film before bedtime, and after 2 weeks, they viewed control non-humorous film and vice-versa. However the randomization strategy was not sufficiently described. Viewing the control film had no effect on night-time awakening in AD patients, while viewing the humorous film decreased night-time awakening in AD patients. The salivary ghrelin levels reflect this; at 2:00 in the morning the salivary ghrelin levels were at 40 for the patients with AD when they watched the control film, and at baseline, but after they watched the humorous film, the levels dropped to 29. These results are very similar when conducted for female patients of the same age.

Grillo *et al.* (2006) aimed to measure outcomes of educational interventions including: subjective and objective measures of the severity of eczema and patient QOL. The study was designed as a randomized controlled trial to examine the impact of an educational intervention on QOL, family impact, and severity of paediatric AD. The study population comprised 61 paediatric patients diagnosed with AD and their parents. At baseline, both groups of participants were assessed by using the clinical SCORAD assessment tool, to determine the severity of their eczema. In addition all participants were given QOL and DFI questionnaires to complete. The intervention group undertook the education program through a 2-hour workshop, together with their normal management regimen. The control group received the standard care including routine education, medical consultation, and management. At week 4 and week 12 visits, both groups were assessed using the previously described tests. There was no attempt to conduct blinding even though it was possible to blind the outcome assessors. The difference in SCORAD scores at week 4 and week 12 was highly significant for both groups; nevertheless there was improvement in both groups.

The results from the Niebel *et al.* (2000) study were obtained from the Ersser *et al.* (2007) review because the original article was only accessible in German. It was a hospital-based randomized control trial with 47 participants. The intervention group attended multiple nurse-led eczema education workshops focusing on how parent and child can, as a team, self-manage the eczema. One was a video-based instruction and the other was direct parental instruction. The main outcome measures were disease severity in the child according to the SCORAD index. Still, the randomization strategy was poorly described, and there was no blinding. Base-line measurements were made before the beginning of the workshops. The study concluded that atopic eczema symptoms improved overall, but the effectiveness of the treatments differed significantly; most improvements were observed in the group provided with video assisted instruction compared to the group with direct parental teaching.

Therefore one can conclude that any form of AD education

is better than none at all. Despite two of the studies showing that there was no difference between the control and the intervention groups, other studies demonstrated that any form of educational intervention is helpful in reducing the severity of AD and improving the QOL of patients. The studies in this review showed a deficit in standard randomized control trial protocols as indicated by the Jadad *et al.* (1996) scale scores. As well there were a large number of QOL scales used indicating a need for standardization. SCORAD was effectively used in nearly all the studies.

Education as an intervention on its' own is complex as it can have a range of effects on the patient. The benefits may not be attributable solely to the educational interventions in comparison to the standard program or no educational program. In all the control groups it must be assumed that patients were highly motivated and tried to optimize their therapies. The only different study was observing how viewing humorous films affected night-time awakenings. It called for more studies to be conducted on the relationship between ghrelin and allergic diseases in order for future studies to confirm of their results. In general this method is a cost effective and efficient way of reducing restlessness of children with AD. There are significant opportunities to improve research design to evaluate psychological and educational interventions for children with AD and the reporting standards of such studies. Due to a large variety of educational interventions there is a need for more methodologically designed trials. These would employ intervention formats using validated outcomes measures, before any complete review is undertaken.

Conclusion

This review indicated both strengths and weaknesses in the effectiveness of psychological intervention for children with AD. Although there are many methodological concerns in the articles reviewed, it is evident that AD is a psychologically debilitating disease causing a decrease in the quality of life for both the care-giver and the child, especially when the child is young. The findings of the review indicated that AD educational workshops are a slowly emerging form of treatment that has yet to be further researched in order to correctly assess their effectiveness.

Education as an intervention versus no education at all showed that the intervention group had a larger decrease in disease severity than the control group (Staab, 2006, p. 236). The form of education as a single consult with an AD educated nurse showed no difference between the control and the intervention group (Chinn et al., 2002, p. 437). Nurse-led clinics versus dermatologist-led clinics were tested (Moore et al., 2009, p. 105), concluding that the nurse-led clinics were more successful. Viewing humorous films before bedtime was demonstrated as a successful means of reducing night-time awakenings (Kimata, 2007, p. 283). Also, both specific AD education and routine education and consultations showed improvement in both groups (Grillo et al., 2006, p. 434). Finally AD video-education versus direct parental teaching concluded that the video-education was more effective (Niebel et al., 2000, p. 401).

A key objective of the review was to ascertain if educational and psychological interventions can result in clinically significant changes in outcome for children with atopic dermatitis. There is insufficient evidence of the effectiveness of psychological interventions, as an addition to conventional topical therapy, to help manage children with AD. This is due to a lack of quality and quantity of data from individual studies and therefore an inability to undertake data synthesis subsequently (Ersser et al., 2007, p. 4). There is a significant drive to undertake methodologically sound trials to evaluate theoretically based psychological interventions that may enhance the management of AD in children.

Acknowledgements

I would like to sincerely thank Prof. Jeffrey Jutai, without whom this paper would not have been possible.

References

Ben-Gashir, M. A., Seed, P. T., & Hay, R. J. (2004). Quality of life and disease severity are correlated in children with atopic dermatitis. *The British Journal of Dermatology, 150* (2), 284-290. doi: 10.1111/j.1365-2133.2004.05776.x

Boguniewicz, M., & Beltrani, V. (2002). Chapter 8: Atopic dermatitis and contact dermatitis. In Adelman, D, Casale, T & Corren, J (Eds.), Manual of allergy and immunology (4th ed., pp.165-175). Philadelphia: Lippincott Williams & Wilkins.

Chida,Y., Steptoe, A., Hirakawa, N., Sudo, N., & Kubo, C. (2007). The effects of psychological intervention on atopic

dermatitis. A systematic review and meta-analysis. *International Archives of Allergy & Immunology, 144*(1), 1-9. doi: 10.1159/000101940

Chinn, D. J., Poyner, T., & Sibley, G. (2002). Randomized controlled trial of a single dermatology nurse consultation in primary care on the quality of life of children with atopic eczema. *The British Journal of Dermatology, 146*(3), 432-439. doi: 10.1046/j.1365-2133.2002.04603.x

Ersser, S. J., Latter, S., Sibley, A., Satherley, P. A., & Welbourne S. (2007). Psychological and educational interventions for atopic eczema in children. Cochrane Database of Systematic Reviews, (3), CD004054. doi: 10.1002/14651858.CD004054.pub2

Grillo, M., Gassner, L., Marshman, G., Dunn, S., & Hudson, P. (2006). Pediatric atopic eczema: The impact of an educational intervention. *Pediatric Dermatology, 23*(5), 428-436. doi: 10.1111/j.1525-1470.2006.00277.x

Hoare, C., Li Wan Po, A., & Williams, H. (2000). Systematic review of treatments for atopic eczema. *Health Technology Assessment, 4*(37), 1-191. Retrieved from http://dx.doi.org/10.3310/hta4370

Jadad, A. R., Moore, R. A., Carroll, D., Jenkinson, C., Reynolds, D. J. M., Gavaghan, D. J., & McQuay, H. J. (1996). Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Controlled Clinical Trials*, *17*(1), 1–12. doi: 10.1016/0197-2456(95)00134-4

Jones, S. M., Buchanan, A., & Burks, A. W. (2007). Chapter 13: Atopic dermatitis. In Lieberman P., & Anderson J. (Eds.), Allergic diseases: Diagnosis and treatment (3rd ed., pp. 218- 219, 246). Totowa, N.J.: Humana Press.

Kimata, H. (2007). Viewing humorous film improves night -time wakening in children with atopic dermatitis. Indian *Pediatrics, 44*(4), 281-285.

Moore, E. J., Williams, A., Manias, E., Varigos, G., & Donath, S. (2009). Eczema workshops reduce severity of childhood atopic eczema. *The Australasian Journal of Dermatology, 50*(2), 100-106. doi: 10.1111/j.1440-0960.2009.00515.x

Niebel, G., Kallweit, C., Lange, I., & Folster-Holst, R. (2000). Direct versus video-aided parent education in atopic eczema in childhood as a supplement to specialty physician treatment. A controlled pilot study. [Direkte versus videovermittelte Elternschulung bei atopischem Ekzem im Kindesalter als Ergänzung fachärztlicher Behandlung Eine kontrollierte Pilotstudie] *Der Hautarzt, 51*(6), 401-411.

Staab, D., Rueden, U., Kehrt, R., Erhart, M., Wenninger, K., Kamtsiuris, P., & Wahn, U. (2002). Evaluation of a parental training program for the management of childhood atopic dermatitis. *Pediatric Allergy and Immunology, 13* (2), 84-90. doi: 10.1034/j.1399-3038.2002.01005.x

Staab, D., Diepgen, T. L., Fartasch, M., Kupfer, J., Lob-Corzilius, T., Ring, J., ... Gieler, U. (2006). Age related, structured educational programs for the management of atopic dermatitis in children and adolescents: Multicentre, randomized controlled trial. *British Medical Journal, 332* (7547), 933-938. Retrieved from http://dx.doi.org/10.1136/bmj.332.7547.933

Appendix

Table 1 Clinical Features of AD

Major Features	*Associated Features*
• Pruritis • Chronic or relapsing course • Typical distribution: Facial and extensor involvement <2 years old; Flexural involvement >2years old • Personal and family history of atopy or allergic disorders	• Early age of onset • Course influenced by environmental and emotional factors • Itch with sweating • Intolerance to wools and other irritants • Xerosis • White dermatographism • Infraorbital darkening • Facial pallor or erythema • Hand or foot dermatitis • Hyperlinear palms • Frequent cutaneous infections, especially • *Staphylococcus aureus*

Adapted from Boguniewicz & Beltrani, 2002, p. 166

Table 2 Selected Studies

Study Details	*Population Characteristics*	*Treatments, Interventions and Outcome measures*	*Results*	*Jadad Score (0-5)*
Staab, 2006	Parents and children with atopic dermatitis aged 3 months to 18 years (n=446) and controls (n=377)	Group sessions of standardized intervention programs for AD once weekly for six weeks or no education (control group). SCORAD and subjective severity (standardized questionnaires), and QOL for parents of affected children aged less than 13 years, were assessed over 12 months.	Significant improvements in severity of eczema and subjective severity were seen in all intervention groups compared with control groups.	5

Table 2 continued: Selected Studies

Study Details	*Population Characteristics*	*Treatments, Interventions and Outcome measures*	*Results*	*Jadad Score (0-5)*
Chinn, 2002	119 intervention and 116 control children aged 0.5-16 years.	Randomized control trial to evaluate the effects of a single consultation with a primary care nurse on the QOL of children with atopic eczema and the impact of the disease on their families. The (CDLQI), the (IDQOL) and the (FDI) were completed by the parent participants to judge QOL.	The scores on these measures were skewed at baseline, 20% of children had a zero score on the FDI, indicating no impact on family life. No significant improvements were found on the CDQOL and IDQOL measures between baseline, 4 and 12 weeks respectively ($p>0.05$) . There was a suggestion of marginal improvement in FDI score at 4 weeks in the intervention group.	3
Moore, 2009	99 patients referred to dermatology department of children's hospital diagnosed with AD, ages 16 or less	Randomized control trial where 49 caregivers of children with AD were selected to attend eczema educational workshop. The other 50 children participated in a standard dermatologist-led clinic. Patients underwent baseline assessment and followed-up 4 weeks after the intervention. The primary outcome was the severity of eczema.	At the 4-week review the mean improvement in SCORAD was significantly greater in those patients attending the eczema workshop than those attending the dermatologist-led clinic. The rest of the study compared how effective various treatments were in the two groups.	5
Kimata, 2007	40 male and 40 female patients; mean age 5 years without AD, and 40 male and 40 female patients, mean age 5 years with AD	Randomized control trial; Ghrelin is involved in night-time wakening and stress which is associated with AD. Thus salivary ghrelin levels were measured for children with AD during the night; to observe effectiveness of watching humorous films before sleep. Males and females were in separate comparison groups because ghrelin secretion levels vary significantly.	Neither viewing non-humorous film nor viewing humorous film had any effect on healthy children (control group). In contrast, viewing humorous film improved night-time wakening and reduced elevation of salivary ghrelin levels in patients with AD, while viewing control film failed to do so.	3
Grillo, 2006	61 paediatric patients (0-16 years), diagnosed with AD and their parents, excluding severe eczema	Randomized control trial where the participants were put into either the routine education control group or specific AD education group. Outcomes of educational interventions were measured over a 12 week period including: (a) subjective and objective measures of the severity of eczema and (b) patient QOL. Of secondary interest was any impact on the family.	Key findings demonstrated that education decreases the severity of eczema regardless which group the patient was in. QOL measures did not significantly improve with decreased severity of eczema	2
Niebel, 2000	47 mothers and their AD-children (mean age 4 years) participated in the study.	Does behaviour-based parental education in groups (DPE) or standardized video-education (VPE) enhance dermatological treatment effects and reduce skin-damaging behaviours in children and stress in their mothers. 18 mothers underwent the DPE (10 sessions), 15 mothers worked with VPE at home.	AD-symptoms improved overall, but parent education showed the most improvement with VPE rather than DPE. Psychological problems of mothers were equally reduced with DPE and VPE.	2

Portrayals of Childbirth: An Examination of Internet Based Media

Tiffany L. HOLDSWORTH-TAYLOR* [1]

[1] Student, University of Ottawa, Canada

* *Auteur(e) correspondant* | *Corresponding author*: N/A

Abstract:

More pregnant women turn to reality-based television programs and the Internet than to prenatal classes. Scant research examines the portrayal of childbirth in these new media. Although its impact is unknown, we do know that up to 20% of pregnant women fear giving birth; consequences include avoiding pregnancy, termination, depression, and increased maternal morbidity.

Overall internet content tended to be contradictory but largely reflected two categories: natural and mainstream, with two different portrayals of childbirth. Natural sources focused on eliminating fear, discrediting hospital births, and promoting 'alternative' options such as homebirth and midwifery. Mainstream sources reinforced fears, discredited home births, reported statistics from studies, and employed misinformation. Popular Internet sources tended to have the goal of educating whereas media uncovered in the purposive searches tended towards entertainment goals. Conflicting and misinformation from the Internet may entrench rather than assuage fears. Women may become confused and develop a heavily biased representation of birth. This could strongly impact a woman's approach to and experience of birth.

Keywords

Media, childbirth, Internet, fear

Introduction

Women spend an ever-growing amount of time on the Internet. Media analysis shows that the Internet affects how people communicate and live (Kung, 2008). It has also found traditional media including film, television and print misrepresent childbirth realities (Karpf, 1988). Despite this inaccuracy, more women turn to birth shows than prenatal classes (VandeVusse, 2008). Many also go online for information. As a new trend, scant research exists that evaluates Internet portrayals of childbirth. To learn about women's childbirth choices, it is important to evaluate their information sources—including online text and video.

Twentieth-century medicalization of childbirth has resulted in a loss of community knowledge creating an information void—enter popular media. Many women develop 'experience' of birth through TV, magazines, or web browsing. Many children also learn about birth this way (Kitzinger, 2001). Media analysis shows pregnancy and childbirth are often portrayed as risky (Seale, 2002). A consequence may be a fear of birth.

Tokophobia—pathological fear of childbirth—is characterized by avoiding pregnancy, termination, depression, increased morbidity, and elective caesareans (Hofberg & Brockingston, 2000; Hofberg & Ward, 2003). Although it is reasonable to have some fears and anxieties during pregnancy, especially the third trimester, tokophobia is debilitating (Hofberg & Brockingston, 2000). This little understood phobia affects women young and old:

> *Over 20% of pregnant women report fear and 6% describe a fear that is disabling. Altogether, 13% of non-gravid women report fear of childbirth sufficient to postpone or avoid pregnancy (Hofberg & Ward, 2003).*

With many fearful and tokophobic women, it is not surprising that suicide is the leading cause of maternal death (Hogberg &Ward, 2003). This fear is in part due to second-hand "knowledge". Many women report fear originating from alarming publications, sex-education videos, or 'horror stories' (Melender, 2002). Some state they must leave the room if a childbirth scene is on television (Sadie, 2007). With a potential link between media and tokophobia, it is imperative to understand the media's portrayal of birth and its impact.

Media studies show television can alter viewer perception and behaviour (Clement, 1997). Change in behaviour after watching certain programs has also been observed. There is evidence that "people alter their estimates of real-world phenomenon in line with television statistics" (Clement, 1997). Women thus perceive great risk in pregnancy and delivery, possibly linking tokophobia with the media. Unfortunately, few studies on childbirth in the media exist, so the true impact of watching clamorous labours is undetermined. Internet studies are surprisingly rare (Seale, 2003) given that pregnant women acknowledge Internet-use as a significant source of information. This study will begin to fill the research gap regarding the portrayal of childbirth in online media.

Research Questions

1. What are the different portrayals of childbirth on the web?

2. How has Internet media influenced women's perceptions of birth?

3. Does the Internet contribute to a cultural fear of childbirth?

Methods

To discover different portrayals of childbirth on the Internet, and analyze their relation to fear, a broad qualitative approach was undertaken involving web searches for

video and text-based information. Both popular and purposive searches were undertaken. Popular searches evaluated the most frequently occurring results of keyword searches. Purposive searches evaluated television programs—*A Baby Story, Baby Week, Deliver Me*—and magazines that are available online. This merging of other forms of media with the Internet is becoming increasingly popular and was therefore important to include in this study.

Data Collection

Data collection was intended to mimic searches by childbearing women by using search terms suggested by Google and YouTube. Popular text and video were found using these common searches.

Google text search-terms included: "childbirth", "birth",

"home birth", "labour pain", "labour pregnancy", "childbirth and labour", "water birth", "birth labor", "labour and delivery", and "childbirth methods". Popular video content was retrieved from YouTube by entering: "childbirth scene", "birth scene", "childbirth", "labour", "birth video", "childbirth pain", "childbirth delivery", "childbirth at home", "labour and delivery", and "labour live" into the search box. The top ten text and video results were evaluated. YouTube viewer comments were recorded as insight into audience perception.

Purposive searches included known popular sources. Sampling also evaluated other media including magazines and online versions of television programs.

Inclusion criteria included English and intrapartum[1]-related content only. Exclusion criteria included blogs, advertised results, PDFs, 'about us' sections, animal birth content, links to external content, pregnancy and postpartum information, news articles, Google results other than 'web' (video, news, scholar etc., academic results, and websites created by midwives, doulas, hospitals or birth centers to recruit clients). Organization websites were included unless selling an item or service. Many sites were dedicated to a book, DVD, etc. and were excluded as their purpose was to sell items rather than inform the public. Those selling a wide variety of items were included in this study as these web pages often sold products from other companies and did not have a vested interest.

Appendix 1 includes URLs and each search's assigned code.

Data Analysis

While searches took place a formal qualitative analysis was conducted. Notable themes, quotations, and information were recorded on coding sheets and a frequency table. This record provided insight into online childbirth portrayal.

Each media source was compared against an analytic/thematic template. Codes were determined based on the existing research and emerging issues such as the location and safety of breech delivery. Blank spaces were left on the coding sheets to allow the addition of further unanticipated/emerging themes during the data collection process. The first time a topic outside the coding template arose it was included in a blank space of the table. Because these themes were added during the data collection process as they appeared it is unlikely content was missed in earlier data collection. Most changes to the thematic template involved restructuring or reordering the codes. In these cases it was unnecessary to return to data to rerecord information. Both key and representative quotations from data sources were recorded in these templates. Collecting the quotations from ten articles provided sufficient evidence of the tone of the websites and examples of knowledge depth.

Frequencies of codes were also recorded throughout the data collection

process. Each search category (magazines, *Baby Week, Deliver Me, A Baby Story,* popular video and popular text) was recorded separately. The same thematic template used for collecting quotations was used in tabular form. This table will be presented and discussed below (Appendix 2).

Results

Common Themes

Themes throughout *all* media are most likely to be discovered by average consumers, likely having the greatest impact on childbearing women. Common themes were identified based on their presence in all search results.

Host country

Websites and videos were hosted from many countries. Magazines and popular text came from the US, New Zealand, UK, and India with the US and UK most prevalent. Not limited to Canadian content, little mention was made of birth in Canada; thus, not all sites' information is applicable to Canadians.

UK and New Zealand media discussed TENS[2] machines at-length. The following account describes its use during labour:

> *I used the TENS[2] machine for the majority of my delivery, and it was a fantastic device. I felt a sense of control during the labor because I was able to adjust the knobs as I desired, to experience more or less of the currents as I needed it. It also gave me something to focus upon and to do during the long hours of labor (Popular Text [PT] 10).*

Despite this discussion, TENS machines are not a common option for Canadians. A woman wishing to use the device

must supply her own.

Natural vs. Mainstream content

Two types of content emerged from all searches: what I will refer to as natural and mainstream. Both text and video sources could be divided into natural or mainstream categories.

Natural content highlighted women's ability to give birth without intervention or complications. These sources also emphasized eliminating fear, discredited use of pharmaceuticals and the generally medicalized hospital birth environment, promoted 'alternative' options including homebirth, midwifery, and in some cases, unassisted birth. For example:

> *If the mother experiences a lot of pain during labor in a hospital, she will probably be given pain medications, even if she doesn't want them and is trying to have a natural delivery (PT8).*

Mainstream websites focused on hospital birth and audience education in procedures and interventions. These tended to promote fears through topic selection, vocabulary, and commentary. They also discredited homebirths by citing out-dated information. Misrepresentation of literature was common in mainstream content. As consumers are unaware when authors cite out-dated or questionable studies, any reference implies validity. Referring to disproved literature is one method in which misinformation was employed. The following describes a procedure sometimes used in labour, however, justification for which is based on old inaccurate literature:

> *An episiotomy can considerably shorten the time-consuming, painful and pushing stage of labour. It prevents injury to the muscles of the vagina and perineum and protects the foetal head from being compressed through a smaller opening… Moreover, it is certainly better to have a proper incision made rather than suffering a vaginal laceration (PT5).*

Text and Video: Key Differences

Many themes pervaded popular and purposive searches, but differed in text and video sources. Commonalities between popular and purposive searches include in-text references to media portrayal, omissions from video, and viewer comments. Because text and video are seen regardless of search type they likely arise in pregnant women's internet searches, making them important to understand.

In-Text Reference to Media Portrayals

Many of the analyzed textual websites referred to media warping the process of birth:

> *You might think that you'll be most comfortable lying on the bed, perhaps because you've seen lots of women in labour on the TV doing so; however, keeping as upright as you can will help your labour to progress and will help you and your baby to cope better during labour (PT2).*

> *You will hear (particularity on the internet) about how awful inductions are from some women, but others report it being not much different to when they went into labour on*

Table 1 Frequency of topics in Text vs. Video: Content (Popular and Purposive)

Code	Text	Video
Episiotomy	20	0
Hypnobirth[3]	6	1
Tearing	4	0
Placenta	8	0
Orgasmic birth	5	1
Accupuncture/Accupressure	2	0
TENS	6	0

Code	Text	Video
VBAC[4]	12	1
Premature labour	17	0
Use of castor oil	4	0
Childbirth education	11	1
Birth plan	14	0
Stages of labour discussed	11	2

their own (PT10).

Such generalised media analysis is a common theme. Authors may refer to media depictions of birth to make their article sound more authentic, and to discredit opposing claims. Controversial topics such as the safety of epidurals appear especially vulnerable to this type of authentication. For example:

> *While the Internet has immeasurably increased the quantity and accessibility of medical information, it has also fostered the spread of misinformation about pain management and childbirth… Pain management has no effect on labor, except in rare and exceptional cases… Contrary to claims frequently cited on the Internet, there's no credible evidence to show that epidurals or other forms of pain management slow speed of labor, lead to Cesarean sections or are associated with a higher incidence of depressed infants (PT1).*

This quotation sounds convincing, but is not evidence-based. The literature states the opposite: epidurals slow labour, lead to caesareans, and cause the infant to be "sleepy" (Mauberry, 2002).

Video Omissions

Several codes were recorded amongst text-based content (magazines and popular text) that were absent or rare in video content. No topics observed in videos were absent from text. This is likely because texts are intended to inform whereas videos more often seek to entertain. Table 1 shows themes present only in text. A major consequence of video omissions is promoting fear and distorting *when* labour ends

Emphasising the unlikely

Episiotomy is discussed 20 times in texts but never seen in videos: Vaginal birth injury with visible tears or episiotomies are common (PT9).

This is likely because displaying an episiotomy on video would require showing an incision of women's genitalia—avoided for privacy or viewer-rating reasons. There is, however, an option of discussing the procedure on film as it takes place or afterwards. This was not included in video, possibly due to the procedure's rarity. Episiotomy, once routine, is seldom-used and only in emergencies. It is therefore expected that they are absent from video or text discussions. Their widespread discussion, without demonstration, may lead women to fear what is highly unlikely to happen. It is also worth noting that episiotomies are rarely performed in today's birthing practices, yet are discussed as often as common procedures such as induction or caesarean section. This may be due to fear that women have of episiotomies. No website, however, commented on their rarity.

The end is not the end: Stages of labour

The stages of labour were often discussed in text in conjunction with information regarding childbirth education. Textbook examples of the three stages of dilation and the stages of labour ensue. Not observing a woman in distinct phases of labour makes for a skewed image of labour and delivery. Videos often only show women in transition and stage two - pushing. This suggests labouring women are in intense pain throughout the process. Nuances in the timing and intensity of contractions go unlearned. This information does not create 'drama' and thus is excluded from videos.

The placenta is discussed 8 times in text and not at all in video. Text discussed its importance to the foetus, and its expulsion in the third stage of labour. This stage is omitted from videos, and labour is instead shown to end at the second stage. The third stage is an important part of birth. Many complications, such a haemorrhage, can occur in this stage. Fear would not explain this omission as expelling the placenta is not painful. The sight of blood could explain the placenta's absence.

Viewer comments

Comments on videos often referred to pain during labour, expressing surprise if the mother was not "screaming":

> *OMG!!!!! I'm never having kids! (PV6)*

> *I'm amazed at how calm the mother is. I would imagine she would be screaming her head off at this point (PV7).*

> *Oh no giving birth it's so painful. I don't even want to remember it's painful but real beautiful when u see that baby (PV5).*

This suggests that many viewers are unfamiliar with the birthing process and fear the pain. Misinformation was common in comments:

> *If I got pregnant I would like to give birth at home too. I was born at home. Risky but so natural (PV7).*

Here homebirth is considered less safe than hospital birth—a common myth. Some comment threads include attempts to correct misinformation. This was often done in a judgmental way, and was just as likely to be misinformed:

> *PITOCIN IS EVIL!!!!! (BS3).*

Many viewers were misinformed and demonstrated fear of childbirth. This suggests that popular Internet video does not provide deep understanding of childbirth. Women who feared childbirth appeared either surprised by the calmness of a labouring woman or had fears confirmed by misinformed viewer comments.

Popular and Purposive Searches

Overall, popular searches presented a more balanced portrait of childbirth likely due to education goals. Conversely, the goal of drama and lack of concern over fears and accuracy distanced the purposive samples from the popular. Conflicting information was more common in popular searches though it did occur in the magazines. The natural / mainstream duality was observed across both purposive and popular searches with natural content being more common in popular media.

Topic frequencies can be found in Appendix 2 but will not be discussed at length as their importance to viewer searches relies heavily on which type of search a woman conducts. Thus, general conclusions cannot be formed.

Discussion

The Internet is a popular information destination for pregnant women. For this reason evaluating its accuracy and portrayal of childbirth is important. The findings and implications of this media analysis are discussed below.

1. Childbirth Portrayals

This study examined ways in which childbirth is portrayed in online media. Many portrayals of online media were found. Content could be divided into popular/purposive, text/video and mainstream/natural. Similarities were found across all media, but the differences have unique implications for childbearing women. These differences likely result from competition for an audience.

2. Media's Influence

With an infinite amount of content online, webhosts must compete for audiences. Competition is divided between natural birth and mainstream, video and text, as well as magazines and other texts. Each medium approaches childbirth differently. Beyond the mentioned divisions, sites part further between popular education-driven sites and purposive entertainment media. Competition for consumers has resulted in an invisible battle between hosts. Information from one website to another often conflicts such as the safety of pain medications. Authors resort to strategies such as citing academic journals, credible or not, and referring to media misrepresentation to gain an edge over competitors. The effect of this background battle on consumers is little known. Comments related to videos suggest women are misinformed and scared about childbirth as was seen regarding the safety of homebirth. More research is needed to determine the effects of the internet on women's perceptions of childbirth.

3. Cultural fear of childbirth

Media analysis shows that childbirth is portrayed as risky for mother and foetus (Seale, 2002). This theme is reflected in Internet content in a more complex manner. As on television, women frequently discussed fears of labour, pain being the most common. Purposive content furthered this fearful portrayal by adding physicians' fearful commentary or dramatic narration. As this content originated as television and magazine media, it is possible that these representations have a more fearful overtone.

Popular searches acknowledged the culture of fear around childbirth and attempted to alleviate it by informing readers. This portrayal of fear is quite different from that commonly seen on TV and in the purposive searches. Despite the presence of articles directly targeting fear, others directly contributed to fears. Discussions of interventions, infant deaths, and pain management all had an air of danger.

The natural birth oriented webpages are most likely to be successful in empowering its readers to not fear childbirth. They focused on a woman's natural ability to give birth, as opposed to the mainstream question of whether a woman will be able to endure the pain.

It is thus possible that the Internet contributes to society's fear of childbirth. With such a wide spectrum of portrayal, the fear a woman experiences regarding birth is likely to depend on which type of internet media she subscribes to. To fully understand to relationship between Internet media and tokophobia, more research is required.

Methodological limitations

The Internet, an interactive medium, changes daily. Content analyzed during this study will change over time. Each month, magazines post new articles, new websites and new searches will become popular and viewer comments will change. Although unproblematic in the short term, this will render the results obsolete in the long-run.

Text and video provided different amounts of information making it impossible to quantify data. Frequencies gave only a qualitative sense of themes that are addressed or ignored.

Implications from this study could only be drawn based on existing research and viewer comments. To fully understand the implications of childbirth media on women, further studies are required.

Future Research

The scale of this study presented some limitations. A larger study should be conducted to examine more specific search terms that women would frequently use such as common interventions and diagnoses. A study of what women tend to focus on in searches and self-education would also be useful.

As mentioned above, further studies are needed to determine the impact of study findings on childbearing women. Fear and misinformation should be given particular focus.

Online childbirth education classes are becoming popular amongst childbearing women but were not included in this analysis. A study should be conducted comparing these classes to classes offered by hospitals and childbirth education organizations.

Further forms of media such as news stories further influence the Internet's portrayal of childbirth. Again, due to the small scale of this study, these sources were excluded. As much of the content analyzed was from international websites, a study of exclusively Canadian sources ought to be done. Since Google has an option to search only Canadian content, some women may limit their searches in this way. Misinformation due to foreign sources of self-education media would be eliminated from such a study.

Conclusion

This study shows there is wide variation in online childbirth portrayal. From unassisted birth to cascading interventions, each portrayal of childbirth has its own set of implications. Misinformation and conflicting information were found to be quite common. Viewer comments suggest that audience members are confused about childbirth—perhaps from this tangled web of misinformation. Further studies should investigate this relationship. The competition to attract women to particular websites may cause of the vast amount of conflicting information. Website authors discredit other media and cite literature to make their website stand out. These messages tell women that each website is authentic, whereas all others should not be trusted. As communicators are granted the ability to shape their information environment, individuals, organizations and public bodies each want a piece of the Internet (Ward, 1993). Search results show that each portrayal of birth takes a different angle in attracting and maintaining an audience. Each source portrays birth in a particular way and these particularities have an important effect on women's attitudes and childbirth choices.

Notes

[1] During labour and delivery.

[2] A transcutaneous electrical nerve stimulation (TENS) machine sends small electrical pulses to electrodes placed on the skin. During labour, the electrodes are placed on a woman's back to relieve pain.

[3] Hypnobirth is a method of childbirth education that focuses on birth guided by natural instinct and self-hypnosis techniques (HypnoBirth, 2009).

[4] Vaginal birth after caesarean (VBAC).

References

Baxley, E., & Gobbo, R. (2004). Shoulder dystocia. *American Family Physician, 69*(7), 1707 1714.

Clement, S. (1998). Television gives a distorted picture of birth as well as death. *British Medical Journal, 317*(7153), 284.

Clement, S. (1997). Childbirth on television. *British Journal of Midwifery, 5*(1), 37-42. Retrieved from http://dx.doi.org/10.12968/bjom.1997.5.1.37

Laboring under and illusion: Mass media childbirth vs the real thing. Elson, V. (Director). (2009).[Video/DVD]

Gaskin, I. (2003). Scary birth gets high ratings. Ina may's guide to childbirth (pp. 164). New York: Bantam Del.

Hofberg, K., & Brockington, I. (2000). Tokophobia: and unreasoning dread of childbirth. *British Journal of Psychiatry, 176*(1), 83-85. doi: 10.1192/bjp.176.1.83

Hofberg, K., & Ward, M. (2003). Fear of pregnancy and childbirth. *Postgraduate Medical Journal, 79*(935), 505-510. doi: 10.1136/pmj.79.935.505

HypnoBirthing® - the mongan method. (2009). Retrieved from http://www.hypnobirthing.com/

Karpf, A. (1988). It's a natural: Childbirth and the media. Doctoring the media: The reporting of health and medicine (pp. 72-81). New York: Routledge.

Kitzinger, S., & Kitzinger, J. (2001). Letters from europe: Childbirth and breastfeeding in the british media. *BIRTH, 28*(1), 60. doi: 10.1046/j.1523-536x.2001.00060.x

Klaus, M., Kennell, J., & Klaus, P. (1993). Mothering the mother. How a doula can help you have a shorter, easier, and healthier birth. Massachusetts: Addison-Wesley Publishing Company.

Kung, L., Picard, R., & Towes, R. (2008). The impact of the internet on users. The internet and the mass media (pp. 86-101). London: SAGE.

Mason, J. (1988). Midwifery in Canada. The midwife challenge (pp. 100-129). London: Pandora Press.

Mayberry, L., & Clemmens, D. (2002). Epidural analgesia side effects, co-interventions, and care of women during childbirth: A systematic review. *American Journal of Obstetrics and Gynecology, 186*(5), S81-S93. doi: 10.1016/S0002-9378(02)70184-1

Melender, H. (2002). Fears and coping strategies associated with pregnancy and childbirth in finland. *Journal of Midwifery & Women's Health, 47*(4), 256-263. doi: 10.1016/S1526-9523(02)00263-5

Merck. (2005). Preeclampsia and eclampsia. Retrieved from http://www.merck.com.proxy.bib.uottawa.ca/mmpe/sec18/ch263/ch263j.html

Nicholas, S. (2007). Are you a tokophobic? the women who are too terrified to give birth. Retrieved from http://www.dailymail.co.uk/femail/article-489776/Are-tokophobic-The-women-terrified-birth.html

Robotham, M. (2000). Fast and furious: Childbirth on TV. *MIDIRS Midwifery Digest, 10*(1), 77-78.

Robotham, M. (2001). In my view. the painful birth of a new television genre. *Nursing Times, 97*(35), 17-17.

Rutherford, M., & Gallo-Cruz, S. (2008). Selling the ideal birth: Rationalization and re-enchantment in the marketing of maternity care. Advances in medical sociology (pp. 75-98). Bingley: Emerald Group.

Seale, C. (2002). Pregnancy and childbirth. Media and health (pp. 198-199). London: SAGE.

Seale, C. (2003). Health and media: An overview. *Sociology of Health and Illness, 25*(6), 513-531. doi: 10.1111/1467-9566.t01-1-00356

Stillerman, E. (2007). The media skews the message. *Massage Today, 7*(10). Retrieved from http://www.massagetoday.com/mpacms/mt/article.php?id=13691

VandeVusse, A. (2008). A baby story as a source of information about childbirth: The messages and their implications. *Journal of Midwifery & Women's Health, 53*(5), 482-482.

Ward, J., & Hansen, K. (1993). Search strategies in mass communication. White Plains, N.Y.: Longman.

Appendix 1: Search Terms and URL Codes

Purposive Sampling

A baby Story

BS1 http://www.youtube.com/watch?v=KI5b4OqPVlU&feature=related
BS2 http://www.youtube.com/watch?v=H8AijSoJjxM&feature=related
BS3 http://www.youtube.com/watch?v=e05vFKlzJvQ&feature=related
BS4-http://tlc.discovery.com/beyond/?playerId=203711705&categoryId=566566872&lineupId=151749457
BS5-http://tlc.discovery.com/beyond/?playerId=203711705&categoryId=566566872&lineupId=151749457
BS6-http://tlc.discovery.com/beyond/?playerId=203711705&categoryId=566566872&lineupId=151749457
no other videos of a baby story were accessible on the internet.

Baby Week

BW1 http://health.discovery.com/videos/exclusive-i-didnt-know-i-was-pregnant-webisode-part-1.html
Or
http://www.youtube.com/watch?v=CJqqftBWT0w
BW2 http://health.discovery.com/videos/baby-week-amazing-births-part-2.html
BW3 http://health.discovery.com/videos/baby-week-i-didnt-know-i-was-pregnant.html
BW4 http://health.discovery.com/videos/baby-week-quads-with-2-moms.html
No further videos were found

Deliver me

DM1 http://health.discovery.com/fansites/deliver-me/video.html
DM2 http://health.discovery.com/fansites/deliver-me/video.html
DM3 http://health.discovery.com/fansites/deliver-me/video.html
DM4 http://health.discovery.com/fansites/deliver-me/video.html
DM5 http://www.youtube.com/watch?v=S0qc7rRAId0
DM6 http://www.youtube.com/watch?v=_PLl7TbpVs4&feature=related
No additional episodes and videos could be found

Pregnancy magazine

M1 http://www.pregnancymagazine.com/the-big-day
M2 http://www.fitpregnancy.com/yourpregnancy/labor_delivery/
M3 http://www.babyexpert.com/
M4 http://www.askamum.co.uk/Birth/
M5 http://www.todayspregnancy.com/article.htm
M6 http://www.fitpregnancy.co.za/birth/
M7 http://www.ayushveda.com/magazine/category/pregnancy/
M8 http://www.mothering.com/pregnancy-birth
M9 http://www.compleatmother.com/
M10 http://www.parents.com/pregnancy/giving-birth/labor-and-delivery/

Popular Video

Childbirth scene
PV1 http://www.youtube.com/watch?v=YYkpnJtT7vQ
Birth Scene
PV2 http://www.youtube.com/watch?v=JujmtUzEXLc
Childbirth
PV3 http://www.youtube.com/watch?v=6AdFdmE9A84
Labour
PV4 http://www.youtube.com/watch?v=h5bm9-B6Ec4
Birth Video
PV5 http://www.youtube.com/watch?v=yABbpMjYbMk
Childbirth Pain
PV6 http://www.youtube.com/watch?v=_eQFJR8wM00
Childbirth delivery
PV7 http://www.youtube.com/watch?v=brL02wfFvfM
Childbirth at home
PV8 http://www.youtube.com/watch?v=7E-wULAaD50
Labour and delivery
PV9 http://www.youtube.com/watch?v=gUOsy4bS2ZE
Labour live
PV10 http://www.youtube.com/watch?v=syNRYD1Q1cA

Popular Text

PT1 www.babycenter.com
PT2 www.babycentre.co.uk
PT3 www.childbirth.org
PT4 www.gentlebirth.org
PT5 www.indiaparenting.com
PT6 www.parenting.ivillage.com
PT7 www.unassistedchildbirth.com
PT8 www.waterbirthinfo.com
PT9 www.wikipedia.com
PT10 www.womens-health.co.uk

Appendix 2: Popular vs. Purposive Searches

Code	Purposive Searches	Popular Searches
Interventions		
epidural uneffective or complications	8	2
epidural received/ discussed	2	16
Induction	15	15
Caesarean	18	20
AROM	7	3
Narcotics	5	4
Forceps / vacuum	3	9
IV	1	3
EFM	3	6
Gas and air	2	6
Episiotomy	7	13
Cascade of interventions	2	1
Natural Birth		
Waterbirth	5	14
Homebirth	5	15
Hypnobirth	3	4
Tearing	1	3
Discussion of placenta	2	6
Orgasmic birth	2	5
Body design pos	1	4
Bpdy design neg	2	1
Coping strategies suggested	3	8
Acupuncture / pressure	1	3
TENS	2	4
Position		
- on back	8	7
- all fours	3	6
- side laying	3	3
- squatting	4	3
- other	6	6
Fear—other	7	0
Pelvic disproportion	0	0
Pain	10	9
Panic / cant handle	3	2
Stuck baby	0	0
Maternal / infant death	4	0
Complications	4	1
Fear acknowledged	4	1
Fear addressed by provider	2	0

Code	Purposive Searches	Popular Searches
Confident	1	1
Complications	6	2
Breech	3	11
Undiagnosed health problem	0	0
Pre-ecclampsia / ecclampsia	2	4
Hemorrhage	0	4
Shoulder dystocia	0	3
VBAC	3	10
Baby not breathing well	5	4
Premature	4	13
Fast labour	5	3
Large baby	6	4
Multiple birth	4	8
Place of Birth		
Hospital	18	7
Intended home	0	3
Unintended home	1	3
Birth Centre	1	4
Caregiver		
Ob	9	7
Midwife	11	9
Doula	11	7
Unknown	0	1
Unassisted	1	1
Breathing		
Hyperventilating	1	1
Instructed to break properly	1	5
Breathing well	2	3
Holding breath	1	0
High pitch screaming	3	4
Other		
Water broke and women immediately		
Shown in stage 2 of labour	1	1
Use of castor oil	2	2
Childbirth Education	7	5
Birth Plan	8	6
Stages of labour discussed	5	8

A Review of Xq28 and the Effect on Homosexuality

Philip M. LEE* [1]

[1] Student, University of Ottawa, Canada

* *Auteur(e) correspondant* | *Corresponding author*: N/A

Abstract:

The cause of homosexuality remains a hotly contested debate to this day. Although the role of genetics has diminished over the past decade because of the popularity of environmental influences, it continues to be a relevant correlative possibility. Since its inception in the early 1990's from a study conducted by Dr. Dean Hamer, the genetic locus Xq28 has become amongst one of the most important genetic factors of sexual orientation. Subsequent studies attempting replication have improved on the original experiment although the initial measures and methods of experimentation may have biased the results of the findings. Consequently, contention between advocates for and against Xq28 continues over 15 years later with mounting evidence weakening the link of Xq28 and homosexuality. Even though the majority of genetic discussion revolves around Hamer's original findings, more recent genetic markers have also now been found which may show positive connections and provide the basis for further research.

Keywords:

Homosexuality, genetics, Xq28

Introduction

Sexual orientation is a critical part of a person's identity which can influence their decisions and actions during life. Once thought of as a paired trait, sexuality is now commonly described as a continuous spectrum of varying degrees of attraction to one sex or another (Pederson & Kristiansen, 2008). This has, however, lead to difficulty in estimating homosexual prevalence in society. As social acceptance continues to grow for people with same-sex orientations there is a continued interest in the natural underlying causes. Many possible speculations have arisen, ranging from differences in neural anatomy to environmental factors (Hamer, Hu, Hu, Magnunson, & Pattatucci, 1993). The area from which perhaps the most interest has been garnered is in the role of genetics. Evidence regarding such a heritable correlation began with homosexual twin studies (Mustanski et al., 2005). Subsequent research has focused on mapping specific genetic components. Whether or not a genetic linkage can be verified is important in both the social and scientific understanding of sexual orientation. Homosexuality is and will be defined within these contexts as a sexual attraction and preference for other members of the same sex (Hamer et al., 1993). In keeping with the available studies, discussion and investigation focuses almost exclusively on male human homosexuality.

Discussion of Measures/Methods in genetic studies

Over the past twenty years, much research and controversy has surrounded a possible correlation between homosexuality and a maternal sex-linked genetic marker, Xq28 (Paterson, 1998). In the first study to map this connection, participants were taken randomly via newspaper and magazine advertisements that catered to homosexual communities (Rice, Anderson, Risch, & Ebers, 1999). A problem arising from this method of collection is the selectivity of the sample as participants consist only of self-identified volunteers. An unrepresentative subset may consequently be taken because of such an unsystematic method (Bailey et al., 1999). Due to the added complexity for females who have two X-chromosomes, where one is randomly inactivated, the samples consisted only of men. Participants who had homosexual fathers or sons were also omitted to withhold influences by unknown Y chromosome contributions. This was conducted through pedigree analysis using family histories (Hamer et al., 1993). The homosexual criterion of participants was identified through taking sexual histories and Kinsey scales, an approved ordinal self-rating scale ranging from 0 (exclusively heterosexual) to 6 (exclusively homosexual), where scores of 5 and 6 were chosen (Hamer et al., 1993). This bimodal treatment of homosexuality was justified by Hamer because of the overlap between various groups in the study created by the Kinsey method. Also, since scaling techniques risk obtaining false positives, the size of effect attributed on the outcome is an area of criticism (Bailey et al., 1999). The last criterion of sample selection was that the participants had to be in pairs of homosexual brothers (sibling pairs). This criterion helps legitimize an X chromosome linkage for homosexuality, as related males should have distinguishing marks in similar regions (Hamer et al., 1993). The DNA of the mothers was also sampled if it was available, to corroborate maternal transmission. After an initial analysis, a polymerase chain reaction of 22 predetermined areas of the sample DNA from the homosexual sibling pairs was conducted. Using these pairs is a more stable method to errors when compared to broader pedigree techniques (Hamer et al., 1993). The results demonstrated statistically significant markers at Xq28 (Hamer et al., 1993). Subsequent studies have used similar methods of data collection and measurement to analyze the accuracy of this connection.

Discussion of Genes

The Xq28 locus has been the most scrutinized genetic region for homosexuality. It is suggested that a component in the Xq28 location with heritable maternal material influences homosexual predisposition. As such, related males (brothers, maternal uncles & cousins) should share an excessive amount of allelic material in that region (Rice et al., 1999). Although the terminal portion of Xq28 may code for homosexuality as indicated by the markers, it is difficult to establish any direct gene products. Even though the X-chromosome codes for relatively few genes, hundreds of candidate genes may still be coded for in that band (Hamer et al., 1993). Possible genes mapped within Xq28 may be associated with neural functioning, however, these are all in different sub-bands of the same locus (Wilke, Gaul, Klauk, & Poustka, 1997). There has yet to be a study large enough to confirm and isolate a specific gene product. As a result, relevant studies focus on the potential of Xq28 to correlate with homosexuality as opposed to the prospective products. Despite criticism, the Xq28 markers continue to be the strongest sex-linked candidates of homosexuality.

Support for Xq28

Primary support for Xq28 is found in the original study by Dean Hamer, which linked 33 of 40 Caucasian homosexual sibling pairs (83%) with the distinct markers. A study done in the same year led by Stella Hu, with a similar team, also found a significant relationship. In addition to using homosexual sibling pairs, this study sampled heterosexual brothers to see if they had similar linkages in the Xq28 region. The results demonstrated that 67% of the homosexual pairs and only 22% of the heterosexual pairs shared any X-linked connection (Hu et al., 1995). Even though this confirms that heterosexual males lack certain Xq28 regions, the sample sizes were smaller, using only 32 homosexual pairs and 11 heterosexual pairs. The continued risk of obtaining unrepresentative samples remains a legitimate concern. This study was also the first to attempt and find similar outcomes in females. The results demonstrated no significant sharing of Xq28 markers in both heterosexual and homosexual sibling pairs (Hu et al., 1995). Within the study itself, there was acknowledgement that although this likely indicates different mechanisms for females, the sample sizes were too limited to make a more definitive statement (Hu et al., 1995). Another explanation for the findings is that the Xq28 locus might be recessive in females signifying that female homosexuality may not be influenced by sex-linked genes (Hu et al., 1995). Subsequently, Xq28 continues to only be a plausible factor of male homosexuality as females and heterosexual males show no excessive links. These findings along with pedigree analyses also confirm the lack of paternal transmission for Xq28 in women.

Criticism of Xq28

A highly referenced study that contrasts with the significance of Xq28 was conducted by George Rice. The study was markedly similar to the original with the main exceptions being that the sample sizes were larger at 52 sibling pairs and taken from Canada, as opposed to Italy (Rice et al., 1999). The resultant data was determined to have only a 55% correlation found in Xq28 sharing (Rice et al., 1999). Comparatively to both Hamer and Hu's findings of 83% and 67% correlations, the final conclusion did not support Xq28 in a significant manner. This discrepancy is largely unaccounted for except a possibility that tighter controls in the previous studies may have been used to exclude potential candidates depending on homosexual relatives (Rice et al., 1999). Still, because the variations between the studies were minimal, the reliability of the original findings can be legitimately questioned. In 1999, John Bailey's study was the first to attempt to garner a more representative subset through different sampling techniques. The study took two significantly larger samples than Hamer from an HIV clinic and a gay pride parade where they incidentally sampled male participants who would consent during that period (Bailey et al., 1999). Although there continues to be a sampling bias from this method, it has more validity than collecting volunteers through advertisements. Consequently, this study found no definitive support for Xq28 but reiterates that it does not exclude the possibility of a moderate linkage (Bailey et al., 1999).

Over the last decade there has been continuing research in the consistency of the Xq28 link as well as deviations into other possible genes of interest. The first study to implement a complete genome scan for sexual orientation in males denotes several possible new genes and mild support for Xq28. In the genomic scan study, maximum likelihood of estimation scores were used for genetic analysis in which results higher than 1.8 were given significance (Kruglyak & Lander, 1995). The sample size was significantly larger than previous studies having a total of 456 homosexual individuals (Mustanski et al., 2005). The findings showed three new genetic markers of interest at 7q36, 8p12 and 10q26. The latter two loci have equal inheritance from maternal and paternal lines, suggesting more influence from autosomal instead of sex-linked genes (Mustanski et al., 2005). The region at 8p12 participates in the coding of Gonadotropin-releasing hormone which stimulates both luteinizing and follicle-stimulating hormones that are important in steroidogenesis (Adelman et al. 1986). 10q26 has been linked with some neural proteins in the brain (Mustanski et al., 2005). The most significant marker, 7q36, has coding regions for neurotransmitter and hormone gene products for the hypothalamus (Mustanski et al., 2005). This may suggest plausible relationships with neural gene products. These three genetic markers provide support for the idea of multiple gene interactions in homosexuality. Regarding support for Xq28, the markers had to be selectively controlled in this case to demonstrate a mildly significant score of 1.99 (Mustanski et al., 2005). Accordingly, Xq28 represents a more minor aspect of homosexuality than previously believed.

Some recent research has gone into the influences of various gene products such as sex hormones. Specifically, an analysis of gene CYP19, which aids conversion of andro-

gens into estrogen, showed no significant effects in male homosexuality (DuPree, Mustanski, Bocklandt, Nievergelt, & Hamer, 2004). Still, due to the strength of data from outside studies on animals, sex hormones and androgen receptors continue to be a viable path of interest for homosexual causation (Dupree et al., 2004).

Conclusion

The inconclusive genetic findings present only possible explanations of genotypic information underlying homosexual expression. Since the results of the original Xq28 study have never been replicated to such a significant degree, the validity of the outcome has been weakened. It is quite evident in alternate studies that as sample sizes become larger and more selective (increasing statistical power) the visibility of such a relationship becomes diminished. Although Xq28 remains the most prominent sex-linked candidate, support has been shifting towards the more probable influence of autosomal genes (Mustanski et al., 2005). Currently, such new genes of interest potentially code for products such as neurotransmitters and prenatal hormones (Mustanski et al., 2005). Unfortunately there is no substantial evidence to suggest that these genes are related to homosexuality in a considerable manner. As no genetic link is strongly correlated enough to demonstrate causation, it is appropriate to assume that no single gene is responsible for homosexuality. Instead, it is a combination of different genes that provide a propensity towards homosexuality. Although abundant research has focused upon genetic influence, homosexuality may be solely a behavioural characteristic and subsequently the weight of the environment needs to be considered. Regarding the social environment, the idea that homosexual parents are prone to have a higher prevalence of homosexual children has been largely discredited (Morrison, 2007). It is illogical to deduce that homosexuals would have had any significant deviation from “normal” parenting methods. Using twin studies has provided evidence that sexual orientation can be impacted, in part, by non-shared environmental influences (Mustanski et al., 2005). It has proven very difficult to isolate what those unique factors could be. Nevertheless, the rich complexity of physical and social elements likely shape beliefs and characteristics to some degree. Consequently, more studies are still required to facilitate further understanding of genetic influence and which gene products, if any, can be strongly linked. Environmental studies should continue in the social context until more specific genes can help identify possible physical factors. A focus also needs to center on female homosexuality, although it is more complex to study, it should not be ignored as a crucial part of this variant behavior. The recent autosomal genetic markers may provide a link between both sexes. Thus, as the current evidence suggests, regardless of future studies, it is likely a multitude of possible genes working in conjunction with environmental factors and triggers that produces homosexual behavior.

References

Adelman, J. P., Mason, A. J., Hayflick, J. S., & Seeburg, P. H. (1986). Isolation of the gene and hypothalamic cDNA for the common precursor of gonadotropin-releasing hormone and prolacting release-inhibiting factor in human and rat. *Proc Natl Acad Sci USA, 83*(1):179-183. Retrieved from http://www.jstor.org/stable/26821

Bailey, J. M., Pillard, R. C., Dawood, K., Miller, M.B., Farrer, L. A., Trivedi, S., & Murphy, R. L. (1999) A family history study of male sexual orientation using three independent samples. *Behavior Genetics, 29*(2), 79-85. doi: 10.1023/A:1021652204405

DuPree, M. G., Mustanski, B. S., Bocklandt, S., Nievergelt, C., & Hamer, D. H. (2004). A candidate gene study of CYP19 (aromatase) and male sexual orientation. *Behavior Genetics, 34*(3), 243-250. doi: 10.1023/B:BEGE.0000017870.77610.52

Hamer, D. H., Hu, N., Hu, S., Magnunson, V.L., & Pattatucci, A.M.L. (1993). A linkage between DNA markers on the X chromosome and male sexual orientation. *Science, 261*(5119):321-327. doi: 10.1126/science.8332896

Hu, S., Pattatucci, A. M., Patterson, C., Li, L., Fulker, D. W., Cherny, S. S., Kruglyak, L., & Hamer, D. H. (1995). Linkage between sexual orientation and chromosome Xq28 in males but not in females. Nature Genetics, 11, 248-256. doi: 10.1038/ng1195-248

Kruglyak, L., & Lander, E.S. (1995). Complete multipoint sib-pair analysis of qualitative and quantitative traits. *The American Society of Human Genetics, 57*, 439-454.

Morrison, T. G. (2007). Children of homosexuals and transsexuals more apt to be homosexual: A reply to cameron. *Journal of Biosocial Science, 39*, 153-154. Retrieved from http://dx.doi.org/10.1017/S0021932006001714

Mustanski, B. S., DuPree, M. G., Nievergelt, C. M., Bocklandt, S., Schork, N. J., & Hamer, D. H. (2005). A genomewide scan of male sexual orientation. *Human Genetics, 116*(4), 272-278. doi: 10.1007/s00439-004-1241-4

Paterson, A. D. (1998). X-chromosome workshop. *Psychiatric Genetics, 8*(2), 121-126.

Pedersen, W., & Kristiansen, H. W. (2008). Homosexual experience, desire and identity among young adults. *Journal of Homosexuality, 54*(1/2), 74-84. doi: 10.1080/00918360801951962

Rice, G., Anderson, C., Risch, N., & Ebers, G. (1999). Male homosexuality: Absence of linkage to microsatellite markers at Xq28. *Science, 284*(5414), 665-667. doi: 10.1126/science.284.5414.665

Wilke, K., Gaul, R., Klauk, S.M., & Poustka, A. (1997). A gene in human chromosome band Xq28 (GABRE) defines a putative new subunit class of the GABA neurotransmitter receptor. *Genomics, 45*(1), 1-10. doi: 10.1006/geno.1997.4885

Social Media and its Use in Health Promotion

Joëlle J. LEVAC* [1], Tracey O'SULLIVAN [2]

[1] Student, University of Ottawa, Canada
[2] Professor, University of Ottawa, Canada

* *Auteur(e) correspondant* | *Corresponding author*: N/A

Abstract:

Social media holds considerable potential for health promotion and other health intervention activities, as it addresses some of the limitations in traditional health communication by increasing accessibility, interaction, engagement, empowerment and customization. The use of social media increases the potential for easy access to preventive medicine, interaction with health care providers, interprofessional communication in emergency management, and public health. However, more research is needed to determine its long term effectiveness and to maximize the strategic presence of health organizations on social networking websites. This paper provides encouraging information about the possibilities of using social media to improve access to health information and health care providers, as well as to promote positive health behaviour change. It is essential for health promotion organizations to capitalize on the opportunities provided by social media, in order to modernize strategies to reach all age groups and to tailor programs to current communication trends, all of which are offered at a relatively low cost.

Keywords:

Social media, social networking, health promotion, health communication, online health information, emergency management, interprofessional communication

Introduction

Facebook, Twitter, Google, Bing, and Buzz are new terms but they are used every day by millions of people across the world. The impressive growth in social media has been fascinating to watch, but intriguing as well, when you consider the multitude of applications these tools have unleashed, and their potential to influence population health.

Interest in the internet as a health promotion tool has grown immensely in the past decade (Korp, 2006). The internet has become a powerful global communication method for health interventions, providing public access to a wide range of health promotion programs, and opportunities for people to communicate with others, and with health professionals (Cassell et al., 1998). According to Pew Research Center Publications (2009), 61% of American adults now look online for health information. Because people have actively adopted the internet for health communication, and many people believe it improves their health (Neuhauser & Kreps, 2003; Fox et al., 2000), the internet is regarded by health promotion specialists as an efficient strategy for promoting positive health behaviour change (Mangunkusumo et al., 2007; Fotheringham et al., 2000).

High risk, preventable health behaviours, such as smoking, alcohol abuse, insufficient exercise and unhealthy diets still contribute to a substantial number of deaths in North America (Canadian Institute for Health Information, 2006; Danaei et al., 2009). This underscores the necessity of ensuring access to accurate health information and effective health interventions. Canada's Advisory Council on Health Infostructure emphasized that health information "is an essential public good which should be readily available and accessible to all Canadians" (Health Canada, 2005; Health Canada, 2001; Advisory Council on Health Infostructure, 1999).

Health promotion specialists continually search for new and efficient methods of reaching people of various ages. The use of new technology, more precisely social media, could be a key strategy in helping to solve some of the challenges faced by those in the health promotion field. Interventions incorporating social media channels hold considerable potential for health promotion and address some of the limitations observed by traditional health communication strategies by increasing the potential for interaction, engagement, customization and participation.

The Evolution of Communication

Communication is a method for offering social support – which is directly linked to positive health behaviours (Abroms & Maibach, 2008). Research on health communication interventions has shown that a number of conditions are required for communication to be effective, including the message reaching people on emotional and rational levels (Neuhauser & Kreps, 2003; Rubin & Rubin, 2001). Tailored messages are more effective than generic messages since they are customized to the needs of the recipients, interactive communication is more effective than linear (ie. one-way) communication, and gain-framed messages appear to be more effective than loss-framed messages in terms of the persuasiveness of a message (Latimer et al., 2007; Rothman et al., in press). Finally, a combination of interpersonal and mass media communication is essential for creating more of an impact on health behaviour (Neuhauser & Kreps, 2003). Social media has the potential to address each of these elements for effective communication in health promotion.

Social media, or social networking, is a configuration of people connected to each other through interactive links that form online communities (Coyle & Vaughn, 2008). It is a way for people to interact, communicate and share information. The users, a term used to describe the people that use these sites, create a profile page where they can upload messages, videos and blogs and link their pages to their friends' pages, creating a social network. Users may also form groups based on common interests and ask their friends to join these groups. This process creates a haven for viral marketing (Freeman & Chapman, 2008), which can be leveraged to spread positive health behaviour messages. Although published research is limited due to its modernity, there is positive evidence that social media is effective in health behaviour change (Hartoonian, 2008).

The Advantages of Social Media

The evidence regarding the accessibility of social networking shows that it is ideal for reaching the general population. People can feel connected and experience a sense of support without the need for face to face interaction. The information is available 24 hours per day, 7 days per week, making it extremely accessible. It is an ideal way to communicate because busy people are able to trade information rapidly (Farhi, 2009). According to Kreps & Neuhauser (2010), the internet's vast scope and accessibility is

perfect for providing people with motivational information concerning healthy behaviours.

In today's technology-dependent world, most people have either heard of, visited, or even have an account of their own on a social networking site. As of January 2008, participation in social media had risen to the 'early majority phase' when an innovation is diffusing through a population. This means it has been accepted among the adopting culture as a viable method of communication (Deloitte, 2009; Livingston, 2008). Over 54% of Americans use social networking sites and 45% have their own profile (Internet World Stats, 2009). Facebook currently has more than 300 million active users, 50% of whom login on any given day. Participation rates continue to rise, with an average of 250 000 people registering daily (Facebook, 2009). MySpace and Twitter are also popular networks with 110 million and 50 million active users, respectively (Ostrow, 2009). Innovators and early adopters are currently taking advantage of this phenomenon: The Canadian Cancer Society, the American Medical Association and Weight Watchers are all examples of health organizations using these sites to disseminate information ("Facebook", 2009).

Social media's role in promoting positive health behaviours is also related to the origin of the information. Instead of receiving health promoting messages from experts, which might be inadvertently disempowering for some people, the messages come from within social networks, which include friends, family members, co-workers, or other social contacts (Kreps & Neuhauser, 2010; Neuhauser & Kreps, 2003; Smedley & Syme, 2000). Messages from close contacts may seem more positive, and thus be more effective.

According to Kreps & Neuhauser (2010), health behaviour change requires changing shared social practices. People's attitudes, values, and beliefs about health are a direct product of social interaction (Kreps & Neuhauser, 2010; Bunton et al., 1991). Social networking provides users the opportunity to connect to one another, which could thus prove favourable for positive health behaviour change. Social modeling and social influence also play a key role, since an individual's actions are affected by observing the behaviours of others. For example, curiosity may spark after observing a friend's post about a new training program which they enjoy. After trying the new program, this person might write about it on their own profile, thus enabling viral communication (VC) to their network connections. VC, also known as 'word of mouth marketing', is the passing of information from person to person. Because of the personal nature of the communication between users, the credibility of the subject is perceived to be superior to more formal forms of promotion methods (Grewal et al., 2003). Research also suggests that VC is more influential than traditional media channels (Cheema & Kaikati, 2010; Godes & Mayzlin, 2004; Herr et al., 1991). Marketing companies are taking advantage of these findings; for example, in hopes of creating buzz about the 2010 release of their new Fiesta model, Ford Motors gave away 100 of the cars to 100 bloggers for six months. In exchange for the cars, the bloggers posted monthly updates and videos about the cars on their social networking pages and on YouTube. So far, the 'Fiesta Movement' has proved to be favourable for Ford: there are a few hundred videos, pictures, blogs and tweets about the new car, and all but few are positive (Barry, 2009).

Social media offers an alternative to traditional methods of mass communication. A study by Coyle & Vaughn (2008) found that the average college student visits their social networking account three times per day, while it is estimated that most of the students had never visited a health organization's website. Health promotion agencies can increase the likelihood of reaching students by posting on a social networking site, rather than on a traditional government-run website.

The early adopters of social media innovations were predominantly teenagers; however, social networking sites have strategically targeted other age cohorts, as this innovation has diffused through the population. According to Facebook (2009), the fastest growing demographic of new users are people aged 35 and over. People aged 35-49 were also the largest single group of "tweeters" (people using Twitter) last year, making up approximately 42 percent of total users in February 2009 (Farhi, 2009).

Social networking websites actively try to attract and retain users; continually customizing according to the tendencies and preferences of their priority populations. For example, Facebook recently launched an application called "social ads" to provide advertisements based on the activities and preferences of the user and their friends. If the user were to write "baseball" as an interest on their profile page, then advertising related to sports equipment, merchandise, tickets, etc. would appear on their profile and their friends' profiles. These same strategies can be used in health promotion or other health interventions.

Social Media and Healthcare

Health promotion specialists are not the only professionals adopting social media as a means to reach the public. Social websites have been adopted by some doctors to disseminate simple information to their patients, eliminating waiting time and a trip to the clinic for many patients. As cited by Cohen (2009), Dr. J. James Rohack, president of the American Medical Association, was reported to have said that communication with existing patients online can add value to the patient-physician relationship. According to Korp (2006), health promotion mediated by the internet has enhanced opportunities for patients to be more actively engaged in their care, because patients who use this form of communication are more involved in coping with their problems and in communicating with their doctor, compared to those who did not use the internet as a communication mediator.

In a study by Manhattan Research (2009), it was reported that, as of January 2009, about 60% of physicians were already using or were interested in using physician online communities, a type of social networking used only for medical purposes. As a result, health care providers are able to update patients on relevant health news by directly delivering personalized messages, reminders and alerts. Of course, vigilance must be used, because some information exchange should not be managed online. Although it would be beneficial for activities such as prescription refills and answering simple health questions, social media would be inappropriate and not feasible for more demanding requests such as diagnostics and treatments, where face-to-face contact is required.

Applications for Public Health and Emergency Management

In public health promotion, social media sites allow individuals to benefit from easy access to preventive medicine information. The U.S. Preventive Medicine, for example, has social networking accounts on Facebook, Twitter and MySpace (U.S. Preventive Medicine, 2008). The Ottawa Health Decision Centre, in partnership with the Ottawa Health Research Institute, also recently launched a page on Facebook entitled “iShould” in hopes of providing decision aids to a vast population (Ottawa Health Decision Centre, 2009). Decision aids are tools that prepare patients for shared decision making with their healthcare professionals. They include the latest medical information, feedback from other patient’s decisions, and guidance in decision making. According to their research, patients who use decision aids are more informed, are more active in their treatment, know more about available alternatives, and chose treatments with features they value the most (Ottawa Health Decision Centre, 2009).

Another important application of social media is its ability to enable individuals and organizations to cooperate in all phases of emergency management: mitigation, preparedness, response and recovery (White et al., 2009). Social media provides a unique opportunity for the public to engage in critical public health issues, such as the H1N1 pandemic, where sharing of information, collaboration and interactivity are encouraged (U.S. Department of Health & Human Services, 2010). Emergency notification systems can utilize social media to distribute information because of the opportunities they hold: fast distribution, mass communication for large groups, low cost and ease of use, and international diversity (White et al., 2009). For example, Health Canada and the Public Health Agency of Canada both have their own pages on social media websites and use them to broadcast information on anything from preventable diseases and immunization to nutrition and product recalls (Health Canada, 2010; Public Health Agency of Canada, 2009). The American Center for Disease Control and Prevention (CDC) regularly updates its Facebook page to disseminate messages, videos, links, pictures and graphs to over 50 000 people (facebook.com, 2009). Social networking sites should therefore be considered as a viable tool in emergency management sectors.

Expected Benefits

Expected benefits of pairing social media and health promotion include widespread dissemination of information, customized and accessible information available to diverse audiences, easy connections to others for social support, and more intense and personal engagement and participation of the user because of the interactivity involved with social networking (Eng & Gustafson, 1999; Neuhauser & Kreps, 2003). The most influential advantage remains its cost-benefit feature; social media has the ability to reach an increasing number of people without the high cost of traditional marketing (Frick, 2006; Neuhauser & Kreps, 2003; Institute of Medicine, 2001a; National Research Council, 2000; Science Panel on Interactive Communication and Health (SPICH), 1999). Instead of spending significant funding to develop new websites or other tradi-

tional methods of communication, health promoters should exploit and take advantage of social media websites (Freeman & Chapman, 2008).

Health promotion mediated by social media, paired with other methods of communication, would be most beneficial: numerous studies have shown that multidimensional interventions and participant interactivity are most successful at reaching diverse audiences (Thomas, 2006). It is best to reach people multiple times, in multiple settings and from multiple sources (Neuhauser & Kreps, 2003). Social media has the potential to empower the user by putting more control in their hands, as compared to traditional methods of communication (Korp, 2006; Walch, 1999). Akesson *et al.* (2007) found that patients who used interactive health communication had enhanced knowledge, confidence, and health, and that their relationship with health professionals was reinforced due to the superior feeling of empowerment they felt.

Challenges and Limitations

One important challenge in using social marketing for health promotion is that unlike traditional marketing, where money is exchanged for a tangible item and the related benefits appear almost immediately, the benefits of positive health behaviour change are often not noticeable for a long time (McKenzie et al. 2009). For example, weight loss and a reduced risk of heart disease and diabetes are all expected benefits of improved knowledge in a nutritional content value. However, these benefits are not apparent right away and could therefore lead to short-term support.

Another limitation of social media pertains to the digital divide in the population. Socially disadvantaged groups often do not have access to new media and social networking due to language, literacy disability or other barriers (Korp, 2006). Also, when the server is down or when the internet connection is not available, participants are disconnected from the program and do not have access to the information available on these websites.

Another limiting factor relates to the authenticity of the information posted on social media sites. Readers need to be wary of the health information they encounter, because the users are in control, there is no filter to screen what information is posted. Several studies have shown moderate legitimacy of information on general health topics, even on websites identified as being 'credible' (Neuhauser & Kreps, 2003; Kunst et al., 2002). To ensure accuracy, quality and credibility of information, better evaluation methods need to be developed. The Government of Canada has created a Chief Information Officer Branch (CIOB) to provide "strategic direction and leadership for the government-wide pursuit of excellence in information management and information technology" (Treasury Board of Canada Secretariat, 2007). Amongst the many roles of the CIOB, they provide leadership in the application of social networking technologies by developing standards, guidelines and other tools to enable credibility and privacy protection of online media (Treasury Board of Canada Secretariat, 2007). The CIOB should therefore play a leading role in the evaluation process.

Furthermore, health professionals need to be strategic about their presence on social media sites. Because these sites offer tremendous opportunities to post information or create groups, health professionals must compete for user's attention. In September 2009 on Facebook, for example, only one credible sponsored group appears in the first 50 of 500+ results of the subject "quit smoking". A sponsored group is when an organization or company pays to have their group featured on the website (Freeman & Chapman, 2008). Health organizations can develop sponsored and free groups and pages to better attract viewers.

Because social media is a relatively recent phenomenon, evaluation methods are in the early stages of development. Additionally, it is still too early to tell if these sites will continue to flourish, since they depend on how vigilant users are about them (Landro, 2006). According to research by several marketing organizations, the explosive growth in social networking is expected to plateau by 2012 (Marketing Charts, 2009; Datamonitor, 2007). Rubel (2009) also suggests that Twitter's disorganization and superficiality are likely to make it short-lived and replaceable by the next new media craze. Research in the field of social media and health promotion should be increased, especially to determine its long-term effectiveness and potential influence on health improvement.

Concluding Comments

There is evidently encouraging information about the possibilities of using social media to improve access to health information and health care providers, as well as to promote positive health behaviour

change. New communication technologies offer opportunities to increase the availability of information, broaden the base of support groups, and actively engage people with relatively minimal cost (Abroms & Lefebvre, 2009). By increasing interaction and engagement, social media may complement traditional health promotion by raising awareness, spreading influence, and contributing to health behaviour change. It is essential that health organizations incorporate social media in their tailored communication strategies, to modernize their approaches and increase the likelihood of reaching different age groups.

References

Abroms, L. C., & Lefebvre, R. C. (2009). Obama's Wired Campaign: Lessons for Public Health Communication. *Journal of Health Communications, 14*(5), 415-423. doi: 10.1080/10810730903033000

Abroms, L. C., & Maibach, E. W. (2008). The Effectiveness of Mass Communication to Change Public Behavior. *Annual Review of Public Health, 29*, 219-234. doi: 10.1146/annurev.publhealth.29.020907.090824

Akesson, K. M., Saveman, B. I., & Nilsson, G. (2007). Health care consumers' experiences of information communication technology – a summary of literature. *Intl J Med Inform, 76*(9), 633-645. doi: 10.1016/j.ijmedinf.2006.07.001

Barry, K. (2009). Ford Bets the Fiesta on Social Networking. Retrieved from http://www.wired.com/autopia/2009/04/how-the-fiesta/

Canadian Institute for Health Information (CIHI), improving the health of Canadians: Promoting healthy weights, Report on the Canadian Population Health Initiative, CIHI: Ottawa, Canada, 2006

Cassell, M., Jackson, C., & Cheuvront, B. (1998). Health Communication on the Internet: An Effective Channel for Health Behavior Change? *Journal of Health Communication, 3*(1), 71-79

Cheema, A., & Kaikati, A. (2010). The Effect of Need for Uniqueness on Word of Mouth. *Journal of Marketing Research, 47*(3), 553-563. Retrieved from http://dx.doi.org/10.1509/jmkr.47.3.553

Cohen, E. (2009). Should you "friend" your doctor on Facebook? CNN Health. Retrieved from http://www.cnn.com/2009/HEALTH/09/03/friending.your.doctor/index.html

Coyle, C. L., & Vaughn, H. (2008). Social Networking: Communication Revolution or Evolution? Bell *Labs Technical Journal, 13*(2) 13-18. doi: 10.1002/bltj.20298

Danaei, G., Ding, E. L., Mozaffarian, D., Taylor, B., Rehm, J., Murray, C. J., & Ezzati, M. (2009). The Preventable Causes of Death in the United States: Comparative Risk Assessment of Dietary, Lifestyle, and Metabolic Risk Factors. *PLoS Medicine, 6*(4), e1000058. doi: 10.1371/journal.pmed.1000058

Deloitte Media Predictions, TMT Trends. (2009). Deloitte Touche Tohmatsu, 4-22.

Eng., T. R., & Gustafson, D. H. (1999). Wired for Health and Well-Being: The Emergence of Interactive Health Communication. Science Panel on Interactive Communication and Health. Executive Summary.

Facebook. (2009). *Facebook Statistics*. Retrieved from http://www.facebook.com/facebook?ref=pf#/press/info.php?statistics

Farhi, P. (2009). The Twitter Explosion. *American Journalism Review, 31*(3), 26-31. Retrieved from ajrarchive.org/Article.asp?id=4756

Freeman, B., & Chapman, S. (2008). Gone Viral? Heard the Buzz? A Guide for Public Health Practitioners and Researchers on how Web 2.0 Can Subvert Advertising Restrictions and Spread Health Information. *Journal of Epidemiology and Community Health, 62*(9), 778-782. doi: 10.1136/jech.2008.073759

Frick, K. D. (2006). Cost-effectiveness Studies of Behavior Change Communication Campaigns: Assessing the State of the Science and How to Move the Field Forward. *Journal of Health Communication, 11*(Suppl 2), 163-73. doi: 10.1080/10810730600974894

Hartoonian, N., Ormseth, S., O'Carroll Bantum, E., & Owen, J. (2008). Process and Outcome Evaluation of a Social Networking Website for Health Promotion. *Annals of Behavioral Medicine, B090*, s63

Grewal, R., Cline, T. W., & Davies, A. (2003). Early-Entrant Advantage, Word-of-Mouth Communication, Brand Similarity, and the Consumer Decision-Making Process. *Journal of Consumer Psychology, 13*(3): 187-197. doi:

10.1207/S15327663JCP1303_01

Godes, D. & Mayzlin, D. (2004). Using Online Conversations to Study Word-of-Mouth Communication. *Marketing Science, 23*(4), 545-560. Retrieved from http://dx.doi.org/10.1287/mksc.1040.0071

Health Canada. (2001). Providing the Public with Reliable Health Information: A Key Priority for Health Canada. Healthcare Information Management & Communications Canada, Vol. XV, No.4, 3rd Quarter.

Health Canada. (2005). Office of Health and the Information Highway. Retrieved from http://www.hc-sc.gc.ca/hcs-sss/pubs/ehealth-esante/

Health Canada (2010). Social Media: Stay Connected. Retrieved from http://www.hc-sc.gc.ca/home-accueil/sm-ms/index-eng.php

Internet World Stats. (2009).Usage and Population Statistics. Retrieved from http://www.internetworldstats.com/stats.htm

Korp, P. (2006). Health on the Internet: Implications for Health Promotion. *Health Education Research, 21*(1), 78-86. doi: 10.1093/her/cyh043

Kreps, G. L., & Neuhauser, L. (2010). New directions in eHealth communication: Opportunities and Challenges. *Patient Education and Counseling, 78*(3), 329-336. doi: 10.1016/j.pec.2010.01.013

Latimer, A. E., Salovey, P., & Rothman, A. J. (2007). The Effectiveness of Gain-Framed Messages for Encouraging Disease Prevention Behavior: Is All Hope Lost? *Journal of Health Communication, 12*(7):645-649.

Landro, L. (2006). The Informed Patient: Social Networking Comes to Health Care; Online Tools Give Patients Better Access to Information and Help Build Communities. Wall Street Journal. Retrieved from http://www.wsj.com/articles/SB116717686202159961

Mangunkusumo, R. T., Brug, J., Duisterhout, J. S., de Konin, H. J., & Raat, H. (2007). Feasibility, acceptability, and quality of Internet-administered adolescent health promotion in a preventive-care setting. *Health Education Research, 22*(1):1-13. doi: 10.1093/her/cyl010

Manhattan Research, LLC. (2009). Physician Online Communities: Physician Social Networking and the New Online Opinion Leaders. Retrieved from http://www.manhattanresearch.com/products/Research_Modules/Physician/physician-online-communities.aspx

Marketing Charts. (2009). Social Networking's Explosive Growth to Plateau in Five Years, Watershed Publishing. Retrieved from www.marketingcharts.com

McKenzie, J. F., Neiger, B. L., & Thackeray, R. (2009) *Planning, Implementing, & Evaluating Health Promotion Programs*. United States: Benjamin Cummings.

Neuhauser, L., & Kreps, G. L. (2003). Rethinking Communication in the E-health Era. *Journal of Health Psychology, 8*(1): 7-23.

Ostrow, A. (2009). Mashable: The Social Media Guide. Retrieved from http://mashable.com/

Ottawa Health Decision Centre. (2009). Patient Decision Aids. Ottawa Health Research Institute. Retrieved from http://decisionaid.ohri.ca/index.html

Pew Research Center. (2009). The Shared Search for Health Information on the Internet, Pew Internet & American Life Project.

Public Health Agency of Canada. (2009). Stay informed, stay connected! Mobile and Social Media Tools. Retrieved from http://www.phac-aspc.gc.ca/sm-ms/index-eng.php

Rubel, S. (2009). Twitter is Peaking; Get Ready to Follow the Geeks Onward. *Advertising Age, Communication and Mass Media Complete, 80*(13), 15

Thomas, R. K. (2006). Health Communication: Traditional Approaches to Health Communication, Chapter 9, pg. 119-131. doi: 10.1007/0-387-26116-8_9

Treasury Board of Canada Secretariat. (2007). Government of Canada, Chief Information Officer Branch. Retrieved from www.tbs-sct.gc.ca

U.S. Department of Health & Human Services. (2010). Social Media, Flu.com Know what to do about the flu. Retrieved from www.flu.gov

U.S. Preventive Medicine. (2008). Retrieved from http://www.uspreventivemedicine.com

White, C., Plotnick, L., Kushma, J., Hiltz, S. R., & Turoff, M. (2009). An Online Social Network for Emergency Management. 6th International ISCRAM Conference.

Discussion of Bisphenol A as an Environmental Endocrine Disruptor: The Low Dose Effect and Governmental Regulations Concerning its Use and Disposal: A Literature Review

Derek MCLELLAN* [1]

[1] Student, University of Ottawa, Canada

** Auteur(e) correspondant | Corresponding author*: N/A

Abstract:

The disruptive and potentially harmful effects of naturally occurring and man-made endocrine disrupting compounds found in the environment are a topic of considerable debate within government, industry and the general public. Bisphenol A (BPA) is of particular concern due to its incorporation in many consumer products and its potential for leeching. Scientific study continues with attempts to identify and quantify risk associated with this chemical, in order to support industry and regulatory actions. The issue of greatest concern with regards to BPA is the effects of routine exposure to very low concentration of the chemical. The effects of this phenomenon, called Low Dose Effects, raise a great deal of controversy as it is difficult to accurately assess the health outcomes from these exposures. This paper gives a basic understanding of what constitutes Low Dose effects and also examines several studies conducted to determine the health outcomes as a result of exposure to low dose BPA.

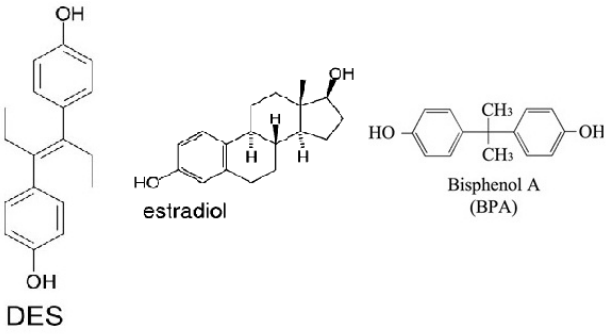
Regulatory activities seek to mitigate risk through enactment of legislation to control the use of and exposure to these compounds. As a result the regulatory agencies in Canada and the U.S. have banned the sale of certain consumer products containing BPA and have imposed strict limits on concentration in industrial effluents and waste water drainage. This paper outlines the conditions and limits put in place by both the Canadian and U.S. government regarding the presence of BPA in effluents and consumer products.

Keywords: Endocrine disruption, male infertility, low dose effect

Introduction

The subject of endocrine disrupting chemicals is currently one of the more controversial issues in environmental toxicology. The prospect that humans are constantly being exposed in the environment to natural and artificial chemicals that modulate the way the endocrine system works (and by extension many other systems in the body) is a troubling thought. One of the most important concerns is the effects this is having on human reproduction. As perceived decreases in sperm counts and increases in infertility (defined as the inability to produce pregnancy while in a stable relationship and engaging in sexual intercourse without contraception for greater than a year (Pflieger-Bruss, Schuppe, & Schill, 2004)) continue to be published, the theories that this may be due to endocrine modulators are increasing in popularity. (Richter et al., 2007) Therefore, increases in research and regulations regarding these chemicals are imperative to ensuring the health of the public. Bisphenol A is a chemical of particular concern due to its presence in many consumer products and also the large number of contradictory results among studies. Along with Diethylstilbestrol (DES), a known estrogenic toxin, BPA has a chemical structure very similar to that of natural estradiol and this is important in considering the possible affects of exposure to this chemical.

Figure 1 The similar chemical structures of Diethylstilbestrol and Bisphenol A as compared to Estradiol result in their estrogen mimicking activity at the body's estrogen receptors. ((Morais-de-Sa, Pereira, Saraiva, & Damas, 2004) (Hashimoto, Okada, & Imaoka, 2008)(Zhao et al., 2007))



A review of several studies (discussed in the Low Dose Effect section) illustrates the ongoing controversy surrounding the issue of exposure to endocrine disrupting chemicals and more importantly the effects of low dose exposures. (vom Saal & Hughes, 2005) Focusing on the issue of the low dose effect, five studies are analyzed that propose either the finding of adverse effects or the lack thereof as a result of exposure of mice or rats to BPA at low doses. While DES is an endocrine disrupting chemical, it can not be considered alongside BPA as it has well documented toxic effects, and as such it is used in all of the studies discussed as a positive control for adverse effects of exposure. The controversial topics of what a low dose is, the concept of environmentally relevant doses (Richter et al., 2007), appropriate animal model selection (Pflieger-Bruss et al., 2004), the need for positive control groups (vom Saal & Hughes, 2005), and the influence of funding sources (vom Saal & Hughes, 2005) are examined in the analysis of these journal articles. The conclusion that there are in fact adverse health effects related to low dose or environmentally relevant exposures is becoming a more prominent finding but still demands significant further research to reinforce this finding. (vom Saal & Hughes, 2005)

Finally, the details of current governmental regulations regarding these chemicals are discussed. Canada was the first country to perform an in depth risk assessment and subsequently place various bans on the use, sale, import and disposal of BPA and DES. The restrictions on BPA placed by both governments focus specifically on the sale of BPA containing consumer products (i.e. Baby bottles), and the BPA levels found in industrial effluents and waste water. (Health Canada, 2008) With regards to DES, there have been long standing restrictions limiting the use of this drug to only non-food producing animals and even then it is highly regulated. (Health Canada, 2003b) Both Canada and the United States have extensive regulations with regards to BPA and DES and are pressing for continued research on the subject.

The Low Dose Effect

The most controversial issue surrounding the potential human health effects of endocrine disrupting chemicals is the topic of the low dose effect.(vom Saal & Hughes, 2005) Low dose commonly refers to a dosage used in studies that would be considered environmentally relevant. (Richter et al., 2007) In other words, doses resulting in test animal serum levels of the endocrine-disrupting chemical being similar to those observed in human serum from routine environmental exposure. (Richter et al., 2007) This dose is determined based on the usual reference dose and the governmentally set "safe dose". (vom Saal & Hughes, 2005) The standard reference dose or lowest observed adverse

effect level (LOAEL) for BPA prior to 1997 was 50mg/kg/day for studies involving rats. (Richter et al., 2007) This value is contested based on evidence that effects can be observed at much lower concentrations. (vom Saal & Hughes, 2005) The U.S. Environmental Protection Agency's (EPA) "safe dose" limit for BPA is set by dividing the LOAEL by 3 log factors or safety factors (i.e. 1000), which gives a value of 50µg/kg/day based on the pre-existing reference dose. (Richter et al., 2007) The issue with BPA is that studies have been published with both no observed effects and significant observed effects in both mice and rats for dosages below the "safe dose". (Pflieger-Bruss et al., 2004)

A review published in 2005, (vom Saal & Hughes, 2005) discusses the existence of both results in published studies but proceeds to make several important points regarding the proportions of the opposing results. In the review by vom Saal(vom Saal & Hughes, 2005), the author discusses a large inconsistency in the data with regards to the source of funding for each study. Vom Saal *et al.* contend that of the studies published at the time of their publication, all those that were funded by industry sources found no effects for low dose exposures. Conversely, the authors point out that of the studies funded by the government, greater than 90% found significant observable effects from low dose exposures to BPA.

Table 1 Source of funding and results of low dose BPA studies. Also compared based on CD-SD rat use as an animal model; due to its low sensitivity to BPA this may affect results. (vom Saal & Hughes, 2005)

	All studies		CD-SD rat studies		All studies except CD-SD rats	
Source of funding	**Harm**	**No harm**	**Harm**	**No Harm**	**Harm**	**No Harm**
Government	94 (90.4)	10 (9.6)	0 (0)	6 (100)	94 (96)	4 (4)
Chemical corporations	0 (0)	11 (100)	0 (0)	3 (100)	0 (0)	8 (100)

Values shown are no. (%)

As shown by the above table the proportion of results that observed harmful effects from low dose BPA exposures far outweigh the number of studies that had the opposite finding.

A review of 4 other low dose BPA studies revealed similarly conflicting results. A study completed by Pflieger-Bruss *et al.* (2004)outlined the common effects of xeno-estrogen compounds, (i.e. BPA and DES) in animal studies as hypospadias, cryptorchidism, decreased sperm count and testicular tumours. This study went on to compare peri- and post- natal exposures to BPA at low doses (2.4µg/Kg/day) in rats, with the observed results being reduced serum leutenizing hormone and testosterone in the postnatally exposed animals and reduced testosterone in adulthood for the perinatally exposed rats. (Pflieger-Bruss et al., 2004)A high dose (300µg/Kg/day) was also administered to the rats with no observed effect.(Pflieger-Bruss et al., 2004) Ultra low dose (0.1µg/Kg/day) tests were also conducted using mice exposed for 28 straight days, with the following results: decreased testicular and epididymal sperm counts, and decreased weights of the testes and seminiferous vesicles. (Pflieger-Bruss et al., 2004)

Two of the other studies reported opposing findings in rats and mice respectively.(Cagen,et al., 1999b)(Cagen, et al., 1999a) The study conducted on rats (Cagen et al., 1999b), used an oral dosing method via the animals' drinking water. Test groups were set up with 0 (control), 0.01, 0.1, 1.0, and 10 ppm of BPA dissolved in their drinking water. A positive control group was also tested using 0.1 ppm DES. Female mice were given these dosages for a period of 7 weeks, starting 2 weeks prior to mating and continuing through to 22 days of lactation. (Cagen et al., 1999b) The males and offspring were not dosed.(Cagen et al., 1999b) Offspring from the F1 generation were sacrificed at 90 days and tissues were analyzed with the following results: BPA exposed rats showed no effects on growth, survival or reproductive parameters (including weights of testes, prostate and preputial gland; sperm count; daily sperm production and testes histopathology). (Cagen et al., 1999b) The DES exposed rats showed a decrease in body weight, body weight change and food consumption in the adult female rats, as well as a decrease in the number of pups per litter and an increase in gestational length. (Cagen et al., 1999b)

The second study with a result of no effect was also published by Cagen *et al.* (1999a) but this study was conducted with mice in lieu of the previously tested rats. A different method of administration was also used in this study. The maternal mice were given oral deposit doses of 0.2, 2, 20 and 200 µg/Kg/day of BPA and a positive control group was given 0.2µg/Kg/day of DES.(Cagen et al., 1999a) These doses were given on gestational days 11 through 17 and the pups of the F1 generation were sacrificed at 90

days old.(Cagen et al., 1999a) Tissue collection and analysis revealed no significant dose response in the BPA test groups.(Cagen et al., 1999a)

The last publication reviewed was itself a review of several studies that found dose response effects from low dose BPA exposures. (Richter et al., 2007) It emphasized several common issues with low dose BPA studies, those being: the selection of appropriate animal strain, the use of a positive control, and the relevance of the dosing method. (Richter et al., 2007) As outlined in the vom Saal and Hughes (2005) article, this article discussed the possible effects of an inappropriate animal model for this type of study. For example CD-SD rats have much lower sensitivity to estrogenic compounds and would therefore register no observed effects in low dose BPA studies where other strains of rat may produce significant dose response effects. (Richter et al., 2007) This consideration must be heeded in order for any study on low dose BPA effects to have significant validity. (vom Saal & Hughes, 2005) In order to determine a strain's sensitivity to estrogenic compounds with hopes of validating the results of a low dose exposure study, a positive control must be used (vom Saal & Hughes, 2005).

DES and Ethynylestradiol are commonly used as positive controls in BPA or other estrogenic compound exposures as they have well characterized and replicated adverse effects. (Odum et al., 2002)(Richter et al., 2007) Despite their known ability to cause dose response effects, it is still necessary to consider if the method of dosing is appropriate with the positive control chemicals as well as the experimental chemical. Certain chemicals can be more or less biologically active depending on the route of administration, as with ethynylestradiol which has a low bioactivity if administered orally. (Richter et al., 2007) It is also important to consider method of dosing with regards to environmental relevance, as this can affect validity of the results when compared to normal human exposure. (Richter et al., 2007) For example, oral administration (such as: oral deposit, oral gavage, drinking water) represents a much more accurate model of regular human exposure and allows for more accurate results given that the drugs will be undergoing the same metabolic processes in the animal models as they would if ingested by a human. (National Toxicology Program (U.S.), 2008) This is an important consideration that adds to the validity of a study.

In conclusion, as a small sample of the numerous studies out there, the five articles reviewed provide compelling evidence to both support and refute the evidence that low dose BPA exposure can have adverse effects on human health. While there appears to be more evidence in support of the argument that there are observable effects at and below the "safe dose", more testing is surely needed prior to these findings being considered absolute. The other considerations voiced by these articles, including appropriate animal model and route of exposure, should also be further tested to determine the most biologically relevant methods to use for a study on the effects of estrogenic endocrine disruptors, specifically BPA.

Governmental Regulations

As testing continues on the effect of environmental endocrine disruptors on the various physiological systems of the human body, government agencies have begun to take notice of the potential for possible health risks and have responded accordingly. In 1996 the U.S. Food Quality Protection Act

contained amendments to the U.S. Federal Food, Drug and Cosmetic Act and amendments were also made that year to the Safe Drinking Water Act. (Stokes, 2004)These amendments require that the U.S. Environmental Protection Agency (EPA) implement the new laws to monitor the endocrine disrupting effects of new chemicals. (Stokes, 2004) In 1998 the EPA proposed the Endocrine Disruptor Screening Program (EDSP) to satisfy these conditions. (Stokes, 2004) The EDSP outlines how the EPA uses both in vitro and in vivo testing to identify chemicals that might adversely affect humans and ecologically important species. (Stokes, 2004)

Bisphenol A is a chemical commonly used in the production of polycarbonate plastics and resins. (National Toxicology Program (U.S.), 2008) Polycarbonate plastics are used to make a wide range of consumer products including: water and infant bottles, impact-resistant safety equipment, compact disks and even some medical equipment. (Stokes, 2004) It is also used in the canning process to generate the protective epoxy coating inside canned food containers to prevent contamination arising from leaching of the metal container into the food (Pflieger-Bruss et al., 2004). This widespread use increases the potential for human exposure on a regular basis. (Richter et al., 2007) As a result, in 2008 Canada became the first country in the world to perform a risk assessment on BPA with the participation of industry and other stakeholders, as well as to conduct a 60 day public comment period on the decision to

ban certain BPA containing products. (Health Canada, 2008) Based on the findings that there were some minor health risks associated with BPA containing baby bottles as well as the public concerns gathered during the comment period, the Canadian government banned the import, sale and advertisement of BPA containing polycarbonate baby bottles in June 2009. (Health Canada, 2009; Health Canada, 2009) In addition to this ban, regulations have been proposed and are under review in a response to the findings that significant amounts of BPA were being found in wastewater and sludge treatment plants. (Health Canada, 2008) These proposed regulations limit the amounts of BPA effluent that is allowed to enter the environment from an industrial source. (Environment Canada, 2009)This limit will be 1.75µg/L in the industrial effluent released from any facility with the exception of wastewater from the treatment of intake water. (Environment Canada, 2009) The proposed implementation date of this regulation is no later than April 2011. (Environment Canada, 2009)

Diethylstilbestrol is a synthetic estrogen used in both human and animal medicine. From 1948 to 1977 DES was used in France to prevent miscarriage and pregnancy related bleeding in pregnant women. (Health Canada, 2003a) Diethylstilbestrol was subsequently recognized as a genotoxin and carcinogen to both humans and animals. (Health Canada, 2003b) As a result, the following regulations were created in Canada: prohibition of the sale of DES or other stilbene compounds for administration to food producing animals; prohibition of the sale of animals treated with these drugs for use as food; prohibition of the sale of food products from animals treated with these drugs; and prohibition of the sale of food products containing residues of these drugs. (Health Canada, 2003b) A full prohibition of the sale of DES and other stilbene compounds was proposed, but there is still sufficient use of these drugs in a veterinary context to prevent this. For example Diethystilbestrol is still used as an effective veterinary treatment for estrogen responsive incontinence in spayed female dogs and to prevent pregnancy in dogs and cats. (Health Canada, 2003b)

In conclusion, both Canada and the United States have imposed strict regulations on the use, content and disposal of BPA in consumer products and waste by-products based on preliminary results concerning its effects on human health. Further research is needed to fully understand the hazardous nature of this chemical in order to be able to set regulatory limits that protect against possible adverse health effects, with special attention to possible low dose effects. As a well characterized hazardous chemical, the strict regulations against the use of DES appear to protect the public from its adverse health effects, while still allowing for its limited range of beneficial uses. DES maintains its uses in veterinary medicine and laboratory testing as a positive control. As more evidence develops on the effects of low dose exposures to BPA, a review of the current regulations will be needed to ensure the ongoing protection of the public against the endocrine disrupting effects of this chemical.

References

Cagen, S. Z., Waechter, J. M., Dimond, S. S., Breslin, W. J., Butala, J. H., Jekat, F. W., ... Harris, L. R. (1999a). Normal reproductive organ development in CF-1 mice following prenatal exposure to bisphenol A. *Toxicological Sciences : An Official Journal of the Society of Toxicology, 50*(1), 36-44.

Cagen, S. Z., Waechter, J. M.,Jr, Dimond, S. S., Breslin, W. J., Butala, J. H., Jekat, F. W., ...Harris, L. R. (1999b). Normal reproductive organ development in wistar rats exposed to bisphenol A in the drinking water. *Regulatory Toxicology and Pharmacology, 30*(2 Pt 1), 130-139. doi: 10.1006/rtph.1999.1340

Environment Canada. (2009). Canadian environmental protection act: Environmental registry: Consultation document bisphenol A. Retrieved December 1, 2009, from http://www.ec.gc.ca/ceparegistry/documents/participation/pba/p5.cfm

Hashimoto, S., Okada, K., & Imaoka, S. (2008). Interaction between bisphenol derivatives and protein disulphide isomerase (PDI) and inhibition of PDI functions: Requirement of chemical structure for binding to PDI. *Journal of Biochemistry, 144*(3), 335-342 . doi: 10.1093/jb/mvn075

Health Canada. (2003a). Advisory on diethylstilbestrol (DES) and the risk of genital and obstetrical complications. Retrieved December 1, 2009, from http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/_2003/des_hpc-cps-eng.php

Health Canada. (2003b). Part II canada gazette - food and drug regulations: Project number 1227 (prohibition of certain veterinary drugs). Retrieved December 1, 2009, from http://www.hc-sc.gc.ca/dhp-mps/vet/legislation/acts-lois/cg-gc_part2-eng.php

Health Canada. (2008). Government of canada takes action on another chemical of concern: Bisphenol A. Retrieved December 1, 2009, from http://www.hc-sc.gc.ca/ahc-asc/media/nr-cp/_2008/2008_59-eng.php

Health Canada. (2009). Government of canada protects families with bisphenol A regulations. Retrieved December 1, 2009, from http://www.chemicalsubstanceschimiques.gc.ca/challenge-defi/batch-lot-2/bisphenol-a/index-eng.php

Morais-de-Sa, E., Pereira, P. J., Saraiva, M. J., & Damas, A. M. (2004). The crystal structure of transthyretin in complex with diethylstilbestrol: A promising template for the design of amyloid inhibitors. *The Journal of Biological Chemistry, 279*(51), 53483-53490. doi: 10.1074/jbc.M408053200

National Toxicology Program (U.S.). (2008). NTP-CERHR monograph on the potential human reproductive and developmental effect of bisphenol A. United States: National Institute of Health, U.S. Department of Health and Human Services.

Odum, J., Lefevre, P. A., Tinwell, H., Van Miller, J. P., Joiner, R. L., Chapin, R. E.,... Ashby, J. (2002). Comparison of the developmental and reproductive toxicity of diethylstilbestrol administered to rats in utero, lactationally, preweaning, or postweaning. *Toxicological Sciences: An Official Journal of the Society of Toxicology, 68*(1), 147-163. doi: 10.1093/toxsci/68.1.147

Pflieger-Bruss, S., Schuppe, H. C., & Schill, W. B. (2004). The male reproductive system and its susceptibility to endocrine disrupting chemicals. *Andrologia, 36*(6), 337-345. doi: 10.1111/j.1439-0272.2004.00641.x

Richter, C. A., Birnbaum, L. S., Farabollini, F., Newbold, R. R., Rubin, B. S., Talsness, C. E.,... vom Saal, F. S. (2007). In vivo effects of bisphenol A in laboratory rodent studies. *Reproductive Toxicology, 24*(2), 199-224. doi: 10.1016/j.reprotox.2007.06.004

Stokes, W. S. (2004). Selecting appropriate animal models and experimental designs for endocrine disruptor research and testing studies. *ILAR Journal / National Research Council, Institute of Laboratory Animal Resources, 45*(4), 387-393. doi: 10.1093/ilar.45.4.387

vom Saal, F. S., & Hughes, C. (2005). An extensive new literature concerning low-dose effects of bisphenol A shows the need for a new risk assessment. *Environmental Health Perspectives, 113*(8), 926-933. doi: 10.1289/ehp.7713

Zhao, L., Jin, C., Mao, Z., Gopinathan, M. B., Rehder, K., & Brinton, R. D. (2007). Design, synthesis, and estrogenic activity of a novel estrogen receptor modulator--a hybrid structure of 17beta-estradiol and vitamin E in hippocampal neurons. *Journal of Medicinal Chemistry, 50*(18), 4471-4481. doi: 10.1021/jm070546x

The Environmental Causes of Cancer: A Literature Review

Premal PATEL* [1], James GOMES [2]

[1] Student, University of Ottawa, Canada
[2] Professor, University of Ottawa, Canada

** Auteur(e) correspondant | Corresponding author*: N/A

Abstract:

Social media holds considerable potential for health promotion and other health intervention activities, as it addresses some of the limitations in traditional health communication by increasing accessibility, interaction, engagement, empowerment and customization. The use of social media increases the potential for easy access to preventive medicine, interaction with health care providers, interprofessional communication in emergency management, and public health. However, more research is needed to determine its long term effectiveness and to maximize the strategic presence of health organizations on social networking websites. This paper provides encouraging information about the possibilities of using social media to improve access to health information and health care providers, as well as to promote positive health behaviour change. It is essential for health promotion organizations to capitalize on the opportunities provided by social media, in order to modernize strategies to reach all age groups and to tailor programs to current communication trends, all of which are offered at a relatively low cost.

Keywords:

Social media, social networking, health promotion, health communication, online health information, emergency management, interprofessional communication

Introduction

Cancer is a multifactorial disease with a long latency and except for a few cancers the risk factors remain to be identified and the etiological relationship remains to be explored. Risk factors can include lifestyle, dietary habits, infections, environmental contaminants, pollution, occupational hazards, and others (Boffetta & Nyberg, 2003). Environmental factors are also believed to risk factors; however, these hazards have been largely overlooked until recently. The difficulty lies in the fact that there are many contaminants in the environment which can influence our health and wellbeing, and their impact on health remains to be documented. Furthermore, the definition of environment is still debatable; some arguing for the broad approach and others suggesting the narrow approach. Some definitions include lifestyle and dietary habits whereas others use a strict definition of contaminants outside the human body. These differences in the definitions change the environmental attributable fraction of cancer.

The World Health Organization (WHO) has stated that roughly 19% (12%-29%) of all cancers are attributable to the environment, which is equivalent to 1.3 million deaths each year (WHO, 2006). In the developed countries, it was estimated that 16% (10—34%) of cancers in men (other than lung cancers), and 13% (10—23%) in women, are attributable to the environment (WHO, 2006). In the developing countries, the corresponding attributable fractions are 18% (10—45%) in men and 16% (10—35%) in women. The uncertainty surrounding these estimates is due to the fact that evidence linking specific environmental and occupational exposures to various cancers is incomplete (WHO, 2006).

In developing countries, the attributable environmental fractions were 33% (6—65%) for men, and 25% (6—37%) for women (WHO, 2006). It was estimated that environmental factors account for 31% of the global disease burden of lung cancer and 30% (6—55%) of the disease burden in developed countries, for both men and women (WHO, 2006). Other studies assessing the environmental attributable fraction of cancer have reported lower estimates. Health Canada estimates that only 10-15% of cancers are linked the environment (Boyd & Genius, 2008). Whereas, other studies have shown the environmental fraction in Canada to be 5-15%, however, this is due to a narrower definition of environmental risk factor than the WHO (Boyd & Genius, 2008). It was estimated that 15.6% of the worldwide incidence of cancer in 1990 could be attributed to infection, however, the range is quite disperse as 10% of cancer is attributable infections in high income countries whereas up to 25% in Africa (Belpomme et al., 2007).

The purpose of this review is to examine and evaluate the scientific literature on environmental cancers and identify potential environmental risk factors and calculate environmental attributable fraction of human cancer. This study reviews the environmental causes of cancer.

Methodology

The first task in this study was to examine the different definitions of the environment. The working definition adopted by several agencies was searched including the Canadian Cancer Society, National Institute of Health Sciences, International Agency on the Research of Cancer (IARC), Environmental Protection Agency (EPA) and the World Health Organization (WHO).

Broad Definition

The National Institute of Health Sciences uses a broad definition that incorporates lifestyle factors, dietary habits, exposure to agents in the ambient environment and in the workplace (Cancer and the Environment, 2003).

Narrow Definition

The WHO applies a narrow definition to the term “environment”. This includes only the physical, chemical and biological factors that are external to the human host, and all related behaviors, but excluding those natural environments that cannot reasonably be modified (Prüss-Üstün & Corvalán, 2006). For the purposes of this study we have adopted the WHO definition of “environment”.

The following databases were searched for this study: Pubmed, Embase, Scopus, and Toxline. The search terms used to retrieve the articles were “environmental cancers, attributable fraction, environment and cancer, environmental burden of cancer”. All articles were then collated and compiled in Refworks. The articles were examined for compatibility with the inclusion and exclusion criteria. All the articles were assessed by reading the title, abstract and the body of the text. Data abstraction was carried out for all

the articles selected for inclusion in this review.

Inclusion Criteria

The following inclusion criteria were used to screen potential studies using the article titles and abstracts:

1. Review articles and original research articles were selected.

2. The term environment defined by the WHO was considered as relevant. Therefore articles focusing on indoor and outdoor air contaminants, contamination of water and food, electromagnetic fields were included

3. Articles on environmental causes of cancer were also included.

Exclusion Criteria

The following exclusion criteria were applied to screen articles that were not relevant for this review:

1. All studies that did not focus on environment and cancer.

2. The definition of the term "environment" that did not include the WHO terms of reference.

3. Studies that did not describe the etiological relationship between environmental factors and cancer.

Results & Discussion

A number of cancers were identified as etiologically associated with environmentally related risk factors. A list of these cancers and the related etiological agent is shown in Table 1. A narrative of this relationship between cancer and

Table 1 Environmental cancers and associated etiological agents

Cancer	Environmental Agent	Cancer	Environmental Agent
Bladder Cancer	Environmental exposure to arsenic. (Boyd & Genius, 2008) Arsenic oxides if inhaled or ingested. (Belpomme et al. 2007)	Lymphoma	Possibly HIV-related Kaposi's sarcoma (WHO, 2006), increased relative risk - indoor Volatile Organic Compound exposure, Indoor use of insecticides (Irigaray et al. 2007)
Cervical	Human papilloma viruses (WHO, 2006)	Melanoma	Possibly UV exposure. (WHO, 2006)
Childhood leukemia	Extremely low-frequency electromagnetic fields (Boyd & Genius, 2008)	Non-Hodgkin's lymphoma	Pesticides and triple the risk (Boyd & Genius, 2008)
Childhood Cancer	In-utero exposure to industrial chemicals, particularly those produced by fossil fuel combustion.	Kidney Cancer	Chromium or Nickel (Irigaray et al. 2007)
Leukemia	Indoor Volatile Organic Compound exposure, Indoor use of insecticides (Irigaray et al. 2007)	Skin Cancer	Asbestos in drinking water (WHO, 2006), environmental exposure to Arsenic and UV radiation. (Boyd & Genius, 2008)
Liver Cancer	Aflatoxins in food, Arsenic oxides if inhaled or ingested. (Belpomme et al. 2007)	Stomach Cancer	Helicobacter pylori, transmission may be facilitated by poor sanitation and crowding. (WHO, 2006)
Lung Cancer	Environmental tobacco smoke, radon, asbestos, chromium, nickel, cadmium, (WHO, 2006) environment exposure to arsenic, particulate air pollution, polycyclic aromatic hydrocarbons. (Boyd & Genius, 2008), Arsenic oxides if inhaled or ingested (Belpomme et al. 2007)	Prostate	Cadium (Irigaray et al. 2007)

respective etiological agents is provided below.

Lung Cancer

Environmental Tobacco Smoke (ETS): ETS is associated with lung cancer and a number of studies support this relationship. The attributable fraction of lung cancer from ETS in those who never smoked and in those who were ex-smokers has been estimated to be 16-24% (Irigaray et al., 2007). A similar study among the residents in Western countries attributed 20-30% of lung cancer to ETS in those residents (Bukowski & Wartenberg, 1997). Boffetta (2002) assessed the incidence of lung cancer each year from ETS with an assumed Relative Risk (RR) of 1.2-1.3; this yielded 300 in Canada, 3000 in the United States and 1100 in the European Union (Boffetta, 2002).

Outdoor Air Pollution: The attributable fraction of lung cancer from traffic-related air pollution in those who never smoked and those who were ex-smokers was estimated to be 5-7%, as reported by Belpomme et al., 2007. Long term exposure to particulates and polycyclic aromatic hydrocarbons in adults is reported to increase the risk of lung cancer mortality by 8%, after controlling for tobacco smoke (Irigaray et al., 2007).

Indoor Air Pollution: A case control study in the Northern Province of South Africa, assessed lung cancer among women using wood or coal as main fuel at home. The increased risk of lung cancer was reported at 1.4 (95% CI 0.6 –3.2) (Boffetta & Nyberg, 2003). Another study conducted in the Los Angelos area in 1981-1982 looked at cancer rates among white women that use coal for cooking and heating in the home during childhood and adolescence. This study reported an odds ratio of 2.3 (95% CI 1.0–5.5) for adenocarcinoma and 1.9 (95% CI 0.5–6.5) for squamous cell cancer (Boffetta & Nyberg, 2003).

Radon: Low radon levels in the home environment are the cause of approximately 10% of lung cancers (Belpomme et al., 2007). The estimated indoor radon exposure was estimated to be 59 Bq/m3 which was determined by a population-weighted average of 29 studies. This radon exposure level would result in an attributable fraction of 4.5% for lung cancers (Boffetta, 2006).

The estimated lung cancer mortality in the United States due to radon and its decay products is 20,000 or more. This value corresponds to roughly 10% of all lung cancer cases in the U.S. The average radon exposure to a U.S. single- family home is 40 Bq/m3, this could result in an excess lung cancer risk exceeding 1 in 1,000, with higher exposure levels causing a risk in excess of 1 in 100 (Bukowski & Wartenberg, 1997).

Mesothelioma

Asbestos: Approximately 5% of the European population is believed to be exposed to residential asbestos according to the WHO. Although, according to Boffetta (2005) the studies selected for the meta-analysis were conducted with populations with high levels of exposure and a more reasonable estimation is in the order of 2% (Boffetta, 2005). A meta-analysis study estimated the RR of mesothelioma from environmental exposure to asbestos at 3.5 (95% CI 1.8–7.0). The corresponding RR to lung cancer was 1.1 (95% CI 0.9–1.5) (Boffetta & Nyberg, 2003). These results indicate that with a prevalence of exposure of 5% would lead to an incidence of 425 mesothelioma cases in men and 56 in women, and; a corresponding incidence of 771 lung cancers in men and 206 in women in the European Union (Boffetta & Nyberg, 2003).

A review and meta-analysis to assess the risk of pleura mesothelioma from environmental (household and neighbourhood) exposure to asbestos indicated an increased risk. The RRs of pleural mesothelioma for household exposure ranged from 4.0 to 23.7 and the summary risk estimate was 8.1 (95% CI 5.3-12) (Bourdès et al., 2000). For neighborhood exposure, RRs ranged between 5.1 and 9.3 (with a single RR of 0.2) and the summary estimate was 7.0 (95% CI 4.7-11). These results indicate an increased risk of pleura mesothelioma from high environmental asbestos exposure; although, the data was unable to offer the magnitude of the excess risk at levels which correspond to environmental exposure to the general population in industrial countries (Bourdès et al., 2000).

Leukemia

Magnetic Fields: A study in England and Wales reported that those living within 200 metres from a high voltage power lines has a RR for leukemia of 1.69 (95% CI 1.13-2.52), and those who are born between 200 to 600 metres have a RR of 1.23 (95% CI 1.02-1.49) compared to those who lived >600 m from a line at birth. This study found a

significant dose-effect dependency in RR with relation to the distance from the line (Belpomme et al, 2007).

Belpomme et al, (2007) has estimated RR of 2 for acute leukemia for children living in areas with an average EMF strength above 0.4 mT and the EMF related RR for childhood leukemia is 2 for about 1% of the overall children population (Belpomme et al, 2007). However, Boffetta (2005) has reported that for childhood leukaemia the attributable fraction, based on the results of the pooled analysis, at 0.6%, corresponding to 18 cases per year in the European Union (Boffetta, 2005).

Traffic pollutants: Several researchers have found positive associations between local traffic density at the time of diagnosis and childhood leukemias. Children are mostly exposed to air pollutants through traffic exhaust; and the estimated RRs is between 1.6 and 4.7 (Belpomme et al., 2007).

Bladder Cancer

A pooled analysis of six epidemiological studies have reported a summary RR of 1.18 (95% CI 1.06 - 1.32) for bladder cancer for exposures above 1 µg/L to trihalomethanes (Boffetta, 2006). However, caution must be used in interpreting these findings because people also consume water outside of their homes and from other sources, which is often overlooked in epidemiological studies The concentration of chlorination by-products in water also varies greatly depending on geographical area, season and by organic contaminants. It is also necessary to consider confounders such as smoking, diet and other lifestyle related factors. It is believed that the environmental attributable fraction of bladder cancer is 10.3% which corresponds to, in the European Union, to 8911 cases in men and 2439 cases in women in 2002 (Boffetta, 2006). A review and meta-analysis of seven studies of bladder cancer risk from consumption of chlorinated water reported a RR of 1.21 (95% CI 1.09–1.34). This estimate was not modified after adjusting for smoking (Boffetta & Nyberg, 2003).

Other studies on bladder cancer in areas with low or intermediate contamination have shown an increased risk of bladder cancer from arsenic (Boffetta & Nyberg, 2003). An ecological study from Finland found a RR 2.44 (95% CI 0.95–1.96) with 3–9 years of latency, and 1.51 (95% CI 0.67–3.38) with 10 or more years of latency for exposure to arsenic at concentrations of higher than 0.5 µg/l compared to less than 0.1 µg/l. In the United States, the RR for a dose of 53 mg or more of arsenic, as opposed to less than 19 mg of arsenic, and the RR was 1.14 (95% CI 0.7–2.9) overall, but the RR was 3.3 (95% CI 1.1–10.3) among smokers (Boffetta & Nyberg, 2003).

Ever consumption of chlorinated drinking water was associated with an increased risk of bladder cancer in men (combined OR=1.4, 95%CI 1.1-1.9) and women (combined OR=1.2, 95%CI 0.7-1.8). The combined OR for mid-term exposure in both genders was 1.1 (95% CI 1.0-1.2) and for long term exposure was 1.4 (95%CI 1.2-1.7). The combined estimate of the slope for a linear increase in risk was 1.13 (95% CI 1.08-1.20) for 20 years and 1.27 (95% CI 1.15-1.43) for 40 years of exposure in both sexes. This review and meta-analysis of the epidemiological literature indicates that long term consumption of chlorinated drinking water is associated with bladder cancer, particularly in men. (Villanueva et al., 2003).

Brain Tumours

Cell Phones: There is inclusive evidence of increased risk of brain cancers from increased use of cell phones. About 25 epidemiological studies were identified that addressed cell phone use and brain tumours. Combined odds ratios (95% confidence intervals) from these studies for glioma, acoustic neuroma, and meningioma were 1.5 (1.2–1.8); 1.3 (0.95–1.9); and 1.1 (0.8–1.4), respectively. The overall evidence speaks in favor of an increased risk, but its magnitude cannot be assessed at present because of insufficient information on long-term use of cell phones. (Kundi, 2009).

Skin Cancer

Existing data on the incidence of human skin cancer were analyzed, as available from two special surveys of non-melanoma skin cancer in the United States. The incidence of non-melanoma skin cancer in the ten regions that were surveyed not only correlated significantly with the ambient UV dose but also with the average daily maximum sunlight in summer. For squamous cell carcinoma the incidence was higher by 5.5% (SE 1.6%) per degree Celsius and for basal cell carcinoma by 2.9% (SE 1.4%) per degree Celsius. These values correspond to an increase of the effective UV dose by about 2% per degree Celsius. Although the precise nature of this correlation with temperature requires fur-

ther studies, it can be concluded that as the temperature rises the intensity of the sunlight increases and amplifies the induction of non-melanoma skin cancers by UV radiation in human populations. (Van der Leun et al., 2008).

Conclusion

Although the term environment has been defined in different ways, this review has used the narrow definition proposed by the WHO. It is necessary to have consensus on appropriate definition for environment. Extensive research has been done to assess the etiological relationship between environmental agents and the risk of cancer. A number of studies have also quantified the risks for some of these agents. Lung cancer, mesothelioma, leukemia, bladder, brain and skin cancer appear to have identified environmental risk factors. Environmental tobacco smoke, indoor and outdoor pollution, radon, asbestos, magnetic fields, traffic pollution, trihalomethanes, cell phones and sunlight appear to the most studied and reported. However, other environmental agents need to be identified and attributable fraction calculated.

References

Boffetta, P. (2002). Involuntary Smoking and Lung Cancer. *Scand J Work Environ Health, 28*(Suppl 2),30-40.

Boffetta, P. , & Nyberg, F. (2003). Contribution of environmental factors to cancer risk. *Br Med Bull., 68*(1), 71-94. doi: 10.1093/bmp/ldg023

Boffetta, P. (2006). Human cancer from environmental pollutants: the epidemiological evidence. *Mutat Res., 608* (2):157-62. doi: 10.1016/j.mrgentox.2006.02.015

Bourdès, V., Boffetta, P., & Pisani, P. (2000). Environmental exposure to asbestos and risk of pleural mesothelioma: review and meta-analysis. *Eur J Epidemiol., 16*(5), 411-7. doi: 10.1023/A:1007691003600

Boyd, D. R., & Genius, S. J. (2008). The environmental burden of disease in Canada: Respiratory disease, cardiovascular disease, cancer, and congenital affliction. Environ *Res., 106*(2), 240-9 . doi: 10.1016/j.envres.2007.08.009

Bukowski, J. A., & Wartenburg, D. (1997). A n Alternative Approach for Investigating the Carcinogenicity of Indoor Air Pollution: Pets as Sentinels of Environmental Cancer Risk. *Environ Health Perspect., 105*(12), 1312–1319.

Cancer and the Environment.. (2003). National Institute of Environmental Health Sciences.

Villanueva, C. M., Fernández, F., Malats, N., Grimalt, J. O., & Kogevinas, M. (2003). Meta-analysis of studies on individual consumption of chlorinated drinking water and bladder cancer. *J Epidemiol Community Health, 57*(3), 166 -173 . doi: 10.1136/jech.57.3.166

Kundi, M. (2009). The Controversy about a Possible Relationship between Mobile Phone Use and Cancer. *Environmental Health Perspectives, 117*(3). doi: 10.1289/ehp.11902

Preventing disease through healthy environments: Towards an estimate of the environmental burden of disease. WHO 2006.

Prüss-Üstün, A., & Corvalán, C. (2006). Preventing disease through healthy environments: Towards an estimate of the environmental burden of disease. World Health Organization.

Trédaniel, J., Boffetta, P., Saracci, R., & Hirsch, A. (1997). Non-smoker lung cancer deaths attributable to exposure to spouse's environmental tobacco smoke. Int *J Epidemiol., 26*(5), 939-44

Van der Leun, J. C., Piacentini, R. D., & Gruij, F. R. (2008). Climate change and human skin cancer. *Photochem Photobiol Sci., 7*(6), 730–733. doi: 10.1039/b719302e

The Effects of Exogenous Estrogens on Estrogen Receptors in Male Reproductive Organs

Mina TOHIDI* [1]

[1] Student, University of Ottawa, Canada

* *Auteur(e) correspondant | Corresponding author*: N/A

Abstract:

There is an essential physiological role for estrogen in male reproduction. Conversely, exposure to exogenous sources of estrogen has negative effects on reproductive physiology and fertility in men. Infertility, affecting nearly 15% of couples, is defined as the inability to conceive after one year of unprotected sexual intercourse. In at least 20% of cases, male reproductive pathology is the major cause for a couple's infertility. Thus, it is essential to investigate potential causes of infertility in adult males. Evidence shows that exposure to certain endocrine disruptors is associated with reduced semen quality and impaired fertility in men. Bisphenol A and Diethylstilbestrol are endocrine disruptors that act as exogenous sources of estrogen and have been associated with male reproductive pathology. This review will examine the role of exogenous estrogens on changes in gene expression of estrogen receptors ERα, ERβ, and GPR30. Previous studies have had conflictive results, suggesting that the effects of exogenous estrogens on male reproduction are multi-faceted. Future studies should focus on determining whether exogenous estrogens have a stimulatory and/or inhibitory effect on gene expression and whether this relationship is dose-dependent or if it follows a more complex dosage pattern.

Keywords:

Estrogen, Bisphenol A (BPA, 2,2-bis(4-hydroxyphenyl)), propane, Diethylstilbestrol (DES), endocrine disruption, GPR30

Introduction

The purpose of this review is to examine the roles of exogenous estrogen on gene expression in the male reproductive system. The first section will briefly describe the function of estrogen and its receptors in regulating normal physiological processes in males. Next, the effects of exogenous estrogens on estrogen receptors ERα, ERβ, and GPR30 will be considered. This review will focus primarily on the effects of two endocrine disruptors, Bisphenol A and Diethylstilbestrol, as sources of exogenous estrogen affecting the male reproductive system.

Estrogen and the Male Reproductive System

Estrogen Ligand

Estrogens are a group of steroid compounds, which include estrone, estradiol, and estriol, that act as hormones regulating reproductive development and function. Although estrogen was historically believed to be a female hormone, there is growing evidence of a biological role of this steroid in male reproduction. Estrogen is said to play a regulatory role in the male reproductive tract because estrogen biosynthesis occurs in the testes, and also because the absence of estrogen receptors (ERs) causes adverse effects on both spermatogenesis and steroidogenesis (O'Donnell et al., 2001).

In males, estrogen may be produced by the liver, adrenal glands, adipose tissue, and in the testes. Aromatase, an enzyme involved the production of estrogen from androgens, has been localized in virtually every cell type within the adult testis, including Sertoli cells, Leydig cells, spermatocytes, spermatids, and spermatozoa. The presence of aromatase confers the ability to synthesize estrogen locally within the male reproductive system (O'Donnell et al., 2001).

Mice with deletion of the aromatase gene (ARKO) are unable to produce endogenous estrogen and show disturbances of spermatogenesis associated with increased apoptosis of developing germ cells. In contrast, overexpression of aromatase induces cryptorchidism as well as spermatogenic arrest in mice (Akingbemi, 2005).

Furthermore, studies have been conducted using mice with deletion of the ER gene (ERKO), which codes for a subtype of estrogen receptors. These mice are able to produce estrogen, but they are unable to carry out responses mediated by this estrogen receptor, which include the production and function of sperm. The ERKO mice exhibit reduced number of sperm in the epididymis, reduced motility, and reduced ability to fertilize oocytes/eggs, supporting the regulatory role of estrogen in male reproduction (Eddy et al., 1996).

Estrogen Receptors

1. Estrogen Receptors Alpha and Beta

Estrogen receptors (ERs) are classic steroid hormone receptors and are members of a ligand-activated nuclear receptor gene superfamily. It was originally believed that only one form of nuclear ER existed (now ERα), until in 1996 the second form (now ERβ) was localized in many species including humans. The two subtypes of ERs are synthesized from separate genes, making them structurally and functionally distinct proteins. However, these receptors share the same organization of a ligand-binding domain, DNA-binding domain, and two transcriptional activation function domains (O'Donnell et al., 2001).

Classic ER action involves the ligand-dependent regulation of gene expression in target tissues (Hall et al., 2001). Estrogen binding to the ER releases the receptor from an inhibitory complex associated with heat shock proteins and chaperone proteins and leads to receptor phosphorylation. Next, the receptor complex homodimerizes and translocates to the nucleus. The ER then binds to estrogen response element (ERE), a 15-bp sequence of DNA located on the promoter region of target genes (Ho & Liao, 2002).

There is considerable tissue specificity with respect to the expression of ERα and ERβ. There has been extensive research on the expression and localization of the two ER subtypes within the adult testes in several mammals including humans. The localization of these subtypes in the Leydig cells, in humans especially, is extremely controversial with some studies showing and others not detecting immunoexpression. Sertoli cells in humans contain ERβ, but do not contain ERα. Furthermore, germ cells have been found to contain both ERs, with ERβ being more predominant (O'Donnell et al., 2001). The considerable conflict in the literature with respect to the expression of ER subtypes arises when comparing studies that use different antibodies in their immunohistochemical techniques. In order to clarify the exact location of ER subtypes in the testes, numerous well-characterized antibodies are required (O'Donnell et al., 2001).

In addition to the classic genomic pathway of ER interaction with target genes, estrogen can have non-genomic effects, presumably through interaction with receptors on the plasma membrane. In various cell types, both ERs can also elicit rapid cellular effects that peak within seconds to minutes after stimulation, making them too rapid to be induced transcriptionally. Furthermore, inhibition of RNA or protein synthesis does not block these effects, supporting the non-nuclear actions of ERs (Ho & Liao, 2002).

These signaling pathways may recruit second messengers including Ca2+ and cAMP, receptor tyrosine kinases including insulin-like growth factor (IGF)-1 receptors and G-Protein Coupled Receptors (GPCRs), serine/threonine kinase Akt, mitogen-activated protein kinases (MAPKs), non -receptor tyrosine kinases, as well as protein Kinases A and C (Ho & Liao, 2002).

The precise nature of these non-genomic receptors is unknown, but many of the pathways involve receptors at the plasma membrane. Thus, investigators are looking to determine if classical estrogen receptors are also present on the plasma membrane. Although the structure of ERα itself does not suggest that it can be anchored to the membrane, there is some evidence to support this theory (Ho & Liao, 2002).

Table 1

Summary of the likely localization of ERα, ERβ, and aromatase in the adult testis. The localization has been obtained from a literature view looking at estrogen and spermatogenesis (see review O'Donnell et al., 2001). The marker (X) indicates the potential presence of each protein in the specified cell type. It is important to note that several inconsistencies still exist regarding the localization of these proteins. This data suggests that estrogen production and action are present in somatic testicular cells as well as germ cells.

Cell Type	ERα	ERβ	Aromatase
Leydig cell	X	X	X
Sertoli cell		X	X
Spermatogonia		X	
Pachytene spermatocyte		X	X
Round spermatid		X	
Elongated spermatid			X
Epididymis	X	X	X

In summary, estrogen can act as a ligand, binding to ERα and ERβ located within the nucleus and inducing its effects through gene transcription. Furthermore, estrogen can also bind to non-nonnuclear ERs, which may be located at the plasma membrane, inducing its effects in a non-genomic manner, such as through the use of secondary messengers or through protein phosphorylation.

2. GPR30

In many reports, the non-genomic estrogen-responsive receptor is proposed to be ERα and/or ERβ, or a modified form of the protein. (Prossnitz et al., 2007). In various organs, however, non-genomic effects of estrogen are not regulated by either membrane-bound ERα or ERβ. Furthermore, aromatase knockout mice show a more severe testicular phenotype than ER knockouts, suggesting that estrogen is still functioning in the absence of ERα and ERβ (Murata et al., 2002). Thus, there is the potential for estrogen action that is unrelated to the ER family of steroid receptors. The same conclusion can be reached by combining findings of studies that have shown the existence of G protein-regulated signaling by estrogen as well the localization of estrogen binding sites to the plasma membrane (Prossnitz et al., 2008).

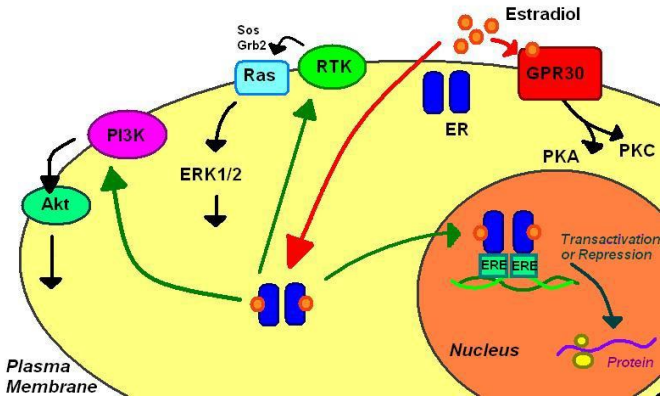
G protein-coupled receptors (GPCRs) are membrane proteins that are activated by ligands such as hormones, neurotransmitters, chemokines, and small peptides. (Funakoshi et al., 2006). The two principal signal transduction pathways involving GPCRs are the cAMP pathway and the phosphatidylinositol signal pathway (Gilman, 1987).

In the late 1990's, a novel G protein-coupled receptor (GPCR) was found which was distinct from any other GPCR. GPR30, a novel 7-transmembrane G protein-coupled receptor, responds to estrogen stimulation and is involved in the regulation of cell growth, including proliferation and apoptosis. There is evidence of GPR30 localization at the plasma membrane and at the endoplasmic reticulum (Prossnitz et al., 2008). An intracellular localization of the receptor is more consistent with estrogen membrane permeability.

It has been determined that the binding of estrogen to GPR30 can be displaced by 17βEstradiol, but not 17αEstradiol, demonstrating the stereo-specificity of the receptor (Thomas et al., 2005). Furthermore, it has been found that GPR30 binds nearly the same amount of estrogen as ERα, suggesting that this receptor does not merely enable estrogen binding, but is involved in estrogen's regulatory fun-

Figure 1

Selected nuclear and nonnuclear actions of estrogen receptors. In classical nuclear pathways, the binding of 17βestradiol to estrogen receptors leads to a translocation of ligand-bound receptor to the nucleus and activation of ERE-dependent transcription. Alternatively, nonnuclear actions may include recruitment of the MAPK pathway, including ERK1/2 through activation of kinases, including Ras. Estrogen receptors can also elicit PI3K and Akt. Ligand binding to GPR30, which is also an estrogen receptor, may lead to activation of several pathways such as PKA and PKC (adapted from Ho & Lia, 2002).

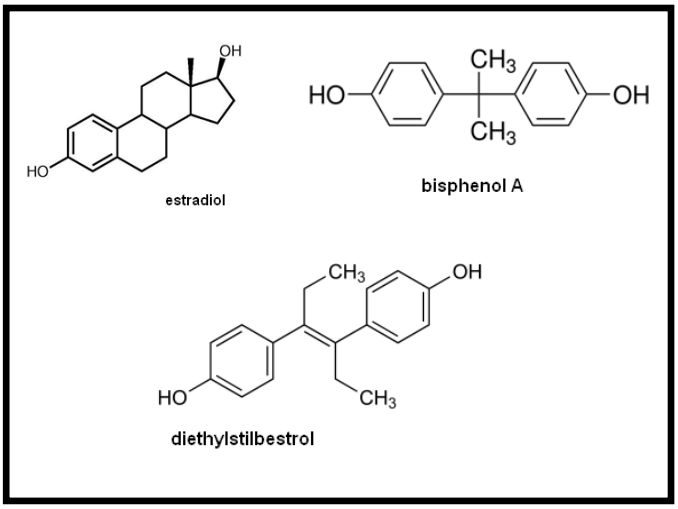


tions within cells (Prossnitz et al., 2008).

The importance of GPR30 in male reproduction is still debatable, and it has even been suggested that GPR30 may be dispensable for the normal development of reproductive organs and reproductive function in mice (Otto et al., 2009). However, there is growing evidence of the involvement of GPR30 with male reproduction. Immunohistochemistry in adult mouse testes was used to demonstrate GPR30 expression in male germ cells, indicating that

Figure 2

Chemical structures of estradiol, Bisphenol A, and diethylstilboestrol.



estrogen effects associated with male reproduction can be induced through this receptor. This study also found, for the first time, that estrogens interacting with GPR30 activate a rapid EGFR/ERK/fos pathway which stimulates mouse spermatogonial cell line proliferation (Sirianni, et al., 2007).

Exogenous Estrogen Ligands

Bisphenol A

Bisphenol A (BPA), is an organic compound with two phenol functional groups and is used as a monomer in polycarbonate plastics. Its structural similarity to estrogen allows BPA to compete with estradiol at binding sites, acting as an exogenous estrogen and endocrine disruptor. One of the highest volume chemicals produced worldwide, BPA can be found in the linings of most food and beverage cans, dental sealants, as well as additives in a wide variety of consumer products (Burridge, 2003). BPA leaches into human food supply through heating of cans, the presence of acidic or basic products in the cans, as well as through repeated washing of polycarbonate products (vom Saal & Hughes, 2005). In the Unites States, BPA has been shown to account for the most estrogenic activity leaching from landfills (Coors et al., 2003).

Suspected of being hazardous to humans since the 1930's, there have been a number of studies of the disruptive effects of BPA to humans. In vitro studies show that BPA's disruptive effects on cells are mediated by genomic and non-genomic estrogen-response mechanisms, with disruptions occurring at doses as low as 1 pM (Wozniak et al., 2005).

A complete background on BPA, although vital, is out of the scope of this review and is available through other sources. A comprehensive document containing references for numerous BPA review articles, mechanisms of action, pharmacokinetics, sources of exposure, and exposure levels in humans, is available online (see review Endocrine Disruptors Group, 2009).

BPA produces estrogenic effects by interacting with ERs. BPA has been shown to be a Selective Estrogen Receptor Modulator (SERM), showing different affinity and regulation of ERα and ERβ and responding differently in various tissues (Routhledge et al., 2000). Furthermore, BPA has recently been shown to act as an androgen antagonist in

the presence of the androgen receptor (AR), blocking testosterone synthesis. Data from this one study, which exposed rats to low doses of BPA, shows that BPA has an inhibitory effect on testicular steroidogenesis. The suppression of pituitary Luteinizing Hormone (LH) along with increased pituitary ERβ mRNA levels in this experiment suggest that BPA's effects are ER mediated (Akingbemi et al., 2004).

With respect to male reproduction, BPA has been shown to decrease daily sperm production and fertility with either developmental or adult exposure in rats. In one study, oral doses of BPA as low as 20 g/kg decreased testicular weight and significantly reduced daily sperm production as well as spermatogenesis (Sakaue et al., 2001).

Diethylstilbestrol

Diethylstilbestrol (DES) is a synthetic, non-steroidal estrogen that has been used traditionally for treatment of multiple pregnancy related problems, including miscarriages, premature birth, and abnormal bleeding (Rubin, 2007).

Synthetic estrogens, such as DES, have been shown to induce bladder, ovarian, testicular, lymphatic, uterine, mammary, and prostatic tumors in mammals (Roy et al., 1997). There is also epidemiological evidence of a slightly increased risk of breast cancer in populations of women exposed to DES (Malone, 1993).

DES has a high affinity for ERs and modifies the expression pattern of androgen and estrogen receptors. Furthermore, neonatal exposure of DES is associated with various reproductive tract anomalies in the male (Goyal et al., 2003; Williams et al., 2001). These changes include reduced growth of the prostate, seminal vesicles, vas deferens, epididymis, and efferent ducts, as well as reduced numbers of Sertoli, Leydig, and germ cells (Williams et al., 2001).

According to another study, DES-exposed rats generally had: (1) altered sperm morphology, (2) decreased sperm production, (3) decreased weight of the testis, epididymis, and seminal vesicles, and (4) decreased sperm fertility as evident from a reduced number of offspring (Goyal et al., 2003).

One study found that prenatal exposure of DES reduces the offspring's Sertoli cell population during adulthood (Sharpe et al., 1998). Here, DES was administered neonatally to rats, and developmental changes in Sertoli cell function were evaluated over time. In adulthood, DES-treated rats had over 60% reduction in testicular weight and very low daily sperm production. Because Sertoli cell population is representative of spermatogenic potential, this finding suggests that neonatal exposure to estrogens may lead to impaired spermatogenesis in adulthood (Sharpe et al., 2003.)

A National Toxicology Program Peer Review Panel stated that DES is an appropriate positive control estrogenic drug that may be used in studies of estrogenic chemicals, such as BPA (Welshons, et al., 2006).

Dose-Response Relationship of Bisphenol A

A review looking at low dose effects of BPA verified the presence of a non-monotonic response function, in which the chemical does not induce change in a classical dose-dependent manner (vom Saal & Hughes, 2005). Instead, it has been shown that low doses of BPA may actually cause a greater response in target cells, while higher doses may inhibit the same response. Several mechanisms could be involved, including changes in tissue expression of affected receptors (Wetherill et al., 2007). Testing the effects of various doses is significant in light of the emerging data concerning the inverted U shape dose-response function of BPA.

Endocrine Disruptors and Estrogen Receptors

The pattern of ER expression is a target for exogenous estrogen action, which can produce either stimulatory or inhibitory effects (Akingbemi, 2005). Although one would assume that an increase in estrogen, whether endogenous or exogenous, would induce increased expression of ERs, the evidence so far suggests a more complex relationship.

A group of mice treated with 50 μg/ml of BPA displayed a significant reduction in mRNA expression of ERβ. In contrast, ERα mRNA expression was increased significantly in the same mice (Takao et al., 2003). Interestingly, a single injection of estradiol benzoate at a 500μg dosage induced the opposite effects in rats, reducing ERα mRNA expression and increasing ERβ mRNA expression (Tena-Sempere et al., 2000). These results suggest that the effects of exogenous estrogen may be differential modulation of ERα and ERβ in the testes. Furthermore, additional research is required to determine whether each endocrine disruptor produces consistent changes in estrogen receptor gene expression, or if the effects may vary with different doses and/or conditions.

The complex effects and disparities of exogenous estrogens on ER expression may be attributed to an inverted U-shaped dosage response, in which low doses of a chemical may be stimulatory but high doses may be inhibitory. Another proposition is that inappropriate estrogen exposure, such as through ingestion of exogenous estrogens, may lead to the down-regulation of ERs. This would result in an estrogen deficiency syndrome, in which mice have deficiencies of ERα similar to ERα knockout mice.

Studies in the testes support this proposal, suggesting that neonatal DES exposure leads to downregulation of ERα and androgen receptor, but an increase in ERβ expression (Tena-Sempere et al., 2000). DES exposure may result in a permanent change in estrogen responsiveness or in estrogen-dependent gene expression (O'Donnell et al., 2001).

Because GPR30 has only recently been recognized as an estrogen receptor in the testes, there is little research studying the effects of endocrine disruptors on gene expression in of this receptor.

Conclusion

Endogenous estrogen plays a significant regulatory role in male reproduction. At the same time, exogenous estrogens, such as endocrine disruptors Bisphenol A and Diethylstilbestrol, have been shown to disrupt development of the male reproductive system and to affect fertility. One mechanism through which these endocrine disruptors can affect reproduction is by changing the expression of estrogen receptor proteins at a cellular level, thus disturbing cellular regulation by endogenous estrogen.

The exact mechanisms through which BPA and DES affect the male reproductive system are complex and may be in part due to changes in the expression of estrogen receptors, which would lead to altered function at a cellular level. Currently, studies show that gene expression of estrogen receptors changes with exposure to BPA or DES, but there is inconclusive evidence as to whether receptor expression is stimulated or inhibited. In fact, gene expression may be influenced differently based on the chemical, dosage, specific estrogen receptor subtype, and tissue (Akingbemi, 2005).

Additional research is required to understand the complex relationship that exists between exogenous estrogens and gene expression of estrogen receptors ERα, ERβ, and GPR30. Future studies should focus on clarifying whether this relationship is stimulatory and/or inhibitory. Furthermore, by studying the effects of different dosages of exogenous estrogens, it may be possible to determine if the changes in gene expression induced are dose-dependent, or if they follow the proposed inverted U-shaped dose-response.

Acknowledgements

I thank Dr. Karen P. Phillips for her assistance in preparing and critically reading this review.

References

Akingbemi, B. T. (2005). Estrogen regulation of testicular function. *Reproductive Biology and Endocrinology, 3,* 51-63. doi: 10.1186/1477-7827-3-51

Akingbemi B.T., Scottas C. M., Koulova A. L., Klinefelter A. M, & Hardy M. P. (2004). Inhibition of testicular steroidogenesis by the xenoestrogen Bisphenol A is associated with reduced pituitary luteinizing hormone secretion and decreased steroidogenic enzyme gene expression in rat Leydig cells. *Endocrinology, 145*(2), 592-603. Retrieved from http://dx.doi.org/10.1210/en.2003-1174#sthash.zwTTkxX4.dpuf

Burridge, E. (2003). Bisphenol A: Product profile. *European Chemical News*, 14-20 April, 17.

Coors, A., Jones, P. D., Giesy, J. P., & Ratte, H. T. (2003). Removal of estrogenic activity from municipal waste landfill leachate assessed with a bioassay based on reporter gene expression. *Environmental Science & Technology, 37* (15), 3430-3434.

Eddy, E. M., Washburn, T. F., Bunch, D. O., Goulding, E. H., Gladen, B. C., Lubahn, D. B., & Korach, K. S. (1996). Targeted disruption of the estrogen receptor gene in male mice causes alteration of spermatogenesis and infertility. Endocrinology. 137(11), 4796–4805. Retrieved from http://dx.doi.org/10.1210/endo.137.11.8895349#sthash.PEufj323.dpuf

Endocrine Disruptors Group. (2009). Bisphenol A References. Columbia, MO: Curators of the University of Missouri. Retrieved from http://

endocrinedisruptors.missouri.edu/pdfarticles/Bisphenol_A_References.doc.

Filardo, E. J., Quinn, J. A., Frackelton, A. R., Jr., & Bland, K. I. (2002). Estrogen action via the G protein-coupled receptor, GPR30: stimulation of adenylyl cyclase and cAMP-mediated attenuation of the epidermal growth factor receptor-to-MAPK signaling axis. *Molecular Endocrinology, 16*(1), 70–84.

Funakoshi, T., Yanai, A., Shinoda, K., Kawano, M. M., & Mizukami, Y. (2006). G protein-coupled receptor 30 is an estrogen receptor in the plasma membrane. *Biochemical and Biophysical Research Communications, 346*(3), 904-910. doi: 10.1016/j.bbrc.2006.05.191

Gilman, A. G. (1987). G Proteins: Transducers of Receptor-Generated Signals. *Annual Review of Biochemistry, 56*, 615–649. doi: 10.1146/annurev.bi.56.070187.003151

Goyal, H. O., Robateau, A., Braden, T. D., Williams, C. S., Srivastava, K. K., & Ali, K. (2003). Neonatal estrogen exposure of male rats alters reproductive functions at adulthood. *Biology of Reproduction, 68*(6), 2081-2091. doi: 10.1095/biolreprod.102.010637

Hall, J. M., Course, J. F., & Korach, K. S. (2001). The multifaceted mechanisms of estradiol and estrogen receptor-signalling. *Journal of Biological Chemistry, 276*, 36869-36872. doi: 10.1074/jbc.R100029200

Hall J. M., & McDonnell, D. P. (1999). The estrogen receptor β-isoform (ERβ) of the human estrogen receptor modulates ER transcriptional activity and is a key regulator of the cellular response to estrogens and antiestrogens. *Endocrinology, 140*(12), 5566–5578. Retrieved from http://dx.doi.org/10.1210/endo.140.12.7179#sthash.sNHlA1yv.dpuf

Ho, K. J., & Liao, J. K. (2002). Nonnuclear Actions of Estrogen. *Aretriosclerosi, Thrombosis, and Vascular Biology, 22*, 1952-1961. doi: 10.1161/01.ATV.0000041200.8594

Kuiper, G. G., Carlsson, B., Grandien, K., Enmark, E., Haggblad, J., Nilsson S., & Gustafsson, J-A. (1997). Comparison of the ligand binding specificity and transcript tissue distribution of estrogen receptors α and β. *Endocrinology, 138*(3), 863–870. Retrieved from http://dx.doi.org/10.1210/endo.138.3.4979#sthash.javzdfDv.dpuf

Malone, K. (1993). Diethylstilbestrol (DES) and breast cancer. *Epidemiological Review, 15*, 108–109.

Murata, Y., Robertson, K. M., Jones, M. E. E., & Simpson, E. R. (2002). Effect of estrogen deficiency in the male: the ArKO mouse model. *Molecular & Cellular Endocrinology, 193*(1-2), 7-12. doi: 10.1016/S0303-7207(02)00090-4

O'Donnell, L., Robertson, K. M., Jones, M. E., & Simpson, E. R. (2001). Estrogen and spermatogenesis. *Endocrine Reviews, 22*(3), 289-318. Retrieved from http://dx.doi.org/10.1210/edrv.22.3.0431#sthash.8rPCkHxy.dpuf

Otto, C., Fuchs, I., Kauselmann, G., Kern, H., Zevnik, B., Andreasen P., ... Fritzemeier, K. H. (2009). GPR30 Does Not Mediate Estrogenic Responses in Reproductive Organs in Mice. *Biology of Reproduction, 80*(1), 34-41. doi: 10.1095/biolreprod.108.071175

Prossnitz, E. R., Arteburn, J. B., & Sklar, L. A. (2007). GPR30: a G protein-coupled receptor for estrogen. Molecular & Cellular Endocrinology, 265-266, 138-142. doi: 10.1016/j.mce.2006.12.010

Prossnitz, E. R., Oprea, T. I., Sklar, L. A., & Arteburn, J. B. (2008). The ins and outs of GPR30: a transmembrane estrogen receptor. *The Journal of Steroid Biochemistry and Molecular Biology, 109* (3-5), 350-353. doi: 10.1016/j.jsbmb.2008.03.006

Routhledge, E. J., White, R., Parker, M. G., & Sumpter, J. P. (2000). Differential effects of xenoestrogens on coactivator recruitment by estrogen receptor (ER) α and (ER) β. *Journal of Biological Chemistry, 275*(46), 35986-35993. doi: 10.1074/jbc.M006777200

Roy, D., Palangat, M., Chen, C., Thomas, R. D., Colerangle, J., Atkinson, A., & Yan, Z. (1997). Biochemical and Molecular Changes at the Cellular Level in Response to Exposure to Environmental Estrogen-like Chemicals. *Journal of Toxicology and Environmental Health, Part A, 50*(1), 10-30.

Sakaue, M., Ohsako, S., Ishimura, R., Kurosawa, S., Kurohmaru, M., Hayashi, Y.,... Tohyama, C. (2001). Bisphenol A affects spermatogenesis in the adult rat even at a low dose. *Journal of Occupational Health, 43*(4), 185-190. Retrieved from http://doi.org/10.1539/joh.43.185

Sharpe, R. M., McKinnell, C., Kivlin, C., & Fisher, J. S. (2003). Proliferation and functional maturation of Sertoli cells, and their relevance to disorders of testis function in adulthood. *Reproduction, 125*(6), 769–784.

Sharpe, R. M., Atanassova, N., McKinnell, C., Parte, P.,

Turner, K. J., Fisher, J. S.,... Saunders, P. T. (1998). Abnormalities in functional development of the Sertoli cells in rats treated neonatally with diethylstilbestrol: A possible role for estrogens in Sertoli cell development. *Biological Reproduction, 59*(5), 1084–1094. doi: 10.1095/biolreprod59.5.1084

Sirianni, R., Chimento, A., Ruggiero, C., De Luca, A., Lappano, R., Ando, S.,... Pezzi, V. (2007). The Novel Estrogen Receptor, G Protein-Coupled Receptor 30, Mediates the Proliferative Effects Induced by 17β-Estradiol on Mouse Spermatogonial GC-1 Cell Line. *Endocrinology, 149*(10), 5043-5051. doi: 10.1210/en.2007-1593

Takao, T., Nanamiya, W., Nazarloo, H. P., Matsumoto, R., Asaba, K., & Hashimoto, K. (2003). Exposure to the environmental estrogen bisphenol A differentially modulated estrogen receptor-alpha and –beta immunoreactivity and mRNA in male mouse testis. *Life Sciences, 72*(10), 1159-1169. doi: 10.1016/S0024-3205(02)02364-0

Tena-Sempere, M., Navarro, J., Pinilla, L., Gonzalez L. C., Huhtaniemi, I., & Aguilar, E. (2000). Neonatal exposure to estrogen differentially alters estrogen receptor alpha and beta mRNA expression in rat testis during postnatal development. *Journal of Endocrinology, 165*(2), 345-357.

Thomas, P., Pang, Y., Filardo, E. J., & Dong, J. (2005). Identity of an Estrogen Membrane Receptor Coupled to a G-protein in Human Breast Cancer Cells. *Endocrinology, 146*(2), 624-632. Retrieved from http://dx.doi.org/10.1210/en.2004-1064#sthash.nJq2TT3z.dpuf

vom Saal, F., & Hughes, C. (2005). An Extensive New Literature Concerning Low-Dose Effects of Bisphenol A Shows the Need for a New Risk Assessment. *Environmental Health Perspectives, 113*(8), 926-933. doi: 10.1289/ehp.7713

Welshons, W. V., Thayer, K. S., Taylor, J., Judy, B. M., & vom Saal, F. S. (2003). Large effects from small exposures. I. Mechanisms for endocrine-disrupting chemicals with estrogenic activity. *Environmental Health Perspectives, 111*(8), 994-1006.

Wetherill, Y. B., Akingbemi, B. T., Kanno, J., McLachlan, J. A., Nadal, A.,... Belcher, S. M. (2007). In vitro molecular mechanisms of Bisphenol A action. *Reproductive Toxicology, 24*(2), 178-198. doi: 10.1016/j.reprotox.2007.05.010

Williams, K., McKinnell, C., Saunders, P. T. K., Walker, M., Fisher, J. S., Turner, K. J.,...Sharpe, R. M. (2001). Neonatal exposure to potent and environmental oestrogens and abnormalities of the male reproductive system in the rat: Evidence for importance of the androgen-oestrogen balance and assessment of the relevance to man. *Human Reproduction Update, 7*(3), 236–247.

Wozniak, A. L., Bulayeva, N. N., & Watson, C. S. (2005). Xenoestrogens at picomolar to nanomolar concentrations trigger membrane estrogen receptor-alpha-mediated Ca2+ fluxes and protein release in GH3/B6 pituitary tumor cells. *Environmental Health Perspectives, 113*(4), 431-439. doi: 10.1289/ehp.7505

Personal Health Responsibility: Blaming Victims or Empowering Nations?

Nicholas VALELA* [1]

[1] Student, University of Ottawa, Canada

* *Auteur(e) correspondant* | *Corresponding author*: N/A

Abstract:

The place for personal responsibility within healthcare has been highly contested within academic debate. Meanwhile, leading causes of death within the United States have shifted to chronic disease as a result of lifestyle behaviours suggesting the need for health promotion to take action. In this position paper, I will argue that the less punitive element of personal responsibility implied by health promotion is both ethically justifiable and beneficial as a means of empowering the individual, population and healthcare system as a whole. Several counter-arguments are presented and subsequently refuted: health responsibility unduly places blame upon vulnerable populations; administration of negative sanctions based on health responsibility is difficult; and actions detrimentally affecting health are not certain to be autonomously undertaken by the individual. Arguments in favour are then presented: a dependence of the population upon the healthcare system has been created; empowerment is effective as the central guiding principle of health promotion; and sensible care for oneself should be a duty of citizens, which they are required to fulfill as the healthcare system is not in a position to act as an unlimited resource. As such, health promotion must continue to emphasize the importance of sensible health behaviour as a means of empowering individuals through self responsibility.

Keywords: N/A

Introduction

When debating criteria for rationing within healthcare systems, personal responsibility seldom receives good press (Buyx, 2008). Holding individuals personally responsible has often been perceived as a way of 'blaming the victim,' which is contrary to the aims of contemporary medicine (Buyx, 2008). However, at present in the United States, it has been estimated that approximately forty percent of premature deaths in the population are attributable to personal health and lifestyle behaviours (Adler & Stewart, 2009). In essence, this is indicative of a high degree of dependency by citizens on their healthcare system as a result of the overly medicalized society in which we live. And the outcomes are clear. Within the past fifty years, the life expectancy of the United States population at birth has increased steadily. During the same time, the leading causes of death have shifted from infectious to chronic diseases resulting from 'lifestyle' behaviours, which include smoking, diet, exercise, and sexual practices (Adler & Stewart, 2009). Such a changeover within a relatively brief period of time has led to widespread calls for people to review their behaviour (Schmidt, 2009). Preventative medicine and health promotion, two components of contemporary medicine, implicitly involve the use of personal responsibility as means of empowering populations to better their health themselves. Rather than punishing or withholding treatment from individuals who choose otherwise, the element of self-responsibility encourages autonomy and aids the individual in making beneficial lifestyle choices. In this position paper, I will argue that the less punitive element of personal responsibility implied by behaviourally focused health promotion is not only ethically justifiable, but also beneficial as a means of empowering the individual, population and healthcare system as a whole.

Cross Arguments and Refutes

The central focus of the recent health responsibility debate has been centered on the justification or criticism of responsibility as a sufficient criterion to impose controversial negative sanctions, primarily the denial of healthcare treatment (Schmidt, 2009). I am suggesting that a more nuanced and less punitive model of self-responsibility, rather than the outright denial of services, is the most efficacious mode of implementing health responsibility to yield positive behavioural changes. However, not all are in agreement.

Health responsibility is still viewed by many as unduly placing blame on the victims, as well as adding further pressure on vulnerable groups within the population (Buyx, 2008). In addition, identifying a direct causal link between behaviour and resulting conditions is nearly impossible as the causes of conditions most often cited as preventable through healthy behavioural choices are multifactorial (Buyx, 2008). It may be possible to clearly identify responsibility for an injury as a result of skiing, whereas it is impossible to unambiguously say whether lung cancer was the result of choosing to smoke (Denier, 2005). However, if we acknowledge that it is unjust to hold individuals responsible for conditions over which they do not have control, it follows that they will only be held responsible for partaking in healthy behaviours when they have full access to the resources that enable those behaviours (Adler & Stewart, 2009). Therefore this places a primary moral responsibility on society, rather than the individual, to provide equal opportunities and resources for all people to be able to make healthier choices (Adler & Stewart, 2009). That said, it would be nearly impossible for one to be able to gain access to healthcare by primarily relying upon one's own possessions (Denier, 2005). Healthcare resources are unequally distributed, needs are highly unpredictable, and healthcare often can be very costly (Denier, 2005). This furthers the importance of society's provision of equal opportunities for all, rather than blaming the unfortunate.

Practically speaking, the notion of implementing negative sanctions based on health responsibility is administratively arduous (Schmidt, 2009). Location of voluntary risk takers would involve, at minimum, the regular and routine breach of individual privacy and confidentiality by government officials to investigate potential health abuses (Denier, 2005). However, I am not advocating for the punishment of irresponsible health behaviours. This practice would be without a doubt demeaning, costly and intrusive (Schmidt, 2009). Instead health responsibility needs to be viewed as a tool used to direct the health behaviours towards a positive route, rather than for the purposes of removing a fundamental human right.

Furthermore, we must be certain that the personal activities in question were autonomously undertaken by the individual, as a lack of autonomy is frequently mentioned as a counterargument. (Denier, 2005). It should be noted that most health behaviours are not impulsively undertaken, but rather are subject to the process of conscious choice (Schmidt, 2009). Yet this process is influenced by numerous factors including socioeconomic status, socialization

and education, family influence, social and peer values, advertisement, addictions and so forth (Schmidt, 2009). A denial of treatment, placement of blame, or emphasis on health responsibility would be considered unjust if the person could not have acted otherwise, or could have only acted otherwise with great difficulty (Denier, 2005). This was emphasized in Norman Daniels' 1985 *Just healthcare and just health: meeting health needs fairly* (Schmidt, 2009).

> *"Too much emphasis on [personal responsibility] ignores egalitarian considerations central to democratic equality. Our health needs, however they arise, interfere with our ability to function as free and equal citizens. [We] must meet the[se] needs however they have arisen, since capabilities can be undermined by bad luck" (p. 69, cf p. 68).*

However, Daniels further noted that even if an emphasis is not placed upon responsibility in assigning obligations of justice, we can still apply this concept through the use of education and incentive strategies (Schmidt, 2009). Urging and directing the population toward the adoption of beneficial health behaviours is not contradictory to this approach (Schmidt, 2009). In fact, present day health promotion strategies makes use of health responsibility as a tool of empowering people through the provision of education and resources rather than punishment and the denial of services.

Arguments

The immense progress of medicalization throughout society has been heavily criticized in recent years as more and more of peoples' behaviour has become subject to medical intervention (Clark, p. 32, 2008). Ivan Illich, in *Limits to Medicine* (1976), offered an influential critique of medicalization. According to Illich, contemporary medicine is *iatrogenic*, that is, it creates disease and illness even as it provides medical assistance (Clark, p. 32, 2008). Illich further proposes structural iatrogenesis, in which the responsibility of good health and self-autonomy has been removed from the individual as a result of the imposition of the medical model (Clark, p. 33, 2008). What has resulted is a dependency on the healthcare system that in turn diminishes any remaining sense of self-empowerment or proactivity within the respective population.

The basic human right to healthcare is not being called into question, however citizens need not only act as passive recipients (Denier, 2005). As the costs of healthcare progressively rise, individuals should feel compelled to aid where possible. Contemporary healthcare has been described by Denier as being built upon an elaborate and diverse framework of institutions, services, and policies that aim at the prevention, restoration, and support for those in need. Rather than simply treating and curing as proscribed in the medical model, behaviourally focused health promotion is mandated to prevent foreseeable conditions and strive for a high quality of life for all.

Health promotion initially gained popularity in the United States during the 1980s as, "wellness programs" (Galloway, 2003). Corporations eagerly adopted these programs in response to the desire to establish healthy habits within the workplace and consequently increase productivity (Galloway, 2003). Since then, community empowerment has acted as a guiding principle for both theory and practice in health promotion (Braunack-Mayer & Louise, 2008). "At the heart of this process is the empowerment of communities, their ownership and control of their endeavours and destinies," (Braunack-Mayer & Louise, 2008). Each empowered community thus is composed of empowered individuals with the responsibility and capability to go about their lives in prescribed ways which are beneficial to their health.

Responsibility is an important value as people's behaviour undoubtedly impacts their health (Denier, 2005). Often, it is the unfortunate reality that the truth regarding lifestyle behaviours is not considered convenient or favourable in the eyes of individuals (Guiet, 2008). Humans on the whole do not react well to forced change and will only do so when a considerable level of suffering has been reached (Guiet, 2008). Thus, it is the work of health promotion to act in the best ways possible to prevent this from happening. Framing health damaging behaviours in terms of choice generates appeal and this way of framing causality can give people a greater sense of control over and responsibility for their own health (Galloway, 2003). Moreover, health promotion should not hesitate to emphasize the importance of sensible health behaviour by generating awareness of the influence that behaviours have on health needs (Denier, 2005).

Taken one step further, personal responsibility should be seen as a practice that can be expected, to a degree, from individuals. In the literature, personal responsibility is found to be an underlying thread to a quasi form of Liberal

-egalitarianism with an added element of solidarity (Buyx, 2008). Liberal egalitarians most certainly call attention to the importance of individual freedoms within society, yet they are also committed to equality of opportunity - the founding justification of healthcare for all (Buyx, 2008). From this, the idea of solidarity reflects the high degree of interdependencies within societies (Buyx, 2008). It is important to ensure that this is not mistaken for the idea of charity or welfare in which only a special group is supported (Buyx, 2008). Rather personal responsibility reflects a dual-sided system that implicates reciprocity, ensuring at least a rudimentary level of assistance and support for all (Buyx, 2008). As said in the outset, people cannot only act as passive recipients. This theory promotes that one should take an active role in trying to avoid damaging effects toward the system (Buyx, 2008). Furthermore, according to Buyx, "[individuals] should act responsibly when it comes to their health and that it is justified to expect this to a reasonable degree." Such efforts will likely lead to the more effective use of healthcare resources, a better quality of life for the individual and the preservation of the system for the long run.

In December of 2001, Winnipeg family physician Frederick Ross took a stand against self-destructive vices and delivered an ultimatum to his patients which attracted the attention of international media (Segal, 2005). Ross' patients were warned that if they were not able to quit smoking within the following three month period, then they would be dropped from his roster. Ross notably stated, "I got fed up with wasting my time treating people with smoking-related diseases. People who continue to smoke are obviously not interested in maintaining their health" (Segal, p. 149, 2005). Although the latter may not necessarily be the case, Ross' strong-willed approach and high expectations of the behaviour of his patients delivered decisive results. Fewer than one dozen patients chose to quit seeing Dr. Ross, while many others found this to be incentive to quit smoking altogether (Segal, 2005). This suggests that further research into the effects of patient responsibility and resulting compliance with prescribed treatment is fully warranted. If in fact responsibility is found to secure compliance, this method could be implemented into mainstream society to significantly reduce the prevalence of "smoking-related diseases" and the like as well as the financial burden on the healthcare system.

Funding is key to a well functioning healthcare system. In recent years, the United States' system in particular has been criticized for the high level of costs associated with the provision of care and delivery of healthcare services. Healthcare expenditures in the United States have risen dramatically from roughly $73 billion in 1970 to an estimated $1,600 billion in 2003 as Americans continue to look to the government for solutions to their health dilemmas (Galloway, 2003). With such a substantial financial commitment, society has the right to expect a return on the investments it has made in the health of individuals through the expenditure of the system's resources (Denier, 2005). That being said, citizens have a basic human right to healthcare services but associated with that right are obligations and duties (Denier, 2005). Sensible care for oneself should be seen as a citizen's duty as required in maintaining one's membership in society (Denier, 2005). One mechanism to address this theoretical duty is to reduce financial stress on the healthcare system through implementation of treatments for preventable clinical conditions.

Within the North American culture, there has been longstanding tension between empowering those who are obese to manage their weight and in contrast, blaming them for failing to do so successfully (Adler & Stewart, 2009). In 2009, Nancy Adler and Judith Stewart at the University of California published work specifically addressing attempts to reduce obesity through empowerment without blaming the individuals. Their findings coincide well with what is being argued here within. Adler and Stewart propose that the obese members of society are already a stigmatized group. It is also felt that their situation will likely worsen unless the general public becomes educated. There needs to be greater awareness with regards to the dire need of people who are obese for resources to enable them to engage in health-promoting activities, thus reducing the harmful placement of blame. Adler and Stewart are not suggesting the complete absolution of blame, but rather highlight the need to provide resources to enable free choice and equality of opportunity. Ultimately, the best way to achieve o this would be to maintain both individuals' autonomy and responsibility for lifestyle behaviours as well as society's responsibility to provide proper health-promoting surroundings (Adler & Stewart, 2009).

Conclusion

According to Illich, the most onerous example of medicalization in present day society is the ever growing dependence of the population upon its healthcare system (Clark,

2008). The vast surge of spending by governments on medical treatment, on hospitalization and on pharmaceuticals is highly indicative of this approach to healthcare (Clark, 2008). But with increasing rates of chronic disease associated with lifestyle behaviours rather than infectious disease, the need for intervention strategies within primary care could be greater than ever before. A more nuanced and less punitive version of health responsibility should be both ethically justifiable and practical in its implementation. The outright denial of healthcare services based upon the concept of personal responsibility is not acceptable as the healthcare system is in no position to place judgement on its patients and may be viewed as victim-blaming. Health promoters have the responsibility to continue to educate the public and facilitate the positive direction of health behaviours without passing judgement. In return, society can expect individuals, as members of a cooperative healthcare system, to make a conscious effort to avoid damaging the system by acting responsibly towards their personal health. Such efforts will likely lead

to the more effective use of healthcare resources, a better quality of life for the individual, and the preservation of the healthcare system for future generations. Thus, health promotion must continue to emphasize the importance of sensible health behaviour as a means of empowering individuals through self responsibility.

References

Adler, N. E., & Stewart, J. (2009). Reducing Obesity: Motivating Action While Not Blaming the Victim. *Milbank Quarterly, 87*(1), 49-70. doi: 10.1111/j.1468-0009.2009.00547.x.

Ampt, A. J., Amaroso, C., Harris, M. F., McKenzie. S. H., Rose, V. K., & Taggart, J. R. (2009). Attitudes, Norms and Controls influencing Lifestyle Risk Factor Management in General Practice. *BioMed Central Family Practice, 10*, 59. doi: 10.1186/1471-2296-10-59

Braunack-Mayer, A., & Louise, J. (2008). The ethics of Community Empowerment: tensions in health promotion theory and practice. *Promotion and Education, 15*(5), 5-8. doi: 10.1177/1025382308095648

Buyx, A. M. (2008). Personal responsibility for health as a rationing criteria: why we don't like it and why maybe we should." *Journal of Medical Ethics, 34*(12), 871-74. doi: 10.1136/jme.2007.024059

Clark, J. N. (2008). Health, Illness, and Medicine in Canada. 5th ed. Don Mills: Oxford UP.

Denier, Y. (2005). On Personal Responsibility and the Human Right to Healthcare. *Cambridge Quarterly of Health Ethics 14*(2), 224-34. Retrieved from http://dx.doi.org/10.1017/S0963180105050309

Galloway, R. D. (2003). Health Promotion: Causes, Beliefs and Measurements. *Clinical Medicine and Research, 1*(3), 249-58.

Guiet, C. Student Health Coordinator, uOttawa Health Promotion. The Element of Health Responsibility within Health Promotion. Personal interview. 11 Nov. 2009.

Schmidt, H. (2009). Just Health Responsibility. Journal of Medical Ethics, 35, 21-26. doi: 10.1136/jme.2008.024315

Segal, J. (2005). Health and the Rhetoric of Medicine. Carbondale: Southern Illinois UP.

Sethna, C. Medicalization. History of Healthcare. University of Ottawa, Ottawa. Apr. 2009 Lecture.

Predisposition to Impulsivity and Risk-taking: Dopamine D4 Receptor (DRD4) Polymorphic Gene Linked to "Novelty Seeking" Personality Trait

Robyn WINTERBOTTOM* [1]

[1] Student, University of Ottawa, Canada

* *Auteur(e) correspondant* | *Corresponding author*: N/A

Abstract:

Genetic variation may play a significant role in the expression of complex personality and psychological traits. This article examines the relationship between heritable biological mechanisms and the psychological trait, impulsivity. In particular, dopamine is proposed to play a role in impulsive behaviours, and numerous studies have implicated functional polymorphisms of dopamine-related genes in impulsivity. This article reviews several studies concerning the role of dopamine receptor (DRD4) polymorphisms in the expression of an impulsivity sub-trait known as "novelty seeking". Furthermore, this article focuses on recent approaches to the study of genetic variation, approaches to the measurement of novelty seeking, as well as other possible regulators of the trait in addition to genetics.

Keywords: Impulsivity; novelty-seeking; dopamine; DRD4; genetic polymorphisms

Introduction

Impulsivity is a complex, psychological construct that appears in various forms and to different degrees in major systems of personality (Whiteside & Lynam, 2000, p. 669). Because of its multifaceted nature, impulsivity has been difficult to exclusively define and measure. Some major features include disinhibition and risk-taking, a tendency to act rapidly without forethought and complete planning, and acting to immediately satisfy a desire, without regard for possible consequences (Dickman, 1993, p. 151). Impulsivity is conceptualized on a continuum. This continuum is fairly subjective, as it can vary with the stimulus, situation, or individual. For example, "impulsive" individuals can be characterized by those who are outspoken and extroverted, to those who engage in thrill-seeking activities such as bungee jumping or rock climbing, to individuals who engage in inherently dangerous, high-risk behaviour substance abuse, aggression/violence, and reckless driving. Impulsivity has also been used as diagnostic criteria for psychiatric disorders as varied as kleptomania, borderline personality disorder, attention-deficit/hyperactivity disorder, mania, bulimia nervous, substance abuse/addiction, and paraphilias (Whiteside, Lynam, 2000, p. 669). There is evidence to support that genetics may play a role in one's susceptibility to this trait.

For the purpose of analyzing the degree of genetic predisposition in impulsivity, a sub-trait called "novelty seeking" will be used as an objective proxy measurement. This trait relates to the risk-taking aspect of impulsivity. Novelty seeking is defined a lack of planning and the tendency to act impulsively without thinking, as well as experience seeking, or the willingness to take risks for the sake of excitement or novel experiences (Zuckerman et al., 1993, p. 757). The Temperament Character Inventory is a psychometric instrument used to measure seven dimensions of personality traits. Individuals that score higher than average in the novelty-seeking quotient on the TCI tends to be impulsive, extravagant, fickle, quick-tempered, excitable, and exploratory (Cloninger et al., 1991, p. 1047).

A promising candidate gene for influencing the complex personality trait of novelty seeking is the dopamine receptor (DRD4) gene. Research demonstrates that polymorphisms in this gene are associated with variation in novelty seeking and exploratory behaviour in a range of species, including humans.

Measurement of Novelty Seeking in Research Studies

A variety of behavioural methods can be used to evaluate novelty-seeking. These include particular punished/extinction paradigms, reward-choice paradigms, and response disinhibition/attentional paradigms. For example, one study examined the relationship between the DRD4 dopamine receptor gene and novelty seeking in primates. Novelty seeking was measured by the latency to approach a large, potentially threatening novel object placed in the home enclosure (Bailey, Breidenthal, Jorgensen, McCracken, & Fairbanks, 2007, p. 23). Another notable study examined the same association in a wild bird called the great tit. Assessment of great tit personality took place in a testing arena, where the hops and flights between perches on artificial trees were used as a proxy for exploratory behaviour (Bensch & Tschirren, 2010, p. 624). A third study used a place-conditioning method where rats received access to novel objects repeatedly in one environment then spent an equal amount of time in a second environment without exposure to novelty. In subsequent choice testing, it was determined that rats had preference for the environment paired with novelty, indicating that novel stimuli have a rewarding quality (Bevins, 2001, p. 190).

Behavioural measures to study novelty seeking are most commonly used on animal models. The methodology for human studies, on the other hand, usually involves employment of psychometric instruments and personality inventories to measure the novelty seeking trait. Most notably, the Temperament Character Inventory (Cloninger et al., 1991, p. 1047), the Sensation Seeking Scale (Zuckerman, et al., 1993, p. 758), and the NEO Personality Inventory (NEO-PI-R) (Costa & McCrae, 1992) are used. Seminal work in this field by Robert Cloninger used the TCI, to determine research participants' degree of novelty-seeking behaviour patterns. This self-report questionnaire measured four separate domains of personality (novelty-seeking, harm avoidance, reward dependence, and persistence) that are each hypothesized to have distinct genetic and neurochemical bases. Participants are asked to answer 240 questions, among them queries like, "I like to experience new things for the simple enjoyment or thrill of it, even if most people think this is a waste of time," or "It is hard for me to stay interested in the same things for a long time because my attention often gets distracted by other things," and "I would enjoy the sensation of skiing very fast down a high mountain slope" (Cloninger et al., 1991). Quantitatively measuring participants' novelty seeking behaviour patterns allowed researchers to correlate them with certain characteristics of a polymorphic gene coding for a dopamine receptor protein (DRD4).

Biological Pathways Linked to Novelty Seeking and Relevant Studies

Findings from numerous studies suggest that individual degrees of the impulsivity, risk taking, and the novelty seeking trait are linked to genetic variability in the transmission of the neurotransmitter, dopamine. The dopaminergic system has been strongly linked to the reward system of the brain. This neurotransmitter is released in key brain areas in response to natural and primary rewards such as food, drink, and sex, and has been associated with feelings of gratification and reinforcement (Iverson & Iverson, 2007, p. 188). A study done on rats showed that, along with natural rewards, novel stimuli are a determinant of the responsiveness to dopamine in the midbrain. Rats in a non-deprived state that were fed novel, palatable food, elicited a more immediate increase in extracellular dopamine release in the nucleus accumbens than rats given their standard food. These results implicate that novelty is important for activation of mesolimbic dopamine, and that dopamine signals adapt to the repeated presentation of reward (Spanagel & Weiss, 1999, p. 526).

More recently, a link between genetics and the novelty seeking trait has been put forth. A group of researchers at the Herzog Memorial Hospital in Jerusalem and Ben-Gurion University in Israel have shown that novelty seeking is associated to a particular polymorphism of the D4 dopamine receptor (DRD4) gene. The DRD4 gene, found on chromosome 11p15.5, codes for the dopamine receptor D4, which is a G-protein coupled receptor. DRD4 is a D2-like receptor which, when activated, causes inhibition of adenylyl cyclase, thereby reducing intracellular concentration of the second messenger cyclic AMP (Neve, Seamans, & Trantham-Davidson, 2004, p. 165). The Herzog-BenGurion study showed that, among 124 unrelated participants, higher than average TCI novelty seeking scores were significantly associated with an exonic polymorphism, the 7-repeat allele at the locus for DRD4 (Ebstein, 1996, p. 78). The participants donated blood samples, and DNA was isolated using the polymerase chain reaction (PCR) and electrophoresis to measure the exon of the DRD4 gene. These results were corroborated by Benjamin et al. (1996) at the National Institute of Health in Maryland, United States, who studied the relationship between DRD4 exon III sequence variants and NEO-PI-R test scores in a population of 315 mostly male siblings, other family members, and unrelated individuals. In addition to confirming Epstein's results, this study showed that the association is the result of genetic transmission, rather than population stratification (p.84). Not only did the two groups find the same correlation between exon repeat length and novelty seeking using different personality questionnaires, but they found it among different ethnic groups of both sexes, and within family members and unrelated individuals (Ebstein, 1996, p. 80).

A study on the molecular characterization of the DRD4 gene, in both humans and rats, has revealed its highly polymorphic 16-amino acid repeat region in the putative third cytoplasmic loop (Asgari, et al., 2004, p. 364). There is a 48-base pair variable number tandem repeat in exon III which ranges from 2 to 16 repeats. The 7-repeat allele is considered the 'DRD4 long' variant, which results in transcription of a longer receptor protein. Differences in ligand binding have been observed between the most common short receptor (4 repeats) and the long variant (Asgari, et al., 2004, p. 364). This study also shows that the outsized D4 receptor protein has decreased functional ability to bind dopamine. In relation to novelty seeking and impulsivity, it is hypothesized that because of low basal dopaminergic activity and resulting low activity of this natural reward pathway, individuals with this variation of the DRD4 gene are susceptible to compensatory reward-seeking behaviours (such as impulsive action toward novel stimuli, food, sex, and drugs) (Cloninger, 1986, p. 167). Numerous additional studies supporting the hypothesized link between DRD4 gene and novelty seeking should be noted. They include studies showing that the number of exon III repeats affects the binding of ligands to the receptor; that DRD4 is distributed in the prefrontal cortex and limbic areas involving cognition, emotions, and decision-making; that dopamine mediates exploratory behaviour in experimental animals; that the rewarding effects of ampehtamines and cocaine are related to dopamine release; and that novelty seeking scores are low in dopamine-deficient Parkinson's disease patients (Benjamin et al., 1996, p. 84).

Conclusion

It is said that "allelic association studies are the strategy of choice for detecting quantitative trait loci, such as those involved in personality, as they provide the statistical power needed to detect relatively small gene effects that contribute to complex behavioural traits" (Ebstein, 1996, p.80). Epstein's and Benjamin's allelic studies have functional significance in determining a partial genetic link to

the novelty seeking trait. Both groups concluded its correlation with DRD4 exon III repeat length, which seems to have an impact on the ability of dopamine to bind to its D4 receptors. Epstein reports that the repeat sequence may confer other properties to the D4 receptor protein that are undetected in binding studies, and that further investigation of the effects of the polymorphism on receptor activities would be valuable.

Although these studies are informative, the DRD4 gene does not entirely explain the biological basis for novelty seeking. Animal models and twin studies have indicated that about half of novelty seeking behaviour is attributable to genes, while the other half to environmental conditions (Ebstein, 1996, p. 80). Epstein acknowledges that there are probably four or five other genes involved in expression of the trait with the same influence as the D4 receptor, and that DRD4 probably accounts for 10% of the difference in novelty seeking behaviour between individuals.

One must consider other factors that contribute to regulation of this trait, including other associated genes and neurochemical pathways, environmental circumstances, and psychopathological disorders. There is research indicating a possible overlap in the neurobiological processes involved in novelty seeking. Neuroanatomical areas that are involved in dopaminergic activity include the nucleus accumbens, hypothalamus, amygdale, hippocampus, and frontal cortex, and thus study of these systems and their link to novelty seeking should be explored. Additionally, consideration should be given to other neurotransmitters that are involved in reward pathways such as serotonin, acetylcholine, and norepinephrine.

Furthermore, it is important to note that novelty seeking only measures one aspect of impulsivity. Perhaps studies done on the DRD4 gene in relation to other subtraits or risk factors for impulsivity, such as addiction or aggression, could enhance this biological evidence for impulsivity.

References

Asgari, V., Schoots, O., van Kats, S., Ohara, K., Jovanovic, V., Guan, H.,...van Tol, H. (1994). Dopamine D4 receptor repeat: analysis of different native and mutant forms of the human and rat genes. *Molecular Pharmacology, 46*(2), 364-373.

Bailey, J., Breidenthal, S., Jorgensen, M., McCracken, J., & Fairbanks, L. (2007). The association of DRD4 and novelty seeking is found in a nonhuman primate model. *Psychiatric Genetics, 17*(1), 23-27. doi: 10.1097/YPG.0b013e32801140f2

Benjamin, J., Li, L., Patterson, C., Greenberg, B., Murphy, D., & Hamer, D. (1996). Population and familial association between the D4 dopamine receptor gene and measures of Novelty Seeking. *Nature Genetics, 12*, 81-84. doi: 10.1038/ng0196-81

Bevins, R. (2001). Novelty Seeking and Reward: Implications for the study of high-risk behaviours. *Current Directions in Psychological Science, 10*(6), 189-193. doi: 10.1111/1467-8721.00146

Cloninger, C. (1986). A unified biosocial theory of personality and its role in the development of anxiety states. *Psychiatric Development, 4*(3), 167-226.

Cloninger, C. R., Przybeck, T. R., & Svrakic, D. M. (1991). The Tridimensional Personality Questionnaire: US normative data. *Psychological Reports, 69*(3 Pt 1), 1047-1057. doi: 10.2466/pr0.1991.69.3.1047

Costa, Jr. P., & McCrae, R. (1992). Revised NEO personality inventory manual. Psychological Assessment Resources.

Depue, R. A, & Collins, P. F. (1999). Neurobiology of the structure of personality: Dopamine facilitation of incentive motivation and extraversion. *Behavioural and Brain Sciences, 22*(3), 491-569. doi: 10.1017/S0140525X99002046

Dickman, S. (1993). Impulsivity and information processing, in The Impulsive Client: Theory, Research, and Treatment. *American Psychological Association, 1*, 151-184. Retrieved from http://dx.doi.org/10.1037/10500-010

Ebstein, R., Novick, O., Umansky, R., Priel, B., Osher, Y., Blaine, D.,...Belmaker, R. H. (1996). Dopamine D4 receptor (DRD4) exon III polymorphism associated with the human personality trait of novelty seeking. *Nature Genetics, 12*, 78-80. doi: 10.1038/ng0196-78

Iverson, S., & Iverson, L. (2007). Dopamine: 50 years in perspective. *Trends in Neurosciences, 30*(5), 188-193. Retrieved from http://dx.doi.org/10.1016/j.tins.2007.03.002

Neve, K., Seamans, J., & Trantham-Davidson, H. (2004). Dopamine receptor signalling. *Journal of Receptor and Signal Transduction Research, 24*(3), 165-205. doi:

10.1081/RRS-200029981

Spanagel, R., & Weiss, F. (1999). The dopamine hypothesis of reward: past and current status. *Trends in Neuroscience, 22*(11), 521–527. Retrieved from http://dx.doi.org/10.1016/S0166-2236(99)01447-2

Tschirren, B., & Bensch, S. (2010). Genetics of personalities: no simple answers for complex traits. *Molecular Ecology, 19*(4), 624-626. doi: 10.1111/j.1365-294X.2009.04519.x.

Whiteside, S., & Lynam, D. (2000). The Five Factor Model and impulsivity: using a structural model of personality to understand impulsivity. *Personality and Individual Differences, 30*, 669-689. doi: 10.1016/S0191-8869(00)00064-7

Zuckerman, M., Kuhlman, D., Joireman, J., Teta, P., & Kraft, M. (1993). A comparison of three structural models of personality: the big three, the big five, and the alternative five. *Journal of Personality and Social Psychology, 65* (4), 757-768. Retrieved from http://dx.doi.org/10.1037/0022-3514.65.4.757

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 ?*

Nous acceptons des soumissions tout au long de l'année, incluant le printemps et l'été.
Vous serez informé(e) lorsque le Comité éditorial commencera la révision de votre soumission.

Vous trouverez de plus amples informations sur notre site web : www.riss-ijhs.ca

CALL FOR PAPERS

Submission criteria are based on the twelve determinants of health as outlined by Health Canada and the Public Health Agency of Canada. Ideally, anyone who wishes to submit their original work to the IJHS should clearly identify which determinant of health is associated with their paper and the nature of the relationship: *how is the subject related to human health through the chosen determinant of health?*

We accept submissions year round, including spring and summer.
You will be informed once the Editorial Committee begins to review your submission.

You will find more information on our website: www.riss-ijhs.ca