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The World Psychiatric Association (WPA)

The WPA is an association of psychiatric societies aimed to increase knowledge and skills necessary for work in the field of mental health and the care for the mentally ill. Its member societies are presently 123, spanning 106 different countries and representing more than 150,000 psychiatrists. The WPA organizes the World Congress of Psychiatry every three years. It also organizes international and regional congresses and meetings, and thematic conferences. It has 55 scientific sections, aimed to disseminate information and promote collaborative work in specific domains of psychiatry. It has produced recently several educational programmes and series of books. It has developed ethical guidelines for psychiatric practice, including the Madrid Declaration (1996). Further information on the WPA can be found in the website www.wpanet.org.

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World Psychiatry

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EDITORIAL

'5000 Years of Science and Care - Building the Future of Psychiatry': the 13th World Congress of Psychiatry

Ahmed Okasha

President, World Psychiatric Association

The 13th World Congress of Psychiatry will take place in Cairo, Egypt from 10 to 15 September, 2005. This is the first time in the history of the WPA that an African and Arab country hosts the World Congress.

From Egypt came the first calendar, the earliest script, the oldest known love song, the first decorated stone monumental building and the tallest tomb. Egypt also has the oldest university in the world (the Islamic University of Al Azhar). It is home to five World Heritage sites: Memphis, capital of the Old Kingdom, with its associated necropolis; the modern city of Luxor with its temples and tombs; all of the Nubian temples from Abu Simbel to Philae; the early Christian pilgrimage center of Abu Mina, and the ancient Islamic quarter of Cairo.

Ancient Egyptians knew mental disorders 5,000 years ago. In spite of the mystical beliefs, psychiatric patients were cared for and treated, as were those with physical ailments. In the country that has given birth to the foundations of civilization, we shall organize our World Congress of Psychiatry in 2005 around the theme '5,000 Years of Science and Care – Building the Future of Psychiatry', thus discussing the old and the new with a view on future progress.

World Congresses of Psychiatry are held to examine the worldwide status and future directions of psychiatry; increase worldwide exchanges of information among psychiatrists and between psychiatrists and other mental health professionals, as well as patients and their families; improve educational and quality of care standards by providing up-to-date informational and skills development opportunities on important and timely topics, including the presentation of WPA educational programs and other activities; support and stimulate collaborative research in the biological, psychological and social sciences relevant to psychiatry and mental health; strengthen links among WPA Member Societies and Affiliated Associations; make psychiatry more visible at the regional and international levels, as well as promote the institutional effectiveness and international standing of the host Society, and facilitate the exercise of WPA organizational functions through General Assemblies and other business meetings, in a context where diverse cultures have the chance to interact, learn from and about each other.

The Cairo Congress will discuss the state of the art as regards all the complexities of today's psychiatry, through addressing a multiplicity of issues such as human development; biological psychiatry and neurosciences; social and cultural psychiatry; psychiatry in Africa and other developing regions; epidemiology and public health; diagnostic systems; dementia and related cognitive disorders; substance abuse and dependence; schizophrenia and related disorders; mood disorders; anxiety, stress and adjustment disorders; dissociative and somatization disorders; eating, sexual and sleep disorders; personality disorders and accentuated personality; child and adolescent mental and behavioral disorders; suicide and other dangerous behaviors; HIV and psychiatry; primary care and mental health; pharmacotherapies; psychotherapies; sociotherapies; prevention and health promotion; ethics, law, human rights and mental health; mental health economics and services research.

Several symposia with contributions from all the 55 WPA scientific sections will be organized, as well as special, regular and industry-supported symposia, panels, workshops, seminars, meet-the-expert sessions, forums, debates and posters from East and West, North and South, developed and developing countries, in addition to video teleconferences, new book and journal presentations, new research paper sessions and free oral communications.

For the first time in a World Congress, master clinical case conferences will be held with worldwide pioneers in clinical psychiatry, where the opportunity for active participation and intervention of the audience will be available. In fact, over 90% of the participants in the Congress will be clinicians, who need to return home with a matrix for upgrading knowledge and skills, renewing professional and personal relations and establishing new ones. Emphasis on partnership as a vital element of our profession will be the focus of attention, including partnership among mental health professionals, and between them and consumers on the one hand and policy makers on the other, and also the partnership between developed and developing countries. For further details on the Congress and deadlines for submission of contributions, please visit the website www.wpa-cairo2005.com.

The four plenary lectures will be delivered by the WPA President and President Elect, the Egyptian 1999 Nobel laureate in Chemistry Ahmed Zewail, and the winner of the Jean Delay Prize 2005 (this is the Nobel Prize of the WPA, usually awarded to neuroscientists of high caliber, most probably from developed countries).

For the first time in a World Congress of Psychiatry, a special award for two young scientists in developing countries will be presented: the WPA Okasha Award (see the WPA News in this issue of World Psychiatry for further information).

The 13th World Congress of Psychiatry will attempt to translate scientific advances into a better care for mental patients, reflecting the essence of our theme '5000 Years of Science and Care – Building the Future of Psychiatry'.

You are welcome in Egypt to enjoy the recent developments in our profession, while hosted by a country which is the cradle of civilization.

Research for Change: the role of scientific journals publishing mental health research

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There is an enormous gap between the burden of mental disorders and mental health resources in low- and middle-income countries. The Mental Health: Global Action Programme of the World Health Organization (WHO) envisions an active role for research in the multidimensional efforts required to change the current mental health situation in these countries (Research for Change). WHO's strategies to achieve this include developing a research policy and a priority agenda at country level with active collaboration from all stakeholders, building research capacity and infrastructure and involving scientific journals to stimulate and disseminate public health oriented research. A recently agreed joint statement by editors of prominent journals publishing mental health research and WHO sets major objectives and some possible strategies for achieving this. WHO is committed to making Research for Change a reality by working with partners who share this aim.

Key words: Mental health, research, developing countries, scientific journals, World Health Organization

There is an enormous gap between the burden of mental disorders and mental health resources in low- and middle-income (LAMI) countries (1,2). In absolute terms, the burden of neuropsychiatric conditions falls heavily on LAMI countries. In contrast, the resources available to meet mental health challenges in these countries are meagre: an overwhelming majority of countries in African and South East Asian regions spend less than 1% of their limited health budgets on mental health (2). In high-income countries themselves, between 44% and 70% of patients with common and severe mental disorders do not receive treatment (3). The treatment gap in developing countries could be as large as 90%. Closing this gap is a clear obligation; otherwise, no discourse around new classifications, concern about more sophisticated diagnosis, or development of innovative psychopharmacological research can be credible (4).

The Mental Health: Global Action Programme of the World Health Organization (WHO) envisions an active role for research in the multidimensional efforts required to change the current mental health situation at country level (Research for Change) (5). WHO intends to collaborate with countries and all other stakeholders to make research an instrument for change. Research-generated information is perceived as essential to determine needs; to propose new cost-effective interventions of an individual or collective nature, to monitor the process of their implementation and to evaluate the changes sought; and to explore the obstacles that prevent recommended cost-effective action to be carried out. Conceivably, research-generated information will enable LAMI countries to better utilise their meagre mental health resources.

The difference between the research information that is needed to plan the best possible services in a given setting and what is currently available can be called the research gap. All available indications point towards the fact that the research gap is particularly large in LAMI countries.

Doing more research alone does not suffice: research must be relevant to the needs of LAMI countries. The World Health Report 2001 (6) suggests that relevant research in and for LAMI countries should assist them in reducing the burden of common and disabling disorders through evidence based and feasible interventions, while ensuring equity and cultural relevance and safeguarding ethical principles.

Currently, the mental health effort in the developing world is based primarily on evidence from high-income countries. This approach has a serious disadvantage, in that the majority of the available information is collected from vastly different cultural and socio-economic contexts. Culturally relevant research should inform mental health policy and service development, treatment decision-making, and anti-stigma and discrimination programmes.

Similarly, mental health research in relation to LAMI countries that is done by academics from high-income countries (such research forms at least one quarter of the mental health literature available on LAMI countries) often has no real connection to local service development (7). The relevance of research may be better ensured if a consortium, run democratically by researchers, planners and administrators, decision-makers, donors and community representatives jointly establish the research policies of a country for a defined period of time.

STRATEGIES TO ADVANCE RESEARCH IN LAMI COUNTRIES

In order to advance research in LAMI countries, it is first of all necessary to set a priority agenda, viable and zealously tailored to country needs, characteristics and resources. Preferably, the research policy for a country should be developed in harmony with all other components of the national mental health policy and strategies,

since research should provide to most of these components the necessary scientific inputs, with the baseline and evaluation data they require.

Second, a research-friendly cultural environment needs to be created. Policy makers, programme planners and managers, governmental officials, mental health advocates, professionals, users and carers, and university settings of LAMI countries should be involved in research efforts that will underlie national mental health action.

Third, a major undertaking on capacity building and infrastructural support is required. International agencies and donor countries and institutions should play a crucial role in training researchers and in helping them to return and remain in their respective countries of origin. Probably the best ways of doing this is to promote (truly) collaborative research and provide training or technical and scientific support to institutions in LAMI countries.

Fourth, methodologies that do not require sophisticated infrastructural support should be made available widely. Simple methods could solve important research problems and should not be devalued when compared with complex methodologies. Evidence resulting from these methods should not be regarded as unsuitable for application. It is the fit between problem and the method used to solve it that counts.

Fifth, as detailed later, scientific journals have to play a considerably greater role in decreasing the research gap in LAMI countries.

The research efforts from LAMI countries will have greater chances of success if research institutions in high-income countries, research foundations and country donors, and editors of scientific journals provide their fullest and sustained support to national and regional efforts in LAMI countries.

ROLE OF SCIENTIFIC JOURNALS PUBLISHING MENTAL HEALTH RESEARCH

Public mental health in LAMI countries can be improved by facilitating the generation and flow of information. Scientific journals can play a major role in achieving these ends. However, a co-ordinated priority driven program is required for mental health research dissemination and to facilitate the transfer of results of mental health research into policy and practice, as is evidenced by the current state of affairs.

LAMI countries contribute only about 6% of articles to leading psychiatric journals (8,9). Even more worrying is the fact that, in biomedical publications, the gap between countries with low and high level of publications is widening (10). The causes for this could be many, including less mental health research being done in LAMI countries due to low priority for research, lesser resources or limitations in research capacity and difficulties in reporting research due to language. But, it is likely that limited appreciation of the research needs of developing countries at the level of reviewers and editorial boards of international journals could also play a part. Only four out of a total of 530 editorial and advisory board members of the ten psychiatric journals with the highest impact factor rating for the year 2000 were based in LAMI countries (11). Similarly, there is a tendency among biomedical journals to send manuscripts to reviewers within their own region (12). The absence of well-informed interlocutors familiar with research needs of LAMI countries could lead to a bias against publication of research from or about these countries.

The trend towards increased publication of resource-intensive biological research in indexed journals (in order to maintain/increase the impact factor) may be another reason for the low rate of publications from LAMI countries (13). Of the twenty journals in the mental health field with the highest impact factor, ten publish papers exclusively on biological psychiatry and/or psychopharmacology topics and others, like Archives of General Psychiatry, American Journal of Psychiatry and Schizophrenia Bulletin, have increased the proportion of papers on biological psychiatry topics during the last two decades (13,14). Research focusing on mental health services is not less important than biological research, and may be more relevant to answering the mental health needs of LAMI countries. Such research does not need to be complicated and expensive and can certainly be carried out in LAMI countries (13).

As a result of these difficulties, the bulk of research from developing countries gets published in journals that are not easily accessible locally or internationally. The dice is loaded against journals based in LAMI countries becoming and staying visible. They face a multitude of problems, including those of resources for publication and dissemination (financial, managerial, marketing), editorial skills and review process, author pool and language, and perhaps biases in indexing systems (15). An overwhelming majority (98%) of biomedical journals indexed in international databases are from the developed world (16). The lack of visibility affects their dissemination opportunities - e.g., libraries in LAMI countries subscribe mainly to influential journals from the Western countries (17) - and thereby the possibility of application of research results contained in them.

LAMI countries also have problems in accessing scientific materials because of their cost. In the last couple of decades, the subscription costs of many scholarly journals (especially those published by certain powerful commercial publishers) have escalated at a rate far exceeding the rate of inflation (18). In addition, many new journals have been started. Even large academic libraries in high-income countries have had to be fairly selective about subscribing to journals and have indeed carried out extensive journal-cancellation projects in the last few years.

Individual efforts have been made by journals and organizations to remedy the disproportion between research needs of populations and available publications

(13,19,20). The World Psychiatric Association launched its journal World Psychiatry in three language editions (English, Spanish and Chinese), and made printed copies available free of charge to more than 31,000 psychiatrists in 121 countries. A significant improvement has occurred in electronic dissemination of research, due to the cost-effectiveness of this medium. A number of organizations - e.g., the WHO sponsored Health InterNetwork Access to Research Information (HINARI), the Scientific Electronic Library Online (SciELO) project of Latin America, scholarly societies and journals (including World Psychiatry) provide access at no or low cost to LAMI countries (21). These initiatives are beginning to have an impact, but a lot still needs to be done, since freely accessible literature forms only a small proportion of scholarly publishing and LAMI countries have limited access to Internet itself. Similarly, levying of page charges makes it difficult for authors from LAMI countries to publish in open access journals unless page charges are subsidized by research funding agencies or governments (18,21).

EDITORS TAKE UP THE AGENDA OF REDUCING THE RESEARCH GAP

As a part of the Research for Change initiative, the WHO Department of Mental Health and Substance Abuse and the WHO Bulletin organized an international meeting on 'Mental Health Research in Developing Countries: Role of Scientific Journals' on 20-21 November, 2003 in Geneva, Switzerland. The meeting was attended by twenty-five editors representing mental health journals and general and public health journals publishing mental health research. A number of other editors reviewed and contributed to the background and follow-up material.

Issues related to responsibility of scientific journals towards international mental health, supporting mental health researchers from LAMI countries, supporting mental health journals from LAMI countries, and enhancing dissemination of mental health research publications were discussed. It was felt that 'international' journals should strive for a global impact in terms of populations served, burden of diseases, and long-term economics. Editors also felt that there is much that health professionals and policy makers from high-income countries can learn from their counterparts in LAMI countries.

Established journals have an important role to play in developing mental health research and publishing capacity in low- and middle-income countries. Training in research methodology and scientific writing for researchers in LAMI countries could be done through mentoring, personal encouragement, training courses and research collaboration. Author helpful policies (e.g., detailed recommendations for revision, manuscript editing, etc.) could help in attracting more submissions from LAMI countries and in salvaging otherwise useful papers that have not been presented well. Editors' and reviewers' experience with and interest in LAMI countries could be an asset in facilitating such publications.

Journals in LAMI countries, besides being a repository of local mental health wisdom, can also help in educating their authors and in translating mental health research into action through dissemination of relevant local and international information to policy makers and public health officials in their countries and regions. Mentorship, twinning arrangements and training workshops on editorial procedures, peer review and overall journal management may be useful for editors and reviewers of journals based in LAMI countries.

A joint statement (Annex 1) was issued by the participants in the Geneva meeting (Annex 2). A catalogue of ideas (Annex 3) was also developed to guide follow-up actions by individual journals and editorial and international organizations. The joint statement represents a common vision to bring about policy changes to facilitate the publication of research from, enhance research and publishing capacity of researchers and journals from, and enhance dissemination of research to LAMI countries. It is hoped that this shared vision, along with concrete follow-up action, will help in reducing the research gap in LAMI countries.

MEASURES OF CHANGE

The WHO is committed to making Research for Change a reality in the near future. In relation to journals, some of the measurable effects could be:

- Increased participation of researchers from LAMI countries in editorial boards and peer review panels of internationally accessible mental health journals.
- Increase in the number of internationally accessible mental health journals with a multi-lingual approach to publication.
- Increased proportion of published work from LAMI countries in indexed internationally accessible mental health journals.
- Increased number of mental health journals from LAMI countries in international indexing systems and wider availability of these journals.
- Increased collaboration between editors of mental health journals from LAMI and other countries.
- Increase in number of mental health journals giving free access to their contents and increase in the volume of material to which free access is given by journals.

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ANNEX 1. *Joint Statement: 'Galvanising mental health research in low- and middle-income countries: role of scientific journals'*

The Department of Mental Health and Substance Abuse, WHO organized a meeting on 'Mental Health Research in Developing Countries: Role of Scientific Journals' in Geneva on 20 and 21 November 2003 that was attended by twenty-five editors representing journals publishing mental health research. A number of other editors reviewed and contributed to the background and follow-up material. This statement is issued by all participants jointly.

Research is needed to address the enormous unmet mental health needs of low- and middle-income (LAMI) countries. Scientific journals play an important role in production and dissemination of research. However, at present, only a minute proportion of research published in widely accessible mental health and psychiatric journals is from or about these countries. Yet over 85% of the world's population lives in the 153 countries categorized as low-and middle-income, according to World Bank criteria. Even more worrying is the observation that the gap between these and high-income countries may be widening in terms of their number of publications. The meeting was aimed at finding ways of resolving this unsatisfactory situation.

Responsibility of scientific journals towards international mental health

Science, in its quest to accomplish valid generalisations about nature, is inherently global. Researchers from all parts of the world should, desirably, contribute to new knowledge about mental health and mental illness, and publish their reports in widely accessible journals. This process is facilitated by a shared understanding of aims and scientific methods, formats of presentation and reference to previous published work. Mental health research from LAMI countries is needed for advocacy, policy development, establishment and expansion of clinical services and to educate investigators in research skills. A steady stream of information about mental health issues in these countries would also contribute to a greater international and multicultural understanding of mental health and ill-health.

Unfortunately, substantial barriers impede publication of mental health research from LAMI countries in widely accessible journals. Researchers from LAMI countries are often unable to meet the requirements of these journals because of limited access to information, lack of advice on research design and statistics, difficulty in writing in a foreign language, and overall material, financial, policy and infrastructural constraints. Limited appreciation of the research needs of, and realities in LAMI countries and the comparative anonymity of their researchers and research centres in editorial offices of journals may constitute additional barriers. Many researchers from LAMI countries are daunted by the seemingly insurmountable chasm between their research effort and its publication in international journals.

Supporting mental health researchers from low- and middle-income countries

We need to face the challenge of reducing the barriers to publication of mental health research by investigators working in LAMI countries. Time, skills, resources and commitment are needed to publish relevant studies from these countries. Editors' and reviewers' experience with and interest in LAMI countries could be an asset in facilitating publication. Meeting researchers from these countries on 'their home ground' could assist this process. International journals could also help researchers improve their submissions by diligent assessment, detailed recommendations for revision and sympathetic consideration of revised versions, even if it means requesting reviewers to 'take an extra round' to make papers suitable for publication. This is not to say that journals need to lower their standards in publishing papers from LAMI countries;

rather, they should devise strategies to help authors attain those standards. Other approaches to support contributions from LAMI countries could be to launch 'starter' sections such as information pages and special columns or even dedicated issues of the journal.

Capacity building is the paramount factor in the long term. Training in research methodology and scientific writing is needed. This could be done through mentoring, personal encouragement, training courses and research collaboration. Increased access to mental health research publications would, by itself, help in capacity building.

Supporting mental health journals from low- and middle-income countries

A major impediment in accessing mental health research from LAMI countries is the lack of visibility of journals published in these countries. Most of them are not indexed in international databases and are often not available beyond their country or region of origin. These journals are published under strained circumstances, in that they often lack sound financial support and have a hard time becoming self-sufficient. They also have difficulty in obtaining suitable articles for publication because their author pool is limited; moreover, influential authors from this pool prefer to publish their best research in indexed journals. Some authors who submit their articles to LAMI country based journals may have limited skills in conducting research and/or in writing up their reports. However, it must be stressed that some excellent work does find publication in these journals.

The task of strengthening journals in LAMI countries begins from the recognition of their role as contributors to the enhancement of the mental health knowledge base and as partners in the international research community.

Editors of LAMI country based journals require support to elevate standards in editorial procedures, peer review and overall journal management since sufficient expertise and experience may be lacking. This could be achieved through their participation in the publication process of established journals, mentorship, twinning arrangements and training workshops.

Enhancing dissemination of mental health research publications

Many high quality mental health journals have a wide distribution, but most of their subscribers are from high-income countries. Special attention to dissemination of research findings is needed urgently in order to maximize their impact on mental health policy and practice and advance relevant research in LAMI countries. Increasing online availability is cost-effective since little additional expenditure is required to provide access to new users apart from the initial costs of posting material on a website. Free access to many categories of electronic resources is provided by many journals. Initiatives such as the WHO-led Health InterNetwork Access to Research Initiative (HINARI) offer institutions in LAMI countries electronic access to thousands of journals at no or very low cost. The Open Access model provides free online access along with the possibility of unrestricted dissemination of research materials, but charges for publication may be prohibitive for authors from LAMI countries unless support comes from funding agencies and governments, e.g., the Scientific Electronic Library Online (SciELO) project in Latin America. Governments in other LAMI countries need to be made aware of the opportunities provided by information technology for dissemination and application of research knowledge.

The role of various stakeholders

Editors of journals, editors' associations and international organizations, including WHO could help achieve the aforementioned objectives. A catalogue of ideas is presented to act as a starting point for specific action. Although these ideas have been developed for the field of mental health, many of them may apply to other areas of health.

ANNEX 2. *Signatories to the Joint Statement*

Acta Psychiatrica Scandinavica (Povl Munk-Jorgensen)***, American Journal of Orthopsychiatry*** (Carlos Sluzki), ***Annals of General Hospital Psychiatry*** (George St. Kaprinis, Konstantinos N. Fountoulakis), ***Anthropology and Medicine*** (Sushrut Jadhav), ***Australian and New Zealand Journal of Psychiatry*** (Sidney Bloch), ***BioMed Central Psychiatry*** (Pritpal S. Tamber), ***British Journal of Psychiatry*** (Peter Tyrer), ***British Medical Journal*** (Kamran Abbasi), ***Bulletin of World Health Organization*** (Hooman Momen), ***Child Abuse and Neglect, The International Journal*** (John M. Leventhal), ***Chinese Journal of Nervous and Mental Disease*** (Li Yingxi, Guan Jinli), ***Comprehensive Psychiatry*** (David L. Dunner), ***Culture, Medicine and Psychiatry*** (Mary-Jo Delvecchio Good), ***Epidemiologia e Psichiatria Sociale*** (Michele Tansella), ***L'Evolution Psychiatrique*** (Yves Thoret), ***Indian Journal of Psychiatry*** (Utpal Goswami), ***L'Information Psychiatrique*** (Thierry Tremine), ***International Journal of Social Psychiatry*** (Dinesh Bhugra), ***International Psychiatry*** (Hamid Ghodse), ***Journal of Child and Adolescent Mental Health*** (Alan Flisher), ***Journal of Nervous and Mental Disease*** (Eugene B. Brody, Kathy McKnight), ***Lancet*** (Laragh Gollogly), ***Primary Care Psychiatry*** (Sean Lynch), ***Psychiatry: Interpersonal and Biological Processes*** (Robert Ursano), ***Psychiatry Research*** (Monte Buchsbaum), ***Psychological Medicine*** (Eugene Paykel)***, Psychology and Psychotherapy: Theory, Research and Practice*** (Phil Richardson), ***Psychopathologie Africaine*** (Momar Gueye), ***Quarterly Journal of Pakistan Psychiatric Society*** (Amin A. Gadit), ***Revista Brasileira de***

Psiquiatria (Jair Mari), ***Salud Mental*** (Hector Perez-Rincon), ***Social Psychiatry and Psychiatric Epidemiology*** (Paul Bebbington), ***South African Journal of Psychiatry*** (Robin Emsley, Susan Hawkridge), ***Transcultural Psychiatry*** (Laurence J. Kirmayer), ***World Psychiatry*** (Mario Maj), ***Forum for African Medical Editors*** (James K. Tumwine), ***Global Forum for Health Research*** (Andres de Francisco), ***World Association of Medical Editors*** (Ana Marusic, Peush Sahni), ***World Health Organization*** (Shekhar Saxena, Pratap Sharan, Benedetto Saraceno, Barbara Aronson, Vladimir Poznyak, Izthak Levav, Edith Certain, R. Srinivasa Murthy, Tikki Pang).

ANNEX 3. *Catalogue of ideas*

Individual journals

Giving priority to relevant mental health research from low- and middle-income countries

- Educate editors and reviewers on research needs of and research infrastructure in LAMI countries.
- Use surveys of various stakeholders such as readers (including those from other regions) for shaping journals' priorities.
- Sensitize readers and other stakeholders to international mental health issues (e.g., through special sections and dedicated issues, guest editorship and the commissioning of relevant research from LAMI countries).
- Critically re-examine the use and limitation of measures such as citation rates and impact factors.
- Adopt a multilingual approach, such as translation of relevant articles and abstracts into other languages.
- Include reviewers and correspondents with a special interest and expertise in LAMI countries on editorial boards.
- Accept a higher proportion of submissions from LAMI countries for review.
- Encourage general medical journals to publish mental health research especially in countries/regions where no mental health journal exists at present.

Supporting authors/researchers from low- and middle-income countries

- Familiarize researchers from LAMI countries with the peer review process.
- Provide constructive critical feedback/detailed recommendations for revision.
- Make provision for extra rounds of editing, assistance with language and use of technical editors.
- Pay attention to the educational goals of the review process (e.g., availability of reviewer's comments to readers or recruiting young researchers in LAMI countries to referee papers).
- Provide mentorship and support prior to submission.
- Organise training workshops for LAMI country researchers and students on scientific writing and research methodology.
- Facilitate the involvement of researchers in multi-centre projects and research groups.
- Accept and process submissions online.
- Devise strategies to prevent economic exclusion of researchers from LAMI countries in author/input paying publishing models.

Supporting journals from low- and middle-income countries

- Support 'twinning' or 'pairing' arrangements, such as invited editorials, exchange of journals, cross-publication of contents/abstracts/summaries/articles and joint publications.
- Agree to serve on editorial boards or as reviewers.
- Agree to mentor reviewers and editors.
- Provide training workshops for editors and reviewers.
- Support national/regional journals in developing their own websites and/or seeking inclusion in specialized websites on mental health.

Enhancing dissemination

- Participate in electronic dissemination initiatives or provision of free/open access through the journal's website.
- Participate in 'buddy system'/peer sponsoring initiatives.
- Employ user-friendly technology for easier downloads.
- Subsidize journal subscriptions for LAMI countries.
- Explore mechanisms for publication of selected papers in more than one journal for wider dissemination.

Editors' associations

- Develop guidelines for good editorial practice concerning publishing and research ethics and conflicts of interest.
- Facilitate access to literature and bibliographic services (e.g., through a directory of databases).
- Support authors to access appropriate specialized journals and specific audience (e.g., through a database of journals and instructions to authors).
- Facilitate mentoring for editors, reviewers and researchers.
- Organise training of editors, reviewers and researchers from LAMI countries.
- Facilitate the multidirectional flow of articles, resources and expertise (e.g., translation of relevant articles and support with information technology).

International organizations

Supporting mental health research, research infrastructure and publications

- Influence other international institutions to give

priority to mental health research in their agendas for LAMI countries.
- Support national institutions in LAMI countries to urge their governments to give higher priority to mental health research.
- Support inclusion of researchers/editors from LAMI countries in relevant decision-making forums.
- Facilitate capacity building for researchers and journals from LAMI countries.

Enhancing dissemination

- Assess information needs in LAMI countries and raise awareness of these.
- Provide access to journals publishing mental health research (e.g., expansion of HINARI or enabling journals to be open access).
- Encourage and facilitate the application of information technology.

Enhancing collaboration

- Develop networks between editors, editorial organizations, professional bodies, publishers, funding agencies, national and international organizations and the media.
- Adopt a systematic approach for follow up: statement of changes hoped for, development of outcome criteria, assessment of progress.

Gene-environment interactions in mental disorders

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Research clearly shows that both nature and nurture play important roles in the genesis of psychopathology. In this paper, we focus on 'gene-environment interaction' in mental disorders, using genetic control of sensitivity to the environment as our definition of that term. We begin with an examination of methodological issues involving gene-environment interactions, with examples concerning psychiatric and neurological conditions. Then we review the interactions in psychiatric disorders using twin, adoption and association designs. Finally, we consider gene-environment interactions in selected neurodevelopmental disorders (autism and schizophrenia).

Key words: Genetic factors, environment, interaction, neurodevelopmental disorders

Family, twin, and adoption studies have firmly established the roles of both genes and environment in mental disorders. It remains difficult, however, to find genes for these disorders, and to characterize the particular environmental circumstances under which psychopathology emerges. The reason for this difficulty lies in the complex nature of mental disorders. Many disorders – like many normal physiological conditions (e.g., blood pressure) and cognitive abilities (e.g., intelligence) – probably result from the combined action of multiple genes of small effect together with a variety of environmental factors. In addition, genetic and environmental factors interact with each other in complex ways to influence phenotype (1). In other words, individual genes and environmental factors exert their effects only via interaction with other genes and other environmental factors. The issue is no longer one of nature *versus* nurture; rather, we must ask: how do genes and environment *interact* to produce a behavioral phenotype?

In this paper, we will focus on 'gene-environment interaction' in mental disorders, using genetic control of sensitivity to the environment as our definition of that term (2). Gene-environment interaction occurs when environmental influences on a trait differ according to a person's genetic predispositions, or when a person's genetic predispositions are expressed differently in different environments. Interaction phenomena are important. By ignoring interactions, true genetic and environmental effects can be obscured, which leads to false negative results and, more generally, to inconsistent findings in the literature.

The subsequent discussion begins with a consideration of methodological and measurement issues involving gene-environment interactions, with examples concerning psychiatric and neurological conditions. This will be followed by a representative review of interactions in psychiatric disorders using twin, adoption and association designs. Finally, gene-environment interactions will be considered in selected neurodevelopmental disorders (autism and schizophrenia) to highlight their potential to shed light on underlying etiologic mechanisms in this class of psychiatric conditions.

METHODOLOGY AND MEASUREMENT ISSUES

Several excellent reviews discuss some of the methodological issues and problems involved in assessing gene-environment interaction, and the reader is referred to these for a more detailed discussion (3-7). Some of these problems are ones of definition and assessment, i.e., in order to test for gene-environment interaction, individuals must be classified according to presence or absence of genetic and environmental risk, and the specification of both can be difficult. Environmental exposures are difficult to define and measure precisely, and are understudied in the context of genetic research designs (8). Moreover, putative environmental risk factors may not be truly environmental. This phenomenon is known as gene-environment correlation, in which an individual's genotype influences his exposure to the environment. In other words, 'environmental' factors are themselves attributable to genetic influences. Gene-environment interaction is difficult to measure in the presence of gene-environment correlation (4).

On the other hand, there are several different ways of measuring genotype (3). Unfortunately, because of the lack of well-established candidate genes for mental disorders (and relatively little knowledge of the biological processes that give rise to mental disorders), researchers have to rely on less direct ways of classifying a person according to genetic risk. This point underscores the importance and potential impact of the developments in molecular genetics, which will make it easier to identify genes and genetic markers associated with mental disorders. These ongoing advances will eventually allow the assessment of specific genotypes in specific environments, which will facilitate direct and systematic investigations of gene-environment interactions.

The impact of advances in molecular genetics (i.e.,

identifying genetic variants associated with mental disorders) can be illustrated using the case of Alzheimer's disease (AD). An allelic association exists between AD and the ε4 allele of the apolipoprotein E (APOE) gene (9), which results in a 6-fold risk for AD in individuals with one or two copies of this allele (10). APOE is considered a 'susceptibility gene', because it is neither necessary nor sufficient for the development of AD. Other genes or environmental agents must be present for the ε4 allele to increase risk for AD. One of the earliest environmental risk factors associated with AD was a history of head injury (11,12). Because a positive family history was also a risk factor for the disease (13), attempts were made to find evidence for gene-environment interaction, using family history as an indicator of genetic risk. However, results of early studies failed to demonstrate convincing evidence of interaction (14,15). Mayeux et al (16) then studied the combined effects of head injury and genetic susceptibility on risk for AD, and found no increase in risk associated with head injury in the absence of the ε4 allele, a two-fold increase in risk with ε4 alone, and a 10-fold increase in risk with both ε4 and a history of head injury. These findings and those from subsequent studies examining frequency of the APOE-ε4 allele in patients with head injury have led to hypotheses regarding a biological mechanism whereby head injury contributes to the pathogenesis of AD by increasing beta-amyloid precursor protein (APP) deposition in the cerebral cortex, which exacerbates the effect of the APOE-ε4 allele (which is thought to be related to cerebral beta-APP deposition).

Malaspina et al (17) found similar evidence for gene-environment interaction in schizophrenia, another mental disorder that has been associated with head injury. Using membership in multiplex schizophrenia and bipolar pedigrees as proxies for, respectively, greater and lesser genetic loading, they found that schizophrenic subjects from schizophrenic pedigrees were more likely to have experienced a traumatic brain injury (19.6%) than schizophrenic subjects from bipolar pedigrees (4.5%). Within the schizophrenia pedigrees, head injury was associated with a greater risk of schizophrenia (OR = 2.06), consistent with a synergistic effect between genes and environment. While these results are provocative, their implications are limited by the lack of information about schizophrenia susceptibility genes. As was the case with AD, once these have been identified with the aid of advances in molecular genetics, it will be relatively easy to incorporate this information into epidemiological studies, resulting in a rapid increase in knowledge about disease pathogenesis.

Currently, alcohol use provides a paradigm for studying gene-environment interaction similar to AD. Two polymorphisms – in the aldehyde dehydrogenase (ALDH) and alcohol dehydrogenase (ADH) genes – are associated with risk for alcohol dependence in Asian populations (18,19), providing the basis for studies examining the relationship between these genetic risk factors and the effects of known environmental risk/protective factors for alcohol abuse and dependence, such as early family rearing environment.

Until now, however, most knowledge about gene-environment interaction has come from traditional quantitative genetic studies, in which family history and monozygotic/dizygotic (MZ/DZ) concordance are used as indices of genetic risk. While there are methodological limitations to these studies (e.g., the possibility of genetic misclassification), twin and adoption studies have been influential in demonstrating gene-environment interaction effects (3).

TWIN STUDIES

Twins can be a useful tool in the investigation of gene-environment interaction (20). For example, MZ discordant twins can provide evidence for the influence of non-inherited characteristics on a disorder. A greater incidence of obstetric complications (OCs) (21) and of dysmorphological handprint signs suggestive of abnormal fetal development (22) has been observed in MZ twins with schizophrenia than in their unaffected cotwins. A different approach involves comparing heritabilities (i.e., the proportion of phenotypic variance due to genetic variance) according to the presence or absence of identified specific environmental risk factors. In addition to having main effects on rates and/or symptom levels of a disorder, environmental variables may also have moderating effects on the relative magnitude of genetic and environmental influences on the disorder. This is a form of gene-environment interaction: changes in the environment may render genes or environment more or less salient as influences on the behavior. In other words, the amount of variability in a disorder that is due to genetic or environmental influences may differ at different levels of an environmental variable, distinct from any main effect of that variable (i.e., in the absence of phenotypic change).

Several twin studies have examined the impact of broad personal variables on symptoms of mental disorders. Among these, the effects of socioregional variables on adolescent alcohol use were examined in a population-based sample of Finnish twins (23,24). In the first study, Rose et al (24) found that although drinking frequencies were similar for adolescents in urban and rural environments, genetic factors played a larger role in urban areas, whereas shared environment had a greater influence in rural settings. In an effort to better understand the nature of this urban/rural effect, this same group then examined more specific, continuous measures of the environment, and found that the magnitude of genetic influences on drinking frequency was nearly five times greater in environments characterized by a greater percentage of young adults, higher migration rates, and proportionately greater alcohol sales (23).

Marital status has been found to exert moderating

effects on the expression of genetic and environmental influences on alcohol consumption (25) and on symptoms of depression (26) in a sample of female adult Australian twin pairs. Genetic influences accounted for a greater proportion of the variance in both alcohol consumption and symptoms of depression in unmarried twins than in twins involved in a marriage-like relationship. In other words, having a marriage-like relationship reduced the impact of genetic influences on psychiatric symptoms. Religiosity has also been found to have a moderating effect on alcohol use initiation (27) and disinhibition, as measured by the Sensation Seeking Scale (28) in a Dutch twin sample. In both of these studies, while there was no association between religious upbringing and either alcohol use initiation or disinhibition, the influence of genetic factors on these variables was much greater in subjects without a religious background. These results suggest that receiving a religious upbringing, like being involved in a marriage-like relationship, may act as a protective factor in reducing the influence of genetic liability to psychiatric symptoms (26).

These studies are consistent with a sociological perspective that regards heritability as representing an individual's proportion of actualized genetic potential (29). According to this definition, the reason that heritability varies across environmental contexts is because different environments provide different opportunities for genetic potentials to be actualized. Structured situations are those that provide relatively unambiguous cues to guide behavior. Conversely, less structured situations are more ambiguous (30,31). Because there are few salient cues in the environment, individuals must rely to a greater extent on their own disposition to guide behavior. It follows that the causes of behavior in structured situations should be more situational than dispositional, whereas individual differences are more likely to be the causes of behavior in less structured situations. Consistent with this prediction, in the above studies, heritabilities for various clinical problems increased in environments that were less controlling, i.e., in subjects living in urban areas, in subjects who were unmarried, and in subjects without a religious upbringing, and the impact of shared environmental influences was greater in environments that theoretically provided a narrower range of opportunities to express individual differences in behavior. Results such as these, demonstrating differences in genetic and environmental influences in differing environmental circumstances, provide one explanation for the heterogeneity among heritability estimates for the same disorder, and point to the need to incorporate measures of the environment into genetically informative designs.

Kendler and colleagues have also used large population-based twin samples to study the impact of life events on depression and anxiety in women. Studies investigating the comorbidity of generalized anxiety disorder (GAD) and major depression (MD) in female twins found that all of the genes that influenced lifetime risk for GAD and MD appeared to be completely shared between the two disorders (32-34). Common or familial environment was not a factor in the etiology of either disorder. Some non-shared or unique environmental factors, however, may be relatively specific to either GAD or MD (e.g., stressful life events), while others may be both depressogenic and anxiogenic. These results suggest that it is likely that environmental factors are largely responsible for whether a female expresses genetic vulnerability as anxiety or depression. Roy et al (35) replicated these results in a clinical twin sample that included both male and female subjects and suggested that MD may be associated with stressful life events that involve loss, while GAD may be primarily related to life events that involve danger, consistent with the fact that MD and GAD have been associated with different sociodemographic predictors (36).

Following these results, Kendler et al (37) set out to investigate the relationship between stressful life events and the onset of depression in this sample. They found that the risk of onset of a major depressive episode in the month following the occurrence of any of four types of severe life events (death of a close relative, assault, divorce or marriage breakup, serious marital conflict) was highest in those at greatest genetic risk (as gauged by twin concordance). The one-month probability of onset of MD in individuals at lower genetic risk (i.e., with an unaffected cotwin) was 0.5% and 6.2%, respectively, depending on the absence or presence within that month of a severe life event. For individuals at high genetic risk (i.e., with an affected cotwin), the probabilities were 1.1% and 14.6%, respectively. These results are indicative of a gene-environment effect, in which genetic susceptibility increases an individual's sensitivity to the psychological impact of stressful life events.

Genetic factors, however, play a role in individual exposure to life events (37) and, moreover, the genetic liability to experience stressful life events overlaps with the genetic liability for depression (i.e., gene-environment correlation) (38). Thus, Silberg et al (39) conducted a more rigorous test of this gene-environment interaction effect by examining the relationship between risk for anxiety and depression and independent life events, i.e., those life events involving no genetic mediation, in a sample of adolescent female twins. They found a gene-environment effect similar to that of Kendler et al (37), in which the occurrence of an independent stressful life event in the past year (a new stepbrother/stepsister, brother/sister leaving home, father losing his job) had no effect on the depression scores of girls at low genetic risk (as indexed by the absence of parental emotional disorder), but significantly increased the scores of girls who had a parent with a history of depression or anxiety. In addition, life events exerted a moderating effect on the genetic and environmental influences on depression and anxiety, such that genetic variance increased with increasing exposure to

stressful life events, a result in accord with the hypotheses regarding protective environments advanced in the studies discussed above (23,26). This study illustrates just one of the difficulties in finding evidence for gene-environment interaction in complex disorders: genes influence both exposure and susceptibility to environmental risk factors. Gene-environment correlation and gene-environment interaction both operate to influence phenotype, and disentangling the two will require conceptual advances such as that illustrated by this study.

ADOPTION STUDIES

More than twin and family studies, adoption studies allow for the separation of genetic and environmental effects, because children do not share home environments with their biological parents. The major drawback to this type of design is that adoptive homes underrepresent high-risk environments, i.e., those at the extremes of poverty and deprivation (see Rutter and Silberg (4) for additional limitations). This is especially important because it has been suggested that gene-environment interactions may only exist at the extremes of genetic and environmental variation, hence adoption studies may underestimate the effects of environmental risk and protective factors and may not always detect true gene-environment interactions (40).

For the most part, adoption study investigations of gene-environment interaction have used biological family history of mental disorder as an indicator of genetic risk, and examined its relationship to psychosocial risk and protective factors in the adoptive family. Results from studies investigating the effects of family variables such as family conflict, poor cohesion, and deviant communication indicate that a wide range of mental disorders, including alcoholism, antisocial behavior (ASB), depression, and schizophrenia share these risk factors and that, for each disorder, these environmental influences interact with genetic risk to exacerbate psychiatric symptoms.

An early adoption study found that male (but not female) adoptees with an alcoholic biological parent were more likely to develop certain types of alcoholism if they were also at environmental risk, based on adoptive family characteristics, pre-placement conditions, and age at adoptive placement (41). Cutrona et al (42) found evidence for gene-environment interaction in alcoholism in a US sample of adoptees. Neither a biological background of alcoholism nor any family environmental variables increased risk for alcohol abuse or dependence in female adoptees. However, women (but not men) with at least one alcoholic biological parent who also experienced early-life family conflict and/or adoptive family psychopathology were more likely to become alcoholic than those with low levels of family conflict. In other words, neither a biological background of alcoholism nor environmental stress alone was sufficient to lead to alcoholism in the adoptees, but a combination of the two increased the risk.

Adoption studies have also found evidence for a gene-environment effect on ASB, such that individuals at high genetic risk are more sensitive to adoptive family conflict. Cloninger et al (43) found a synergistic effect for genetic and environmental risk factors in a Swedish sample, such that adoptees at both genetic risk (i.e., criminal biological parents) and environmental risk (i.e., adverse rearing experiences and poor quality adoptive placements) had significantly higher rates of petty criminality than adoptees at either biological or environmental risk alone. In other words, adoptees with genetic predispositions towards criminality also were more likely to be affected by negative environmental experiences. Rutter (44) noted that a problem with this type of study involved the use of parental criminality as a measure of genetic risk, both because it was crude, and also because it did not provide information on the mechanism of the genetic effect. Parental criminality could be an index of any of a number of psychopathological, physiological, or cognitive risk factors in the child.

Cadoret and colleagues conducted a series of adoption studies investigating ASB and consistently found evidence for an interaction between a genetic background of ASB and an adverse adoptive home environment (45-48). In the most recent study, antisocial personality disorder (ASPD) and substance abuse/dependence in the biological parent were used as indicators of genetic risk, and environmental risk was indexed by a composite measure of marital, legal, and psychological problems in the adoptive parents (48). These family environmental factors increased the risk for childhood aggression, adolescent aggression, and conduct disorder (but not adult ASB), but only in the presence of a biological background of ASPD. There was virtually no effect of the environment on those adoptees not at genetic risk. Unlike the earlier studies which combined ASB and substance abuse as an index of genetic risk (46), this study was able to separate the genetic influences associated with both. The results showed that a biological background of alcohol abuse did not interact with adverse adoptive home environment to increase risk for ASB, which demonstrates the specificity of the genetic diathesis for ASB.

Not all adoption studies, however, replicated the observed gene-environment interaction between a biological background of antisocial behavior/traits and environmental risk, in the form of adoptive parent antisocial behavior/traits (49,50). Moreover, evidence for gene-environment correlation in adoptee ASB demonstrates that additional factors may be operating to influence child ASB, and that care must be taken when conducting studies investigating gene-environment interaction. Both Ge et al (51) and O'Connor et al (52) found an association between a biological background of antisociality and adoptive parenting behavior that was mediated by the child's behavior, such that adoptee antisociality led to harsh and inconsistent behaviors on the part of the adop-

tive parents, which increased the child's own antisocial behaviors.

The same disturbed adoptive parent variable examined in Cadoret et al (48) also interacts with genetic risk factors to influence MD in women. In another study, for instance, Cadoret et al (53) showed that females (but not males) with a genetic background of alcoholism are at increased risk for MD if they live in an adoptive family with a high number of disturbed behaviors. There was no effect of environmental stress in the absence of an alcoholic background. This finding is in accord with theories suggesting that alcoholism is a marker for genetic risk that leads to depression and alcoholism in females, but only alcoholism in males (54).

An adverse adoptive home environment has also been implicated as a source of potential risk for schizophrenia. Findings from the Finnish adoption studies show an increased risk for schizophrenia in the biological offspring of schizophrenic versus non-schizophrenic parents, but only for those high-risk adoptees who were also exposed to a dysfunctional family rearing environment (55,56). Wahlberg et al (57), also using the Finnish sample, demonstrated that symptoms of thought disorder (i.e., an indicator of schizophrenia vulnerability) in offspring of schizophrenic mothers were more probable when they were raised by adoptive mothers who themselves showed elevated levels of 'communication deviance'. In contrast, offspring of schizophrenic mothers, raised by adoptive parents with low communication deviance, were less likely to show thought disorder. There was no relationship between thought disorder in control adoptees and communication deviance in the adoptive parents. In other words, this gene-environment interaction effect suggests that adoptees without a pre-existing genetic liability were not vulnerable to the effects of a disturbed family environment (at least with respect to thought disorder), and individuals with a pre-existing genetic liability expressed this liability only in the presence of additional adverse environmental factors.

Rutter and Silberg (4) suggested that results such as these from twin and adoption genetic studies, i.e., demonstrating gene-environment interaction, have so far been supportive of the hypothesis that the impact of environmental risk factors on psychopathology is slight in the absence of genetic risk. It is likely that research into gene-environment interaction will progress once genetic marker information can be incorporated into quantitative genetic studies, so that subjects with known genotypes can be exposed to environmental manipulations, allowing for a more experimental approach to the investigation of nature-nurture interplay in human beings. One method of incorporating genotypes into studies of gene-environment interaction is considered in the following section.

ASSOCIATION STUDIES

Association studies provide a potentially useful approach to the detection of gene-environment interactions in mental disorders (i.e., controlling and manipulating both genes and environment). They do provide clues about the interaction in various (non-human) animal protocols (58,59). The risk and protective effects of perinatal rearing experiences (e.g., maternal separation or loss, abuse or neglect, social deprivation) on anxiety- and depression-like behaviors have been demonstrated in both rodents and nonhuman primates (60,61). For example, genetically different strains of rodents that vary in their response to stress show additional differences in gene expression and in behavior when exposed to adverse rearing experiences.

Gene-environment interaction effects might thus provide one explanation for inconsistent findings among association studies between genetic markers and mental disorders, just as they may explain the variability in heritability estimates for the same disorder. For example, the role of the serotonin transporter gene (5-HTT) in anxiety in humans is controversial. While some studies have reported an association between a functional polymorphism in the regulatory region of this gene (5-HTTLPR) and anxiety-related behavior (62,63), others did not replicate the finding (64). Similar contradictory findings have been reported between this polymorphism and both MD and bipolar disorder (64). Studies in rhesus monkeys, however, have demonstrated the role of gene-environment interaction in the association between this polymorphism and anxiety-related behavior (65,66). Monkeys at greater genetic risk (i.e., with a greater number of the high-risk, low-activity allele) show differences in measures of 5-HTT expression that are associated with various adverse behavioral outcomes (e.g., lower rank within a social group, less competent social behavior, and greater impulsive aggression), as well as greater anxiety- and depression-related behavior (e.g., diminished orientation, lower attentional capabilities, and increased affective responding). These genotype effects are more pronounced for peer-raised (i.e., separated at birth from mothers) than for mother-raised monkeys.

Another gene whose association with human behavior is controversial is the dopamine D2 receptor gene (DRD2). Associations have been reported between DRD2 variants and several psychological disorders and traits, including alcoholism and other substance use disorders, schizophrenia, post-traumatic stress disorder, and certain personality traits, although, with the exception of schizophrenia (67), none of these associations has been replicated with enough consistency (68). However, some recent studies using human subjects have demonstrated evidence for association, and for gene-environment interaction, by taking account of environmental measures.

An association between the DRD2 Taq1 polymorphism on chromosome 11 and alcoholism was first reported in 1990 (69). Since that time, many attempts at replication have taken place, with variable results (70). Meta-analyses of DRD2/alcoholism studies found that, overall, alco-

holics had a higher prevalence of the high-risk allele than controls, and that the prevalence was higher in more severe alcoholism than it was in less severe alcoholism (71). Still, the association remains controversial (72-74).

Madrid et al (75) measured alcoholism and stress exposure in a sample of Honduran males, and found that neither was related to DRD2 genotypes. They did find, however, a significant interaction between genotype and stress score, such that individuals homozygous for the low-risk allele had similar alcoholism scores regardless of level of stress exposure. Alcoholism scores for heterozygous individuals increased modestly with increasing stress, and alcoholism scores for individuals homozygous for the high-risk allele increased greatly with stress. These results suggest that: a) individuals at genetic risk have a greater sensitivity to stress than those not at genetic risk; and b) the presence of environmental stress may be necessary for the development of alcoholism in this population.

Similar relationships between DRD2 genotype and environmental stress occur with regard to both cognitive markers and the personality trait of extraversion. Berman and Noble (76) found no relationship between family stress and cognitive markers (including visuospatial ability and event-related potentials, both of which have been linked to alcoholism (77, 78)) in preadolescent boys lacking the Taq1 high-risk allele. However, in boys with one or two copies of this allele, cognitive scores were negatively correlated with family stress scores. There were no differences in performance scores between boys from low-risk and high-risk family environments, regardless of genotype. Ozkaragoz and Noble (79) measured extraversion in a sample of children of alcoholic or control parents, under the hypothesis that children growing up in an alcoholic home would experience more environmental stress than those growing up in a non-alcoholic home. While there were no significant main effects of DRD2 genotype or family environment on extraversion, there was a significant gene-environment interaction such that children with the high-risk allele displayed greater levels of extraversion when living in an alcoholic than in a non-alcoholic home, again suggesting an increased sensitivity to stress in those indidivuals at high genetic risk.

Interestingly, among Honduran males living in a less stressful environment, subjects at low genetic risk (i.e., with no copies of the high-risk allele) received higher alcoholism scores than subjects at high genetic risk (75), and the adolescent boys at low genetic risk received higher extraversion scores when living in a non-alcoholic family than an alcoholic family (79). In other words, results from these studies suggest that greater psychopathology is associated with a less stressful environment in subjects who do not possess the high-risk DRD2 Taq 1 allele. One potential explanation for this phenomenon is that individuals with different DRD2 genotypes might respond to stressors in different ways. For example, Ozkaragoz and Noble (79) suggest that boys possessing the high-risk allele might cope with stress by increasing their level of activity, whereas boys with the low-risk allele might cope with stress by decreasing their activity. Thus it would be that, in a less stressful environment, boys at low genetic risk would appear to be more active than boys at high genetic risk.

GENE-ENVIRONMENT INTERACTION IN NEURODEVELOPMENTAL DISORDERS

Neurodevelopmental disorders are particularly likely to express gene-environment interactions, because development itself is a dynamic process that results from a constant interplay between genetic and environmental determinants. The combination of these etiologic factors begins early in development, with a greater liability for psychopathology arising when genetic susceptibility interacts with adverse biological consequences of untoward environmental events in the pre- or perinatal period. This etiology may result in a variety of outcomes based on the severity of both genetic and environmental 'loadings' for a particular disorder, and also on the presence or absence of other genetic and environmental 'protective factors', which may lower the risk for subsequent psychopathology. Two examples of neurodevelopmental disorders, autism and schizophrenia, will be reviewed for evidence of gene-environmental interactions.

While twin studies provide clear evidence of a genetic basis for autism (80,81), environmental factors also play a major role, although convincing evidence for any particular environmental factor is lacking (82). For example, twin studies show evidence of increased OCs among autistic members of discordant MZ twin pairs (80,83), but perinatal adversity may be a consequence, rather than cause, of autism (84). The work of Pletnikov et al (85,86) provides an example of how animal models may be used to test hypotheses about gene-environment interactions. Viral infections have been hypothesized to play a role in autistic disorders (87,88), and neonatal Borna disease virus (BDV) infection has been used as an experimental teratogen in animal studies to induce neurodevelopmental damage and behavioral deficits similar to those found in autistic spectrum disorders. In one study, Pletnikov et al (85) exposed different strains of rats to BDV neonatally to study potential gene-environment interactions. Significant strain differences were evident in brain pathology, behavior, neurochemistry (monoamine brain systems), and in the response to pharmacological treatments. For instance, one strain displayed a significantly greater thinning of the neocortex compared to the other, which was associated with greater novelty-induced hyperactivity and impaired habituation of the acoustic startle response in a prepulse inhibition paradigm. Results such as these provide support for an interaction between specific environmental risk factors (i.e., viral infection) and genetic liability (i.e., the strain of mouse) in the etiology of a neurodevelop-

mental disorder, and suggest novel avenues for research into other putative disorders of neurodevelopment.

The importance of both genetic and environmental factors in schizophrenia is well-established in behavioral genetic and, more recently, molecular genetic studies (89). While the risk of developing schizophrenia is associated strongly with the number of shared genes between a family member and an individual with schizophrenia, no degree of shared genes results in a certainty of developing the illness. For example, having two parents or an MZ twin with schizophrenia results in a risk of approximately 50% for developing the disorder. If having the same genes were the only etiological factor, then the risk should be close to 100% in these cases (1). Instead, the interaction between genetic liability and environmental factors plays an important role in determining outcome. Environmental factors implicated in the development of schizophrenia range from biological to psychosocial in nature and include, among others, pregnancy and birth complications, location of birth/residence, and family environment (90).

Recently, we modified Paul Meehl's use of the term 'schizotaxia' (91) to describe the liability to schizophrenia or schizophrenia-like conditions based on the theoretical premise that the neurobiological basis for schizophrenia is formed by the integrated effect of genes and adverse environmental risk factors. Our reformulation (92) describes genetically vulnerable individuals who are probably exposed to early adverse events (e.g., OCs) that result in abnormal development of certain brain structures. This liability presents from childhood as schizotaxia, which is expressed through a combination of cognitive, neurobiological and social skill deficits that vary in severity. For most individuals, the condition remains stable throughout their lifespan, but for some, a combination of the liability with later adverse environmental events (e.g., substance abuse, or stressful psychosocial circumstances) may predispose to the development of psychosis and chronic schizophrenia.

Consistent with the view of schizotaxia as resulting from a combination of genetic and environmental factors, several studies demonstrate evidence for an interaction between neonatal insults and genetic susceptibility to schizophrenia. For example, these insults likely include OCs and exposure to viral infections (including herpes simplex) (93). The times of greatest vulnerability to the developing brain may include the 2nd and 3rd trimester of pregnancy. During this period, for example, environmental factors may disrupt neuronal migration of cells to the cortex, which results in abnormal development of the prefrontal cortex, the entorhinal cortex, and the hippocampus (94).

Delivery complications associated with increased risk for schizophrenia include fetal hypoxia, ischemia, extreme prematurity, low birth weight, and post-term birth. Overall, pre-eclampsia is the most significant individual obstetric risk factor for schizophrenia (95). Pre-eclampsia, leading to hypoxia during pregnancy, results in fetal malnutrition including lack of oxygen, iodine, glucose, and iron. Chronic hypoxia can result in restricted fetal growth and subtle damage to brain regions. Moreover, blood and oxygen deprivation due to pre-eclampsia during delivery can also result in injury to the hippocampus and cortex (96). Seidman et al (97), utilizing the New England cohort of the National Collaborative Perinatal Project, demonstrated a relationship between obstetrical complications and neuropsychological deficits in children at 7 years of age. Low birth weight had the strongest association with neuropsychological impairments, followed by an index of inferred hypoxic insults, and then by maternal conditions suggesting chronic hypoxia.

Zornberg et al (98) reported results from a 19-year follow-up study of a large sample of individuals with a previously documented history of birth complications, and of matched controls. The individuals with a history of birth complications were classified according to whether or not the complications were hypoxic-ischemia-related. A significant relationship occurred between hypoxic-ischemia-related complications and increased risk for schizophrenia. These data thus suggested that pregnancy and birth complications interacted with genetic liability to increase the likelihood of subsequently developing schizophrenia. Consistent with these findings, Cannon (99) reported a dose-dependent relationship between risk of schizophrenia and severity of perinatal hypoxia in offspring of schizophrenic parents. In contrast, birth complications were unrelated to the development of schizophrenia in a control, low-risk group whose parents did not have schizophrenia. Similarly, Parnas et al (100) followed up offspring of mothers with severe schizophrenia and found the risk of developing the illness was highest for those who were exposed to perinatal complications. Pregnancy and birth complications themselves occur more frequently in schizophrenic mothers compared to normal controls (93), which raises the level of risk for their (already vulnerable) children further.

Other studies also examined relationships between OCs and structural brain abnormalities in individuals with schizophrenia and their relatives (95,101). Among these relationships, ventricular enlargement in individuals at increasing genetic risk for schizophrenia interacted with OCs, with the association between ventricular enlargement and OCs increasing with the degree of genetic risk. Suddath et al (102) reported larger ventricles and greater temporal lobe volumes in the affected cotwin of MZ pairs discordant for schizophrenia. These structural differences were associated with higher rates of OCs in the affected cotwins (103). Cannon et al (104) reported that fetal hypoxia was associated with reduced cortical gray matter and increased cerebrospinal fluid among patients with schizophrenia and their non-psychotic siblings, but not among controls. Effect sizes were greatest for low birthweight subjects, consistent with other find-

ings showing higher rates of subsequent schizophrenia in individuals subjected to prenatal underdevelopment (105-107). The relationship between hypoxia and brain abnormalities was stronger among patients than siblings, and hypoxia was related to ventricular enlargement only among patients, both findings consistent with a gene-environment interaction model in which the liability to schizophrenia is increased in the presence of environmental risk factors. While hypoxia did not occur more frequently among patients than among their unaffected siblings in this study, Rosso et al (108), using the same sample, found a greater number of hypoxic-associated OCs among early-onset than among late-onset cases or siblings, as well as an almost three-fold increased risk of early-onset schizophrenia per hypoxic OC.

Seasonality of birth is another possible environmental risk factor for schizophrenia, with winter-spring births being associated with increased risk (95). The increase could be due to a higher incidence of maternal infection (e.g., influenza), and the cumulative evidence from many studies suggests that maternal influenza infection in pregnancy, leading to fetal brain damage, is associated with an increased risk for schizophrenia (109). Support for a gene-environment interaction effect involving winter birth comes from a study by Pulver et al (110), in which winter birth was associated with a positive family history in schizophrenic probands, although associations in the absence of family history occur as well (111,112).

CONCLUSIONS

The nature-nurture controversy is far less germane than it once was for understanding psychiatric disorders. Research clearly shows that both nature and nurture play important roles in the genesis of psychopathology. As the preceding discussion showed, gene-environment interactions are evident both in a broad variety of mental disorders, and also in a wide range of experimental methodologies used to assess the relative contributions of genes and environment in mental disorders.

The salience of this issue will only increase as advances in neuroscience and molecular biology identify new potential sources of gene-environment interaction. For example, while many studies have focused on relationships between specific alleles and clinical diagnoses, or between independent measures of clinical function and clinical diagnoses, there is a growing focus on 'endophenotypic' expressions of mental disorders. Endophenotypes are features that are somewhat intermediate between the genotype and phenotype for a particular disorder (113), and often involve cognitive or neurobiological functions. Because endophenotypes may be closer to their underlying etiologies, they open windows on the mechanisms involved in both normal and abnormal mental functions. For example, in both patients with schizophrenia and normal controls, Egan et al (114) showed that a common polymorphism in the catechol-O-methyltransferase (COMT) gene produced a four-fold range in COMT activity and dopamine catabolism. The range of COMT activity in both groups was associated with a related range of performance on a neuropsychological test of executive function, and of the efficiency of prefrontal and cingulate cortical function during an information processing test. Because many mental functions and mental disorders are complex, multifactorial, polygenetic conditions (1,89,115), results from studies like that by Egan et al clarify specific mechanisms that likely contribute to efficient and inefficient biological function, and thus to mental function and dysfunction. This in turn provides increasing opportunities to specify environmental contingencies that interact with these mechanisms to increase or decrease the liability for mental disorders.

Ultimately, then, the study of gene-environment interactions will further our understanding of how to identify, diagnose and treat mental disorders. As the pool of potential treatment targets increases, so will opportunities for the development of early intervention strategies for many common but difficult to treat mental disorders (116-118). While the study of gene-environment interactions is but one of several promising ways to approach that goal, it is one whose potential warrants additional attention.

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Pharmacotherapy in the treatment of Alzheimer's disease: an update

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This review summarises the pharmacological properties of the main classes of drugs in current use for the symptomatic treatment of Alzheimer's disease. These may be divided into two major groups: those enhancing cholinergic function which has been shown to be defective in the disease, and those which either directly or indirectly reduce free radical/inflammatory processes in the brain. To date, none of the drugs available has been shown to reverse the pathological changes associated with the disease. However, a number of drugs are in development which are designed to block the neurotoxic action of amyloid beta peptide and thereby reverse the underlying pathological processes. These include the gamma secretase inhibitors and vaccines against amyloid beta peptide. The limitations of these novel approaches are discussed.

Key words: Cholinomimetics, antioxidants, anti-inflammatories, secretase inhibitors, vaccines

For the past 20 years, an increased understanding of the pathology of Alzheimer's disease (AD) has led to the development of numerous drugs for the treatment of the disorder. At the present time, there are at least 60 drugs estimated to be in development for the symptomatic treatment of AD, some of which may ultimately be expected to affect the development of the disease. The drugs in current use can be broadly divided into those that are designed to enhance cholinergic function, those that reduce the synthesis of free radicals, the anti-inflammatory agents, the oestrogens, and a miscellaneous group of natural products which include the Ginkgo biloba alkaloids. In addition, some drugs are in development which are aimed at counteracting the possible causes of neuronal cell loss by blocking the neurotoxic effects of amyloid beta peptide (Ab). These include the inhibitors of gamma secretase and vaccines against Ab. Some of these drugs will now be considered.

DRUGS ENHANCING CHOLINERGIC FUNCTION

The cholinergic hypothesis of AD is based on the loss of histochemical markers of forebrain cholinergic neurons that correlates with diminished cognitive function and with the degree of accumulation of neuritic plaques and neurofibrillary tangles. Assuming that AD bore some resemblance to Parkinson's disease, in which dopaminergic agonists correct the endogenous deficiency of striatal dopamine, it was speculated that directly and indirectly acting cholinergic agonists should correct the symptoms of the disorder. In the past decade drug development has therefore largely focused on centrally acting anticholinesterases and, to a lesser extent, muscarinic agonists and acetylcholine releasing agents. Other approaches have included the administration of high doses of acetylcholine precursors (such as lecithin and choline), which have not been shown to be therapeutically effective, and more recently galanin receptor antagonists.

Because of the progressive neuronal loss that occurs in AD, drugs that enhance the endogenous cholinergic system are inevitably limited in their duration of action. However, at postmortem the M1 and M4 type of cholinergic receptors appear to remain intact in patients with AD, which has strengthened an interest in drugs which have direct cholinomimetic effects (1).

Anticholinesterases

Tacrine, donepezil, rivastigmine and galantamine are cholinesterase inhibitors which preserve endogenous acetylcholine following its synthesis. The inhibition of the cholinesterase may be either reversible, irreversible or pseudoirreversible. In addition, the inhibitor may be either competitive or non-competitive for true (acetyl) cholinesterase, pseudo (butyryl) cholinesterase or for both types. Some anticholinesterases also have a weak affinity for the nicotinic cholinergic receptors. These drugs also differ in their pharmacokinetic properties (for example, protein binding, elimination half-life) and in their interactions with other drugs.

Tacrine is a non-competitive, irreversible inhibitor of both acetyl and butyryl cholinesterase, with a greater potency for the latter enzyme. Based on the outcome of placebo controlled, double-blind studies, tacrine was the first anticholinesterase to be licenced for the symptomatic treatment of AD in the United States (2,3). The main disadvantage of tacrine lies in its hepatotoxicity (approximately 50% of patients were found to develop elevated liver transaminases, which reversed on discontinuation of the drug). Because of such side effects and limited efficacy, tacrine is no longer widely prescribed.

Donepezil is primarily a reversible inhibitor of acetylcholinesterase with a long elimination half-life. It lacks the hepatotoxicity of tacrine but frequently causes nausea, vom-

iting and diarrhoea (4). These side effects, together with occasional bradycardia, syncope and changes in the sleep architecture, are directly associated with a central and peripheral enhancement of cholinergic function (5). At the present time, donepezil is the most widely prescribed anticholinesterase in the United States and Europe.

Rivastigmine is a pseudoirreversible inhibitor of both acetyl and butyryl cholinesterases. Although the drug initially blocks the enzymes, it is metabolized by them, so that its half-life is relatively short (6). The top dose is often necessary to achieve therapeutic efficacy, at which dose the central and peripheral cholinergic side effects become apparent.

Galantamine, unlike the other anticholinesterases in clinical use, is derived from the alkaloids from the daffodil and snow drop family. It is a reversible, competitive inhibitor of acetylcholinesterase with some inhibitory action on butyryl cholinesterase. It is also an agonist at nicotinic receptor sites. Although a clinically effective drug, galantamine frequently causes gastrointestinal side effects (7).

Other anticholinesterases in development include metrifonate. This is an irreversible organophosphorus inhibitor of acetylcholinesterase and is a pro-drug for dichlorvos (8). The development of metrifonate has been delayed because some patients developed muscle weakness, and a delayed neurotoxicity has been described for compounds that are chemically related to the drug (9).

To complete the list of anticholinesterases, extended release physostigmine has been shown to have some therapeutic efficacy, but has been restricted in its development because of the high frequency of nausea and vomiting (10).

In addition to their ability to increase the endogenous concentrations of acetylcholine, anticholinesterases have also been found in in vitro studies to increase the synthesis of non-amyloidogenic amyloid precursor protein (APP) and to decrease the neurotoxicity of Ab (11). Regarding the effect of some anticholinesterases on nicotinic receptors, there is also evidence that neurodegeneration is delayed, thereby suggesting that such drugs may be neuroprotective. This view has been supported by epidemiological studies in which the incidence of Parkinson's disease has been shown to be lower than expected in cigarette smokers (12).

Muscarinic receptor agonists

The first generation of cholinomimetics, such as arecoline, bethanecol and pilocarpine, were not designed for the treatment of AD and the results of the early clinical trials were consistently disappointing. In addition to their poor bioavailability and short duration of action, any therapeutic benefits were limited by their cholinergic side effects. The second generation of muscarinic agonists were therefore developed to specifically treat AD. These drugs, exemplified by milameline and xanomeline, have improved pharmacokinetic profiles relative to the first generation drugs. In controlled clinical trials, xanomeline has shown moderate clinical efficacy but, despite in vitro data showing that it was selective for M1 and M3 receptors, it still caused mild to moderate parasympathomimetic side effects (13). Milameline has equal affinity in vitro for all five muscarinic receptor subtypes; peripheral cholinergic side effects were clearly evident in the initial clinical trials (14). Neither of these cholinomimetics has been marketed at the present time.

Despite the theoretical interest in specific nicotinic agonists for the treatment of AD, to date none has reached clinical development.

Glutamate receptor antagonists

Glutamate is a major excitatory neurotransmitter in the brain, estimated to be involved in the regulation of 70% of excitatory synapses. Of the two major types of glutamate receptor - the ionotropic N-methyl-D-aspartate (NMDA) and the metabotropic once - the former plays a crucial role in neuroplasticity and memory formation. It is postulated that excessive activation of the NMDA receptors by glutamate plays an important role in the neurodegenerative changes found in AD (15); Ab has been shown to increase the release of glutamate (16). Several experimental studies have shown that NMDA antagonists prevent glutamate induced neurotoxicity (17).

Of the various NMDA antagonists which have undergone clinical investigation, memantine has been shown to be the least toxic in vivo and also to have neuroprotective properties. Memantine has been the subject of a double-blind, placebo controlled trial and proven to be superior to placebo in improving cognitive dysfunction in patients with mild Alzheimer's disease (18). It should be added that this drug has been available for clinical use in Germany for the treatment of AD for the past 10 years. Thus, if the placebo controlled studies are replicated, it is likely to provide a useful treatment for the mild to moderate form of the disease.

Anti-inflammatory drugs

Inflammatory processes are well known to be associated with AD. Elevation in circulating pro-inflammatory cytokines, acute phase proteins and complement and the presence of activated microglia have been described in patients with AD (19-22). It has also been shown that the complement cascade can be activated by Ab and result in neurotoxic changes (23,24). The seminal studies of McGeer and coworkers laid the basis to the preventative strategy for the treatment of AD (25). These investigators showed that the prolonged use of non-steroidal anti-inflammatory drugs for the treatment of arthritis and related conditions was associated with a significant decrease in the incidence of AD. Studies of siblings who had a differential exposure to anti-inflammatory drugs also showed that the incidence of AD was significantly reduced in those to whom such drugs were administered (26,27).

Despite the clinical evidence implicating the involvement of inflammatory processes in the pathology of AD, the mechanisms behind the accumulation of inflammatory mediators are complex. Nevertheless, it would appear that cyclooxygenase 2 (COX2) plays a crucial role. It is known that COX2 activity is elevated in the brain of patients with AD (28) and that there is an increased expression of COX2 mRNA in the frontal cortex of such patients. Furthermore, the severity of the symptoms correlates with both the COX2 activity and the increased expression of Ab (28).

A number of anti-inflammatory drugs have now been tested for their therapeutic efficacy in AD. For example, the steroid prednisolone, which is lipophilic, has been administered to patients with AD for up to a year, but the results were disappointing (29). The potent non-steroidal anti-inflammatories diclofenac and indomethacin have also been tested, but shown to have minimal benefit with a high frequency of side effects (30). Perhaps these results are not surprising, since the inhibition of COX is expected to have little beneficial effect on the symptoms of AD once neuronal death has occurred, as seems likely in the clinical studies in which the patients were in the advanced stage of AD. Another problem arising in the interpretation of the data concerns the effects of the selective COX2 inhibitors such as celecoxib and rofecoxib which, in in vitro studies, have been shown to enhance the formation of the highly neurotoxic form of Ab, Ab42 (31). By contrast, the non-selective COX inhibitors ibruprofen and suldinac were shown to reduce Ab to its less neurotoxic form Ab38. With regard to the mechanism of action of the non-steroidal drugs, it has been speculated that the beneficial effects might be linked to a reduction in the activity of gamma secretase, the enzyme assumed to be responsible for the cleavage of APP to its neurotoxic product. In addition, it is known that these drugs also act as free radical scavengers, which is unconnected with their inhibitory actions on COX.

The most positive result for the action of an anti-inflammatory has been obtained from the studies of propentofyline. This drug inhibits the action of microglia which act as macrophages within the brain and release inflammatory cytokines. However, while there was evidence of some therapeutic benefit, the results were modest and insufficient for the drug to be marketed either in Europe or North America (32,33). Thus the jury is still out regarding the potential therapeutic efficacy of the non-steroidal drugs, at least in the treatment of patients with established AD.

Antioxidants

Free radicals have been considered to play an important role in initiating neuronal death. Neurotoxic processes arising from an overactivity of the glutamatergic system, from ischaemia, and from the direct action of Ab lead to increased oxidative stress and free radical synthesis (15). It would therefore be anticipated that free radical scavengers and antioxidants could delay or prevent the progression of neuronal degeneration due to such causes (34). Of the compounds tested in a clinical situation, vitamin E has been the most extensively studied. The results of a 2-year placebo controlled trial (35) have shown that vitamin E, particularly when combined with the monoamine oxidase B inhibitor and free radical scavenger selegiline, had a significant beneficial effect, but the high doses of vitamin E which were necessary are also known to cause disorders of blood coagulation, so it seems unlikely that this will become a treatment of choice.

Chelating agents

It is known that metals such as zinc and copper become more concentrated in the brain with increasing age and that these metals can induce Ab aggregation, thereby enhancing the deposition of senile plaques. In addition, the presence of these metals with Ab initiates the formation of hydrogen peroxide, which causes oxidative damage to neurons. By using metal chelating agents such as cliquinol, it has been possible to reduce the zinc and copper concentrations in the brains of patients with AD, leading to a small, but significant improvement in cognitive function (36). The use of chelating agents may therefore be of some therapeutic benefit in the future.

Oestrogens

The notion of a potential therapeutic value of the oestrogens came from their protective effect against AD in post-menopausal women (37,38). Experimental studies have shown that oestrogens protect hippocampal dendrites from damage and also augment the activity of choline acetyl transferase. Additional properties of oestrogens which may contribute to their neuroprotective effects include antioxidant properties and a facilitation of the processing of APP along a non-amyloidogenic pathway (39,40).

Despite the promising experimental and epidemiological studies, the clinical trials of the oestrogens in AD have been disappointing. There is some evidence that women who had taken oestrogens for the treatment of post-menopausal symptoms had a better response in terms of an improvement in cognitive symptoms than those who had not taken oestrogens. It seems possible that selective oestrogen receptor modulators (SERMs), which are drugs that act as selective agonists for central oestrogen receptors, may eventually replace the non-selective steroidal oestrogens which have been used to date.

Secretase inhibitors

Amyloid deposition is now regarded as one of the earliest changes that initiate AD. It would appear that,

regardless of the position of the mutation, whether this is in the APP gene, presenilin 1 or 2, the final outcome is the increase in neurotoxic Ab42 in the brain and plasma. A similar finding has been observed with the increased frequency of the apolipoprotein E4 allele (41). This has led to the hypothesis that the aggregated form of Ab is primarily responsible for the symptoms of AD and therefore it might be possible to develop appropriate drugs to prevent the neurotoxic damage by blocking the synthesis of Ab.

It is known that beta and gamma secretases are responsible for cleaving APP to Ab, so that by inhibiting these enzymes it might be possible to block the progression of the disease. Alternatively, enhancing the activity of alpha secretase, leading to the formation of a non-amyloidogenic end product, might also be beneficial. Another approach could involve the increase in the breakdown of Ab once it has been formed. All these possibilities are actively under consideration but so far no drugs have emerged.

Regarding the possibility of developing secretase inhibitors, it appears that the pancreas also contains beta secretase and it is presently unclear what the consequences could be if the pancreatic enzyme was inhibited in addition to the brain enzyme (42). With regard to gamma secretase, it is known to be closely associated with the presenilins, the enzymes that are critically involved in a number of metabolic pathways in addition to the formation of Ab (43). Thus, there may be unexpected toxicity problems which arise by inhibiting gamma secretase.

Despite some exciting experimental findings in mice that have been genetically programmed to develop the human form of Ab, so far there is no evidence to indicate that secretase inhibiting drugs have been developed that offer some prospects for treating AD (44). However, following the recent identification of a novel membrane bound aspartic protease (BAC1) as beta secretase, the possibility still remains that drugs targeting the beta - and gamma - secretases could be developed in the near future (45).

There is evidence that cholesterol contributes to AD by enhancing Ab synthesis (46). This provides a theoretical basis for the use of statins to lower the blood cholesterol concentration. There is also recent evidence that the statins have unexpected anti-inflammatory properties by reducing the adhesion and activation of leucocytes, which may contribute to the moderate improvement in the cognition scores which have been observed in a placebo controlled trial (47).

VACCINES

Transgenic mice that overexpress Ab have been used to determine whether vaccines could be produced to reduce the concentration of the peptide in patients with AD (48). Experimental studies have shown that Ab peptide immunization reduces the cognitive impairments and the formation of plaques in rodent models of AD (44). This finding led to the development of vaccines for human use. While the phase 1 trials in the UK suggested that the vaccine was safe (49), more extensive studies in Europe led to the termination of the clinical trials because 5% of the patients developed meningoencephalitis (50). Further studies are presently underway to induce an immune response against Ab without initiating T-cell activation which underlies the inflammatory process in the brain. The possible mechanism whereby cerebral haemorrhage occurs following anti-Ab immunotherapy has been suggested recently by Pfeifer and coworkers (51).

CONCLUSIONS

Major progress has been made in the past decade to develop drugs to treat the symptoms of AD. To date, important advances have been made regarding the reversal of the disease process, in particular with respect to preventing the accumulation of Ab and preventing the central inflammatory response which appears to initiate the neurotoxic changes. Undoubtedly the following decade will see the development of vaccines and other strategies that will alter the course of the disease. Thus we can expect the therapeutic pessimism of the past to be replaced by therapeutic optimism in the future.

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Diagnosis and management of post-partum disorders: a review

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This paper reviews the psychiatry of the puerperium, in the light of work published during the last eight years. Many distinct disorders are seen. In addition to various psychoses and a heterogeneous group of depressions, there are specific anxiety, obsessional and stress-related disorders. It is important to identify severe disorders of the mother-infant relationship, which usually respond to treatment, but have pernicious effects if untreated. The complexity of post-partum psychiatry requires the deployment of multidisciplinary specialist teams, which can handle the challenges of therapy, prevention, training, research and service development.

Key words: Post-partum psychosis, mother-infant relationship disorders, post-partum depression, post-partum anxiety, mother and baby units

Childbearing, from the standpoint of psychological medicine, is the most complex event in human experience. Recently delivered mothers are vulnerable to the whole spectrum of general psychiatric disorders, as well as those resulting from the physical and psychological changes of childbirth. The old classification under three headings – the maternity blues, post-partum ('postnatal') depression and post-partum ('puerperal') psychosis – is an oversimplification. A four-part classification would be appropriate: psychoses, mother-infant relationship disorders, depression and a miscellaneous group of anxiety and stress-related disorders. Each, with sub-headings, will be discussed here in terms of diagnosis, treatment and prevention.

PSYCHOSES

These fall under three headings – organic, psychogenic and bipolar/polymorphic – of which the last is the least rare. The organic psychoses (1) include post-eclamptic psychosis (2) and infective psychoses. Antenatal care and antibiotics have almost wiped them out, but they may still occur in low-income countries. Recent figures for the frequency of eclampsia and post-eclamptic psychosis in India resemble those in Europe 100 years ago (3). There have been occasional reports of confusional states complicating anaemia, ethanol withdrawal, cerebral venous thrombosis (4), chorea gravidarum and heart disease. Idiopathic confusion, similar to that seen during parturition, can occur. In the ICD-10, these disorders can be classified under F05, with an appropriate coding for the cause. The treatment is of the underlying disorder.

In psychogenic psychosis, the content (usually delusions), as well as the onset, course and outcome, are linked to severe stress. Conjugal jealousy, arising in the puerperium, is an example. Psychogenic psychoses are occasionally seen after adoption of a child (5) or in fathers around childbirth. In the ICD-10, these are classifiable under F23.3, and require psychological as well as antipsychotic drug treatment.

Most cases of post-partum psychosis are manic-depressive in form, and there is much evidence for a close connection between puerperal and bipolar disorders (1). Another literature links post-partum and 'cycloid' (acute polymorphic) psychoses (6). Unfortunately, there is no agreement on the relation between the bipolar and the acute polymorphic group: if they were related, as has been suggested (7), 'puerperal psychosis' would simply fall under an (enlarged) bipolar rubric. ICD-10 recommends classifying all post-partum disorders according to the presenting symptoms, with a second code (099.3) for the puerperium. It has also reserved an entire category (F53) for puerperal disorders, while discouraging its use (8). This is unnecessary. The important thing is for psychiatrists to code the puerperal state, so that epidemiologists can identify all cases. The 'puerperium' can be defined broadly, because it is easy to eliminate distantly related cases by scrutinising the records. Two excellent epidemiological surveys (9,10) have established the incidence of post-partum psychosis as somewhat less than 1/1000 deliveries. The diagnosis presents no exceptional problems, since every form of delusion, verbal hallucinosis, disturbances of the will and self, perplexity, stupor, catatonia and mania can occur, with an acute onset soon after delivery. Treatment is with antipsychotic drugs, but severe side effects have been seen with haloperidol, and second generation antipsychotics may be safer. Lithium is useful in treatment; only one breast-fed infant developed (non-fatal) side effects. If a mother needs admission to hospital, it is probably best to admit the infant too (see below). The psychosis has a recurrence rate of at least 1 in 5 pregnancies. Mothers with a history of non-puerperal mania have a similar enhanced risk. There is some evidence that lithium, given immediately after delivery, reduces this risk.

DISORDERS OF THE MOTHER-INFANT RELATIONSHIP

Developing a relationship with the newborn is the central and most

important psychological process of the puerperium. Disturbances in this process were recognized long ago, when hatred and rejection of children (11-14), child abuse (15) and infanticide were described. Various terms have been used to denote these disturbances. 'Bonding' is a lay term, but 'bonding' and 'attachment' are not descriptive of the essential symptom, which is the mother's emotional response to the infant, including hatred and pathological anger. 'Mother-infant interaction' reflects this, and has the advantage that it can be recorded and measured. But the concept of 'post-natal depression with impaired mother-infant interaction' is inadequate for these eleven reasons:

- A disturbed relationship is a distinct phenomenon. Its affective focus is different from depression.
- 'Impaired mother-infant interaction' is merely the behavioural manifestation of this emotional lesion.
- Depression is associated with many other disorders (e.g., phobias and obsessions), but we still recognize these co-morbid disorders as phenomena worthy of study in their own right.
- 'Impaired interaction' has several causes, of which aversion to the infant is only one – the others include focused anxiety and obsessions of infanticide.
- The mother's aversion to her infant is often disproportionate to depression and can occur without it (16).
- Only a minority of depressed mothers have a relationship problem with their infants. It is important to select them for special treatment, and not to stigmatize the others.
- Mother-infant relationship disorders have their own specific treatment.
- The risks are higher in these mothers. It is probable that emotional deprivation, impaired cognitive and personality development, child abuse, child neglect and infanticide are commoner in this group.
- Those involved in public health planning, therefore, should be aware of these disorders, of the risks they pose and their treatment response, so that facilities can be provided.
- The aetiology is probably different from post-partum depression, with more emphasis on unwanted pregnancy and challenging infant behaviour.
- In research, this concept will sharpen the focus of studies aimed at preventing child abuse and neglect.

Perhaps the main reason for the neglect of these disorders is their absence from ICD-10 and DSM-IV (17). In ICD-10, attachment disorders of childhood (reactive 94.1 and disinhibited 94.2) are diagnosable in the children. There are also 'Z codes' that "capture… a wide variety of things which, although not illnesses or disorders, bring patients into contact with the health services". They include hostility towards the child, and scapegoating, but only in relation to the child's psychiatric state. In DSM-IV the corresponding category is reactive attachment disorder of infancy and childhood (313.89). For adults, the only possible category is 'Parent-child relational problem' (V61.20), which is assigned a mere 50 words on p. 681. The American Psychiatric Association's Diagnostic Classification of Mental Health and Developmental Disorders of Infancy and Early Childhood has various relationship disorders as Axis II, but nothing resembling rejection of the child (18). One of the challenges for ICD-11 and DSM-V is to find a place for these disorders, so that they can be recognized by practitioners, and referred for expert treatment. This will be a difficult innovation, because a mother's hatred of her infant does not fit comfortably with the concept of 'disease' or 'illness'. But the medical profession has the responsibility for conceiving a classification that enables the recognition and scientific study of all morbid states brought by patients for treatment.

Disorders of the mother-infant relationship are prominent in 10-25% of mothers referred to psychiatrists after childbirth (1). At the severe level of rejection of the infant, the mother may try to escape, or may seek permanent transfer of infant care within or without the family. She may express the wish that the baby be stolen, or succumb to cot death. Another manifestation is pathological anger – shouting, cursing or screaming at the infant, accompanied by impulses to strike, shake or smother the child. These disorders are more common, intractable and serious in their effects than puerperal psychosis. With treatment, they can resolve completely. Without it, the risks are high. For evidence of these effects, one must turn to studies of the effects of 'post-natal depression'. Most have not assessed the mother-infant relationship, but, where this has been done (19), the child's cognitive deficits were linked to early mother-infant interaction, not maternal depression. More research should be focused on the effects of these disorders, especially their relationship to child abuse and neglect.

The diagnosis is facilitated by screening questionnaires (20,21), and interviews exploring the mother-infant relationship. Observational data can be obtained in hospital (22,23) or at home (24). Other objective measures, such as videotapes (25), can be used. It is possible that functional magnetic resonance imaging can objectify the emotional lesion. In the management, it is wise to treat depression, even when signs of depression are minimal. The specific psychological treatment is play therapy in various forms (26) or baby massage (27,28), which can be undertaken by nursing staff or psychologists. The aim is to help the mother to enjoy her interactions with the child. There is evidence for the efficacy of prophylactic interventions (29,30).

DEPRESSION

The concept of 'post-natal depression' is another useful lay term. It reduces stigma, and enables mothers with a variety of post-partum psychiatric disorders to recognize that they are ill, and seek help. It is a focus for self-

help groups and lobbying to improve services.

It is less useful, however, as a medical concept. The epidemiological association between the puerperium and depression is weak. Depression is relatively common in all adult women, whether infertile, menopausal, pregnant, puerperal or involved in child-rearing. The rates of depression show little difference between newly delivered mothers and other women (31). There is little confirmation of the severity of post-partum depression in the suicide figures. Record linkage studies in Finland, Denmark and Canada have shown lower rates of suicide in mothers within 12 months of childbirth than are found in other women from the same nation (32-34). Only in economically disadvantaged American mothers have higher rates been found (35). Mothers with 'post-natal depression' are a heterogeneous group. Some have anxiety, obsessional and stress disorders, with little or no depression. Others have depression associated with equally important co-morbid disorders. Even those with depression alone are heterogeneous: they include mothers with chronic dysthymia, pre-partum depression continuing into the puerperium, depression associated with recent adversity, and bipolar depression.

In recent years, there has been a flood of publications on this subject from all over the world, with over 800 papers since 1995. Post-partum psychiatric disorders are common everywhere, and are not just confined to industrialised nations with their particular problems of scattered or disrupted families. Indeed, an 11 centre study (36) showed they were most frequent in India (32%), Korea (36%), Guyana (57%) and Taiwan (61%). But unless it is realized that the term is merely a rubric, it will leave research and clinical practice at a basic level. Not surprisingly, research into causal associations has discovered that they are the same as for depression generally, including genetic factors (37), a previous tendency to depression, adverse events, disturbed relationships, lack of support and social isolation (38,39). One bold experimental study (40) showed that abrupt withdrawal of oestrogen and progesterone led to hypomania or depression in women who had previously suffered from post-partum depression.

The merit of a broad concept of 'post-natal depression' is the public recognition that post-partum disorders are common, promoting the deployment of remedial services. Maternal morbidity can have pervasive effects on the infant, other children and the family. Although deficits are not universal (41), depression can lead to reduced interaction and irritability misdirected at the children. Maternal suicide can be combined with filicide, which, though rare, is a matter of great concern. The development of screening questionnaires has put early diagnosis in the hands of every midwife, nurse or practitioner. The Edinburgh Postnatal Depression Scale (EPDS, 42) has been translated into many languages, and a Norwegian paper reviewed 18 validation studies (43). The EPDS is a general screening tool for the whole gamut of post-partum psychiatric disorders. Other questionnaires can also be used. A positive score on a self-rating questionnaire needs to be followed by an interview clarifying the symptoms of depression and co-morbid psychiatric disorders. It is important to explore the wider context, including the mother's life history, personality and circumstances; the course of the pregnancy including parturition and the puerperium; and relationships with spouse, other children, family of origin and, especially, the infant. In addition to diagnosing depression and other disorders, one must identify vulnerability factors and the availability of support. Treatment is focused on depression and any underlying vulnerability. It will always involve psychotherapy (44), often given by hospital and community nurses, health visitors or lay counsellors. A *Lancet* review tabulated 13 randomised controlled treatment trials using psychological treatments (45), to which two recent studies (46,47) can be added. Almost all interventions were beneficial. An extensive literature has accumulated on drug treatment in lactating women, with over 50 reviews (48). The suckling infant is at risk because of the immaturity of foetal systems – lack of body fat, less plasma protein-binding, immature liver and kidney and undeveloped blood brain barrier. Nevertheless, few adverse effects have been reported. Indeed, Epperson et al (49,50) have demonstrated that neither sertraline nor fluoxetine affects serotonin levels in suckling infants. In general, it is not recommended that antidepressant agents should be withheld, or that breast-feeding stopped. It is wise to use antidepressive drugs cautiously in lactating mothers, and it may be helpful to take the drug after breast-feeding. Oestrogens may be efficacious (51), although replication is necessary.

Prevention is important in mothers with a history of post-partum depression. There is a great opportunity to identify mothers at risk during their attendance at antenatal clinics, where pregnant women with previous episodes, current depression and obvious risk factors such as social problems, substance abuse or unwanted pregnancy can be picked up. Support from community nurses, voluntary agencies or groups can begin during pregnancy, and arrangements made for prompt diagnosis and treatment of a post-partum recurrence. The *Lancet* review (45) tabulated 11 randomised controlled prophylactic trials, using psychological interventions, to which 6 others (52-57) can be added. The involvement of fathers has been positive (58,59), and three intervention studies improved mother-infant interactions (30,60,61). But most prophylactic trials have been disappointing. Even prophylactic antidepressive agents have failed to prevent post-partum depression (62). It is remarkable that a disorder that presents such an excellent opportunity for prevention has proved so resistant to prophylaxis.

DISORDERS RESULTING FROM STRESSFUL PARTURITION

Post-traumatic stress disorder (PTSD)

Since the pioneering study of Bydlowski and Raoul-Duval (63), over 40 papers have appeared on this disorder. There have been eight quantitative studies, showing rates up to 5.6% (64). The stressful experience is usually pain, but loss of control and fear of death may be the focus (65,66). Tension, nightmares and flashbacks persist for some weeks or months, and may recur towards the end of the next pregnancy. They lead to secondary tocophobia: in Sweden half the mothers with a 'very negative' birth experience at their first delivery avoided any further pregnancy (67). These patients should be referred for specific psychological treatment.

Querulant disorders

Childbirth is a key experience, and a mother may feel bitter if delivery is perceived as mismanaged. Complaints are relatively common after emergency Caesarean section (68). In some cases, complaining can preoccupy the mother for weeks or months, and interfere with infant care. These disorders are sometimes confused with depression or PTSD, but the affect is ruminative anger, not depression or anxiety, and the treatment is different – distracting attention from the perceived injury, and redirecting it to positive activity.

SPECIFIC ANXIETY DISORDERS

Post-partum anxiety disorders are underemphasized and may be more common than depression (69-71). A review of eight studies of 'panic disorder' showed that 44% anxious women had an exacerbation, and 10% a new onset, in the puerperium (72). ICD-10 and DSM-IV give criteria for anxiety disorders as a group, but the focus of anxiety is also important, because it may indicate specific psychological treatment. This is a challenge for the next generation of international classifications. De Armond (73) described fear of the newborn based on the awesome responsibility of infant care. Most mothers are shielded from this by family support, but it can be a problem in isolated nuclear families. A mother with infant-focused anxiety may develop a phobia for the infant (74). Fear of cot death can reach a pathological degree (75): the main manifestation is nocturnal vigilance – the mother lying awake listening to the infant's breathing, with frequent checks that lead to exhausting sleep deprivation. Many mothers are excessively anxious about the health and safety of their children – described as 'maternity neurosis' in an early paper (76). Drug treatment can be used, but, in lactating mothers, benzodiazepines should be used with caution. They are well absorbed from the gut, have long half-lives, and are more slowly metabolised by the foetal liver. Lethargy and weight loss have been reported in an infant exposed to diazepam. Post-partum anxiety disorders often require the skills of a clinical psychologist, using relaxation techniques, cognitive therapy, desensitisation and other specific therapies. Involvement of a panel of mothers who have recovered from these disorders is useful, as in other post-partum disorders.

OBSESSIONS OF CHILD HARM, AND OTHER MORBID PREOCCUPATIONS

Obsessions of infanticide were among the first post-partum disorders to be described (77). Classic papers were written by Chapman (78) and Button and Reivich (79). The central symptom is impulses to attack the child, but the setting is different from the pathological anger that precedes child abuse. The mother is gentle and devoted. She experiences extravagant infanticidal impulses, together with fantasies of the family's horror and grief, causing intense distress and leading to reduced contact with the baby. The content can include child sexual abuse (80). Jennings et al (81) found that 21/100 depressed mothers had repeated thoughts of harming their child and took precautions, and 24 were afraid to be alone with the baby. Pregnancy and childbirth are among the main precipitants of obsessional neurosis (82,83). The management involves specific psychological treatment as well as antidepressant therapy. It is important to discourage avoidance of the child, and encourage cuddling and play, strengthening positive maternal feelings.

Other morbid ideas are a problem to some mothers. A disorder akin to dysmorphophobia, based on the bodily changes resulting from pregnancy and childbirth, is common. These women complain of weight gain, stretch marks or scars. They are reluctant to undress in front of their husband, avoid looking at themselves in the bath or the mirror, and sometimes avoid being seen in public. These have not been emphasized in the psychiatric literature, perhaps because no-one can suggest a treatment, except time!

Conjugal jealousy is another disorder sometimes linked to pregnancy and childbirth, as an understandable reaction to pregnancy's effect on sexual life. Apart from case reports, there is just one quantitative study: Schüller (84) found that 6/27 patients with morbid jealousy, attending an Austrian clinic, were breast-feeding.

SPECIALIST TEAMS

Because of the diversity of post-partum mental illness, its risks for the infant, and the skills and resources required, there is a case for setting up specialist services. In 1958, Main (85) pioneered conjoint mother and infant hospitalisation. This has accelerated the growth of knowledge through the concentration of severe cases in mother and baby units. The essence of mother-infant services is the multidisciplinary specialist team, including psychiatrists, psychologists, nurses (probably also nursery nurses) and social workers. Its aims are prevention, early diagnosis, and versatile intervention, with minimal family disruption. Such teams can serve a wide

area, taking over the treatment of severe and intractable illness, developing services, training staff and conducting research. They can provide a trial of mothering in complex cases, and give medico-legal advice. Domiciliary assessment and home treatment are appropriate. A day hospital, with a wide range of interventions – groups, play therapy, motherhood classes, anxiety management and occupational therapy – has the advantage of putting mothers with similar disorders in touch with each other, without disrupting family life; it has been shown to be cost effective (86). If a mother must be hospitalised, joint admission of mother and infant has advantages over admission of the mother alone, because it preserves the mother-infant relationship. Units devoted to post-partum care are probably safer and more effective than conjoint admission to general psychiatric wards. Specialist teams need links with obstetric units, which have an important role, especially in early diagnosis and prevention. They also need links with paediatric units, social services and child protection teams to collaborate in the prevention of child abuse. Links with voluntary agencies are important, because self-help groups provide much support for depressed and isolated mothers, and can collaborate in treatment (87). There are a number of specialist services in UK, Australia and New Zealand, France, Germany, Belgium and The Netherlands, but few elsewhere. There is a case for establishing them in every country, and all major cities and conurbations. Unfortunately, the advantages and safety of these specialist services have not yet been established by systematic service evaluation. This will be a difficult exercise, demanding careful matching of cases for diagnosis and severity. But it is one of the main research priorities in this area of psychiatry.

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Postnatal mental disorder: towards ICD-11

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International classifications of mental disorders, to be useful for practitioners, patients and policy makers, should reflect not only scientific advances in knowledge of causes and consequences, but also common usage. In this regard, Ian Brockington's paper, based on encyclopaedic knowledge of ancient as well as recent literature and clinical common sense, has opened up the debate about the direction of travel towards the ICD-11 and the DSM-V.

The limits of existing classifications for postnatal mental disorder are well known to clinicians and researchers in this field (1). The ICD-10, for example, permits the classification of mental and behavioural disorders associated with the puerperium (F53) only if they onset within six weeks and if they cannot be classified elsewhere. Furthermore, psychiatrists from developing countries who wish to use the puerperal psychosis category should do so, not because there are specific features of puerperal psychoses, but because lack of resources prevents finer points of psychopathology being elicited. The implication that psychiatrists of developing countries (perhaps closer to the insights of traditional/folk perinatal mental disorders) have got it wrong rather than right, has indirectly led to the failure of national statistics to document the personal, professional and public policy implications of these discreet mental disorders.

The DSM-IV, with an even shorter onset specifier of four weeks, is restricted to four diagnoses only, and likewise is rarely used. Ironically, in this system, specific features of postnatal mood disorder are acknowledged in the text (e.g., fluctuating course and mood lability, delusions including the baby at risk of infanticide, disinterest in the infant, guilt because of dissonance between the mother's mood and society's expectation of happiness, and less than optimum development of a mother/infant relationship).

At the Satra Bruk classification workshop held in Sweden in 1999 (2), attended by international experts including Eugene Paykel, Marie Asberg, Gordon Parker and Kathy Wisner, these conditions were reviewed, and specific proposals about revised classifications were considered (3). These included: a) the introduction of a specifier for onset within 3 months post-partum, to cover all diagnoses in mood disorder, psychosis and adjustment disorder sections (ICD-10 F20-29, F30-39, F43; DSM-IV schizophrenia and other psychotic disorders, mood disorders, adjustment disorders); b) the omission of F53 (mental and behavioural disorders associated with the puerperium, not elsewhere classified) from the next revision of ICD-10; c) the introduction in the DSM-V of a further psychotic diagnostic category, not limited to post-partum onsets, but permitting this qualifier, while the following criteria for F23.0 in ICD-10 should also be the same: i) sudden onset not on background of chronic disorder; ii) two or more of the following: mood disorder with lability; delusions not characteristic of mood disorder or schizophrenia; rapid fluctuations; perplexity, confusion or disorientation; iii) does not fit criteria for schizophrenia, depressive episode or manic episode/disorder; d) a defined diagnostic category should be introduced in the mood disorder sections of both classifications for sub-syndromal or minor depression, also permitting the post-partum specifier.

Disorders of mother/infant relationship were not included specifically in these proposals. Brockington has made a responsible case for their inclusion. He does however recognise that depression postpartum is commonly also present and can itself initiate a disorder in mother/infant attachment, leading to neuro-behavioural problems in the infant and young child (especially boys). He argues for the inclusion of mother/infant relationship/bonding problems on the pragmatic ground that a classification to be useful must reflect problems brought by patients for treatment. Quite so.

Postnatal depression is indeed a useful lay and professional term and its ubiquity – the Edinburgh Postnatal Depression Scale (EPDS) (4,5) has been translated into 24 languages with validation studies in most – would suggest that modern society is aware of and troubled by conspicuous mood disturbance at this time, particularly depression postpartum. But why now rather than 30 years ago? Is postnatal depression a global culture bound disorder? Is this greater awareness linked to women and men's health issues, or to less support postpartum because of changing family structures?

The EPDS was developed and specifically validated against Research Diagnostic Criteria for depression as an aid to identifying and screening for depression postpartum. Subsequent clinical interviews are necessary to differentiate incidence from prevalence, and identify less common but important co-morbid conditions (e.g., post-traumatic stress disorder, panic disorder and obsessive-compulsive disorder).

The perinatal mood disorders are thus a diagnostic challenge to international classifiers, as well as a broadening stimulus to life event researchers, because childbirth is a complex biosocial and psycho-spiritual process. They are also a challenge to simplistic primary prevention models. Women at high risk of puerperal psychosis and

postnatal depression can be identified, but antenatal prevention studies are equivocal with regard to the success of prevention programmes (6). Secondary prevention through the identification of early onset postnatal depression and severe postnatal blues is in my opinion more feasible and cost effective. In this regard, researchers should not overlook the possibility of a common neuro-endocrine trigger for the blues, the puerperal psychoses and the early onset non-psychotic depression.

Transcultural studies have shown the importance of grandparents (e.g., mothers-in-law) as providers of social support and also as distinctive stressors in Hong Kong (7) or Asians in Nottingham and in all but one of seven European centres (8). A US study (9) of families and households found that undertaking the primary care of a grandchild was associated with an increase in levels of depression.

In addition to the studies of clinical and cost-effectiveness of postnatal mental health services, measures of mental health in new grandparents and postnatal depression as a trigger of serious marital disruption (separation or divorce) are other pertinent research priorities at the present time.

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An evidence-based approach to post-partum depression

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One of the challenges for psychiatry in the 21st century will be to move away from case reports and expert opinion and toward evidence-based knowledge, which will inform the development of best practices. We recently published an evaluative report of the post-partum depression (PPD) literature in four related areas: a) risk factors; b) detection, prevention, and treatment interventions; c) the impact on the mother-infant relationship and child development; and d) public health interventions which may reduce the impact of PPD on the mother-infant relationship and the child (1).

Our report critically reviewed the literature, identified gaps, and formulated conclusions. As the literature on PPD is vast and extremely variable in quality, the following search criteria were imposed: studies had to be empirically-based, peer-reviewed, published in English between 1990 and 2002 (excluding seminal studies prior to these dates), and state both the diagnostic and temporal criteria of PPD used; only cases of nonpsychotic depression with an onset within 1 year of childbirth were included.

Nineteen comprehensive databases containing medical, psychological and social science literature were searched. Salient journals, conference proceedings and graduate theses were scanned. Relevant studies meeting the inclusion criteria were identified, critically appraised, and their quality graded based on published international standardized methodology.

The studies critiqued varied in sampling procedures, the timing of follow-up assessments, and the measurement of PPD; common methodological limitations included selection bias, lack of randomization, and insufficient power to detect effects. While the report presented recommendations, they should be evaluated in light of the dearth of evidence-based literature.

PPD is a significant public health problem, affecting approximately 13% of women within the first year of childbirth. Although the rates of depression do not appear to be higher in women in the period after childbirth compared to age-matched controls, the rates of first onset and severe depression are elevated at least 3-fold. Depression at this critical period of life carries special meaning and risks to the woman and her family.

There are established antenatal risk factors for PPD: depression or anxiety during pregnancy, stressful recent life events, poor social support, previous history of depression, child care stress, low self esteem, maternal neuroticism, obstetric and pregnancy complications, negative cognitive attributions, single marital status, poor relationship with partner, and low socioeconomic status (in descending order of predictive strengths).

The unacceptably low positive pre-

dictive value of all currently available antenatal screening tools makes it difficult to recommend them for routine care. Several post-partum screening tools exist, but the optimal time for screening and their full applicability to multicultural populations are not yet established. Meta-analyses of depression screening programs generally conclude that depression screening must be combined with systemic paths for referral of cases and well-defined and implemented care plans to achieve outcome benefits. Unfortunately, PPD remains under-diagnosed and under-treated.

Research suggests that PPD is amenable to the same treatment interventions as depression at other times, but few randomized controlled trials exist to guide practice and policies for this specific population. One certainty is that there is no single etiologic pathway by which women develop PPD, thus it is improbable that a single preventive or treatment modality will be effective for all women.

Current research suggests that PPD has salient but selective effects for the mother-infant relationship and child growth and development. Young children of mothers with PPD have greater cognitive, behavioural and interpersonal problems than children of nondepressed mothers. With regard to emotional growth and development, studies support an early effect of PPD on infant affect, but do not support longer effects. Overall, it is the exposure to prolonged episodes of PPD or to recurrent episodes of maternal depression that are most likely to have long term effects on the child.

The potential adverse effects of PPD upon the mother-infant relationship and child development reinforce the need for early identification and effective treatment models. Unfortunately, there are few studies of public health interventions that have been shown to prevent or mitigate the impact of PPD on these outcomes. A few studies of variable quality have explored the impact of interventions such as home visiting, telephone counseling, interactive coaching, group counseling and massage therapy. Public health interventions to reduce or mitigate these impacts are nascent and current evidence makes it difficult to recommend them as standard practice.

Our report highlighted a number of gaps in current literature and identified avenues of future research. One glaring gap was the absence of a woman-centered approach to the prevention and treatment of PPD. Pejorative terms such as rejecting, complaining, hostile, bitter and querulous were sometimes used to describe women who were experiencing frightening illnesses or who reported unpleasant, neglectful or abusive experiences from professional caregivers. It is also imperative to develop and apply evidence-based research findings in helping women make informed decisions about further pregnancy, and treatment or prophylaxis. Research which examines the experience of PPD for the mother and child within diverse ethnic and socio-economic groups is lacking.

Large, well-controlled longitudinal studies that evaluate the effects of promising interventions on the woman, maternal-infant relations, and child development are urgently needed. Next steps in policy and practice include the need for greater awareness among public and healthcare professionals of PPD and the local resources available for its optimal treatment. Programs related to prevention, detection, treatment, and amelioration of the effects of PPD on the mother-infant relationship and child growth and development should all be based on sound evidence as it emerges.

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Childbirth is not only complex: it may also be dangerous

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In Latin America, a pregnant woman has the certainty of having skilled health staff attention during delivery only in Cuba, Costa Rica, Chile, Argentina and Uruguay. The maternal mortality rate in our countries averages 190 per 100,000 live births (1). While there is wide public knowledge of modern contraceptive methods, they are not always available and abortion is illegal in most countries (2). Post-partum disorders must be viewed in this context of lack of attention even to the most visible aspects of childbirth. History taking in overburdened emergency maternity wards does not allow for collection of data about the mother's psychiatric history, let alone her current emotional status. Very short stays and lack of follow-up make early recognition of emotional disorders very unlikely.

And yet, everyday we witness the consequences of undiagnosed and hence untreated puerperal disorders. Accounts of puerperal women killing their children are the most prominent examples, but our high rates of child abuse probably reflect irritability and fatigue in depressive mothers as well as difficulties in the mother-infant relationship, an area that needs to be investigated further, as stated by Ian Brockington. Whether maternal emotional disturbances are causative of developmental delays and adjustment problems in the children or whether they just coexist, being both the result of unfavorable circumstances, needs to be elucidated.

Some researchers in Latin America have looked into the prevalence and incidence of post-partum depression. In Chile, Jadresic and Araya (3) reported

that around a third of post-partum women had depressive symptoms. Risco et al (4), also in Chile, found that up to 48% of women, surveyed 12 weeks post-partum, had a score on the Edinburgh Postnatal Depression Scale above 9. When a sample of Chilean women was compared with two samples of Costa Rican women, the rates of depression and dysphoric mood following childbirth were similar (34% vs. 47% reported current dysphoric mood, 40% vs. 48% reported an episode of major depression sometime during their life and one third of the Costa Rican women reported dysphoric mood following the birth of a child), in spite of differences in demographics.

The current thread in these papers is the importance of psychosocial factors. The findings of Risco et al (4) and Wolf et al (5) clearly show an association between post-partum depression and unwanted pregnancy, having three or more children already, lacking a partner, vaginal delivery, having conjugal conflicts or being single, having few years of education and living in crowded households.

Apparently, the lack of sexual and reproductive health (expressed in unwanted pregnancy) is linked to post-partum mental disorders. Women with less education and lower socioeconomic status seem to be at a higher risk of having a pregnancy they do not desire. Single women, teenagers and women over forty also tend to present more unwanted pregnancies.

Particularly worrisome is the situation of pregnant adolescents. Young age is a recognized risk factor for puerperal depression (5). Pregnancy for a young girl means the interruption of schooling and of personal growth and it is a harbinger of future poverty. It may also mean estrangement from the family, either because the pregnancy is the result of incest or because the family holds very rigid conservative values. For the children of these young mothers, there is an increased risk of rejection and neglect. Young girls living in an institution for pregnant teenagers in Lima showed lack of knowledge about their own anatomy and physiology (even after childbirth), had difficulties relating to their children, who were subject to neglect and abuse, and suffered not only from depression, but also from post-traumatic stress disorder (6). These girls lived under the protection of Catholic nuns, as their own mothers had thrown them away from the house – in an exquisite disqualification of maternal love – and they faced the possibility of becoming live-in maids once they were discharged from the shelter.

Lack of social support becomes more important as people migrate to big cities, fleeing violence or starvation. With the disappearance of the extended family, the rituals that insured that women received social recognition and instrumental help after parturition are falling into oblivion. For the high percentage of women that work in the informal sector, social protection is lacking: no maternity leave, no provisions for breast-feeding, no child care available.

Maternity is overvalued in our countries, and yet it is unprotected: the complex emotional experience of motherhood is not taken into account, as becoming a mother is glorified as if it were indispensable for womanhood. It is very difficult among non-professionals and professionals to recognize that a woman who has had a child recently might be undergoing psychiatric problems, mostly depression, as this contradicts the expectation of bliss and happiness supposed to be part of becoming a mother. Mental health professionals have a tough task: they must educate themselves regarding these disorders and they must disseminate the information at all levels, from the medical schools to the executive and legislative bodies. The improvement of obstetric and mental health services for women in Latin America will not be possible without the participation of knowledgeable users and providers.

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Post-partum psychiatric care in India: the need for integration and innovation

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Brockington emphasises the need for clinicians and researchers to recognise that post-partum psychiatric syndromes go beyond the traditionally accepted triad. There are several distinct clinical conditions that have now been recognised, each with different aetiologies, course, methods of diagnosis and management.

In this regard, research in post-partum psychiatric disorders in India, though limited, has followed two parallel streams. Community-based studies have focussed mainly on post-partum depression (PPD), while hospital-based studies have focussed mainly on clinical descriptions of post-partum psychosis. The last few years have seen

an increase in epidemiological data on PPD in India (1,2). These studies have been extremely important in estimating the prevalence and identifying risk factors for the disorder and have also highlighted specific cultural and social factors that increase risk for the disorder in India.

Two prospective studies on pregnant women, in the states of Goa and rural South India, detected depressive disorder in 23% and 16% respectively, with depression persisting six months after child birth in 11–14% of women (1,2). While the risk factors found in both the studies replicate some of those already established in Western countries (poor marital relationship, antenatal depression), the finding of culture specific risk factors enhances their relevance. Gender based factors emerged as being highly important, with intimate partner violence, unhappiness about the gender of the child, poverty and having a living female child being identified as risk factors both for the occurrence of PPD and for chronicity. Maternal education, on the other hand, appeared to be a protective factor. Both the above studies have highlighted the importance of social factors, specifically poverty and female gender of the infant.

It must be emphasised here that both these studies were carried out in states of India where antenatal and postnatal services are among the best in the country. The National Family Health Survey-2 (3) from India has reported that nearly 34% of pregnant women do not receive even a single antenatal check up and only 35% of deliveries are conducted in health facilities. In some states up to 65% mothers did not get even one antenatal check up. Both antenatal and postnatal check ups were reported to be less among low-income women and those who had low literacy levels, both of which have been identified as risk factors for depression.

The findings of these studies, in the light of national health indicators of maternal health, inform us regarding the need for mental health care in the community to be integrated with other programs, including those on economic growth, alcohol services for men, and those addressing gender specific issues. A purely biomedical approach is unlikely to prevent the occurrence or chronicity of these disorders, given the fact that most mediators do not seem to be biomedical in nature. Mental health professionals, however, have an important role in working closely with maternal and child health workers and offering consultative and training services in early detection and referral.

Severe mental illness (SMI) in the post-partum is another important but neglected area, with most studies in India being descriptive (4). Inadequate post-partum care contributes to organic factors in precipitating or worsening psychosis.

There are very few studies that have assessed mother-infant interaction patterns, including harm to the baby and neglect, which according to Brockington are important consequences of post-partum psychosis (5). Despite India having low resources for some mental health facilities, newer antipsychotics, mood stabilisers and antidepressants are available at reasonable cost (6). A large number of women with SMI will be on psychotropic medication and need special services for preconception counselling and safe use of drugs in the post-partum. Parenting assessments and family planning issues need to be integrated into the routine care of women with SMI. All this will require special effort and training of mental health personnel.

It has been established that joint admissions in specialised mother-baby units are the preferred context for handling post-partum women with SMI with their babies. Mother-baby units are expensive and need specialised personnel. In a resource scarce country such as India, while tertiary care centres can offer specialised services including clinical care, research and training, more cost effective ways of delivering services for mothers with SMI need to be identified. This might include domiciliary care by trained nurses, volunteers or trained peers or even a female relative under supervision.

The challenge that post-partum psychiatry faces in India is to translate research findings into practice by working closely with other agencies, adapting established modes of care to local needs and resources and finding innovative care delivery methods both in the hospital and the community.

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Postnatal depression, social support, and child abuse

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Although social support is recognised as an important protective fac-

tor with respect to the occurrence of post-natal depression, and post-natal depression is regarded as a risk factor for abusive child rearing (1), little research has been conducted on the effects of the lack of social support on the occurrence of infant abuse.

We conducted a two-wave questionnaire study on the influence of psychosocial variables on the extent of abusive parenting by mothers. We recruited 758 women who had recently delivered babies at five obstetric clinics and hospitals in Okayama, Japan. The ages of the women varied between 17 and 41 years (mean 28.7 ± 4.1). About half (47.9%) of the women had delivered their first baby. The women were asked to respond to two sets of questionnaires, the first at day 5 after delivery and the second at one month after delivery.

The day 5 set included the Perceived Social Support (PSS) questionnaire (measuring the amount of and satisfaction with perceived social support in three domains: emotional, information, and instrumental) and the Blues Questionnaire (BQ, 2). The month 1 set included the Life Event Scale (measuring both positive and negative events occurring after the childbirth), the Ways of Coping Check-List (3), the Enacted Social Support questionnaire (measuring the amount of and satisfaction for enacted social support, social undermining, and the 'let down' of support – absence of expected support when it was needed – in three domains: emotional, information and instrumental), the Edinburgh Postnatal Depression Scale (EPDS, 4), and the Conflict Tactics Scale (CTS, 5) to measure parental abuse towards the baby.

The total score of the 1 month CTS was significantly ($p < 0.001$) correlated with the woman's age ($r = -0.13$), the husband's age ($r = -.13$), the BQ score ($r = 0.17$), the EPDS score ($r = 0.22$), the negative life event score ($r = -0.17$), the satisfaction with perceived social support on the PSS ($r = -0.15$), the dissatisfaction with the enacted 'let down' support ($r = 0.13$), and the enacted turning to other coping ($r = 0.13$). First mothers had higher CTS scores than mothers with a child or children. Because of the correlations between these variables, we performed a regression analysis with the total CTS score at 1 month. The entry of independent variables were in the following order: 1) the woman's and husband's ages and the gravity, 2) the EPDS at month 1, 3) the negative life event score, the enacted turning to other coping styles, and the perceived 'let down' support score, and 4) the BQ and PSS satisfaction scores at day 5. The final stage of the regression analysis showed that the CTS at month 1 was predicted by dissatisfaction with the enacted 'let down' support (beta = -0.13), and the perceived social support at day 5 (beta = -0.20).

Our result suggests that poor satisfaction with support at the baseline and disappointment due to the absence of expected support after childbirth, rather than post-natal dysphoria (maternity blues and post-natal depression) itself, are direct causes of abusive parenting. Psychological interventions should focus on interpersonal support in order to prevent infant abuse.

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The challenges of motherhood and mental health

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With increased knowledge about post-partum disorders, responsibility and new challenges come. Some of the clinical implications are outlined in Ian Brockington's paper, where he argues against an oversimplification of these disorders and suggests using commonly known terms to describe depression to new mothers and their relatives. This would help them to understand the disease, reduce the stigma of their illness, and allow them to recognize their need for help.

Post-partum depression should be prioritised as it is a common disorder. A meta-analysis indicates a prevalence rate of about 13% (1), and even higher rates have been reported in non-industrialized societies. Without special attention and use of adequate screening procedures, the disorder can escape diagnosis. The Edinburgh Postnatal Depression Scale (EPDS) is often the preferred cost-effective tool to detect the symptoms of depression. The psychometric properties of this instrument are considered very good. We recently confirmed this in our analysis as a one-factor model measuring depression accounted for 46.6% of the scale's variance (2). With the standard use of simple screening tools at the regular postnatal visit, more cases could be identified. Interventions can then be offered at an early stage, often in a primary care setting.

Treatment of depression in women after childbirth should integrate both psychosocial and biological modalities. Selective serotonin reuptake inhibitors (SSRIs) have been recommended as first line therapy in post-

partum depression (3). The SSRIs are also the treatment of choice for post-partum dysthymia, panic disorder and obsessive-compulsive disorder (4). The mother's desire to breast-feed often adds an extra challenge to the treatment, as there is still some uncertainty about drug exposure and subsequent potentially adverse effects on the infant, yet we must keep in mind that breast-feeding is the best nutritional mode during the first six months of life (5). Based on extensive research, breast-feeding should not be generally discouraged in women using SSRIs. There is still, however, a lack of long-term data concerning infant antidepressant drug exposure through breast milk.

When using the proper diagnostic procedures and tools, groups with particularly high risk for depression and psychosis in the post-partum period can be identified at an early stage. There is evidence that most post-partum psychoses are affective and related to bipolar illness, first shown by Bratfos (6). Both severe depression and psychosis are sometimes coupled with strong suicidal ideation and impulses. Because of this there is an urgent need for high efficacy in treatment and rapid improvement. Newer antipsychotics and electroconvulsive therapy (ECT) may be used in the acute phase. Two recent reports indicate that both these conditions respond particularly well to ECT (7,8). For psychological reasons, the first step should be this type of efficient biological treatment when it is applicable. Joint admission of mother and infant when mothers have to be hospitalized is advantageous for all involved in the recovery, yet units devoted to post-partum care only exist in a few countries (9), and are seldom a result of an official health priority. In densely populated areas around the world there are good arguments for establishing such facilities; some of these arguments are given by Brockington. The higher cost of running mother-baby units compared to standard adult psychiatric units is perhaps one of the reasons why they are more commonly seen in the industrialized world.

Even if most depressed mothers do not have a relationship problem with their neonates, new mothers who are mentally ill may be dysfunctional and experience impaired communication with their newborns. There is growing evidence of possible long-term negative consequences on the cognitive and social development of a child (10) in such a situation. This gives strength to the arguments for increased awareness and more specific treatment modalities.

The growing number of single-parent families in many countries in recent years is of clinical significance, as perceived social isolation is a risk factor for post-partum depression (11). Particular attention should therefore be given to prevention, detection, and early intervention of post-partum disorders in single mothers.

Much can be done to restore distressed mothers to good mental health. In view of cost-effectiveness, the benefits of using more resources on management of post-partum mental disorders should be considered, particularly in national health plans. The risk groups are well known, illness can often be prevented, and the prognosis with proper treatment is in most cases excellent. Acquiring the skills, tools, and resources for early detection and efficient treatment can restore a mother's ability to care for her child. This benefits the mother, the child and, in the long run, society.

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Mother-infant bonding disorders and use of Parental Bonding Questionnaire in clinical practice

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Ian Brockington's paper is a most important review of the perinatal psychiatry research and practice in recent times. The paper proposes to recognize

mother-infant relationship disorders as specific conditions to be diagnosed as such by psychiatrists and general practitioners. Brockington states that there is no single entity and that this is a group of overlapping clinical states, with various morbid elements in the relationship between the mother and the infant. They include a distressing lack of maternal feeling, irritability, hostility and aggressive impulses, pathological ideas and outright rejection. These disorders are quite common in mothers referred for psychiatric help and are present in 22% of post-partum referrals (1) and in 29% of mothers diagnosed with post-natal depression (2). There are three different manifestations of bonding disorders: a) mild disorders (delay, ambivalence or loss in maternal response); b) rejection (threatened or established); c) pathological anger (mild, moderate or severe).

When the mother experiences delay or loss of maternal emotional response, she may express disappointment about her feelings towards her infant (e.g., that she has no feelings, or she feels estranged or distant from him, or she feels that he is not her baby, or that she is baby-sitting for someone else).

When a mother experiences pathological anger towards the infant, she may have a milder form (an experience of anger which is controlled with difficulty) or she may have an impulse to harm or kill the child, or she may lose control at a verbal level and shout and scream at the baby. When the presentation of anger is more pronounced, this may result in handling the baby roughly (e.g., throwing it into the cot or jerking his limbs, shaking him, occluding his breathing), or she may strike, beat, bite, burn or throw him or make a deliberate attempt to kill him.

The third presentation of a bonding disorder is the rejection of the infant (when the mother expresses strong negative feelings about the child: dislike, hatred and regret about his birth). There is absence of affectionate behavior such as kissing, cuddling, cooing, singing, playing. She feels better when away from the infant; she expresses the feeling of being trapped by motherhood. She may express the wish that the infant care is transferred to someone else. She may have the wish that the infant is stolen or dies and she may have run away to escape the care of the infant. All these presentations of bonding disorder have to produce distress and result in an appeal for help from family or professional staff, in order to meet the criteria (2).

The mother-infant interaction is one of the main focuses of perinatal psychiatry. In a recent transcultural study on post-partum depression, the mother-infant interaction was one of the variables assessed to capture the whole spectrum of themes of perinatal illness (3). Leading perinatal psychologists and psychiatrists have developed objective methods of investigating the mother-infant interaction. For the clinician, these methods are sometimes quite difficult to implement. Questionnaires are a very useful tool to evaluate a disordered relationship at the first interview with the mother. This can facilitate the establishment of a treatment plan and the evaluation of treatment progress.

In cases of post-partum depression, the Parental Bonding Questionnaire (PBQ, 2) is best used together with the Edinburgh Postnatal Depression Scale (EPDS, 4), in order to assess the effect of treatment on both variables: depression and difficulties of the mother to relate to her child.

The use of the PBQ allows the clinician to judge the severity of the relationship disorder and even more importantly to evaluate improvement. This is very helpful with the depressed patient, who often does not notice any change. It also enables the therapist to keep the patient hopeful and optimistic, a crucial ingredient in the therapy of depressed patients.

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Implementation of evidence-based treatment for schizophrenic disorders: two-year outcome of an international field trial of optimal treatment

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According to clinical trials literature, every person with a schizophrenic disorder should be provided with the combination of optimal dose antipsychotics, strategies to educate himself and his carers to cope more efficiently with environmental stresses, cognitive-behavioural strategies to enhance work and social goals and reducing residual symptoms, and assertive home-based management to help prevent and resolve major social needs and crises, including recurrent episodes of symptoms. Despite strong scientific support for the routine implementation of these 'evidence-based' strategies, few services provide more than the pharmacotherapy component, and even this is seldom applied in the manner associated with the best results in the clinical trials. An international collaborative group, the Optimal Treatment Project (OTP), has been developed to promote the routine use of evidence-based strategies for schizophrenic disorders. A field trial was started to evaluate the benefits and costs of applying evidence-based strategies over a 5-year period. Centres have been set up in 18 countries. This paper summarises the outcome after 24 months of 'optimal' treatment in 603 cases who had reached this stage in their treatment by the end of 2002. On all measures the evidence-based OTP approach achieved more than double the benefits associated with current best practices. One half of recent cases had achieved full recovery from clinical and social morbidity. These advantages were even more striking in centres where a random-control design was used.

Key words: Evidence-based treatment, schizophrenia, effectiveness, field trial, outcome, multicentre

In the past three decades, treatment strategies have been developed for treatment and rehabilitation of schizophrenic disorders that have been shown to markedly reduce the clinical, social and carer morbidity and improve the efficiency of mental health resources. Several reviews of the clinical trials literature have concluded that every person with a schizophrenic disorder should be provided with the combination of a) optimal dose antipsychotics, b) strategies to educate himself or herself and carers, usually relatives, to cope more efficiently with environmental stresses, and c) assertive home-based management to help prevent and resolve major social needs and crises, including episodes of symptoms (1-6).

Despite strong scientific support for the routine implementation of these 'evidence-based' strategies, few services provide more than the pharmacotherapy component, and even this is seldom applied in the manner associated with the best results in the clinical trials (4). Further, although a 5-year outcome is considered the minimal time period for evaluating modifications in the natural course of major disorders by effective treatment, very few field trials of psychiatric treatment strategies have evaluated prospectively the benefits and risks of treatment for more than one year.

In 1994, an international collaborative group was established with the goal of promoting the routine use of evidence-based strategies for mental disorders with continued evaluation of clinical, social, carer and economic outcomes. This collaboration became known as the Optimal Treatment Project (OTP). This paper reports preliminary results for a cohort of cases with schizophrenic disorders.

METHODS

More than 80 centres in over twenty countries have begun the project since 1994. Lack of research funding and administrative difficulties limited the number of centres with unselected cases that have received 'optimal treatment' according to the project protocol for at least 24 months to 14. These were Ankara (Turkey), Gothenburg, Svenljunga and Lysekil (West Sweden), Como and Benevento (Italy), Trondheim (Norway), Athens (Greece), Bonn (Germany), Valencia (Spain), Auckland (New Zealand), Tokyo (Japan), Budapest and Szekesfehervar (Hungary).

'Optimal treatment' includes the strategies listed in Table 1. In each centre, a multidisciplinary team of psychiatrists, psychologists, social workers, nurses and occupational therapists received between 60 and 100 hours of workshop training in these strategies. Once they had been certified as competent, they began to enter cases in the

Table 1 Evidence-based treatment strategies used in the Optimal Treatment Project (OTP)

- Minimally effective antipsychotic drug strategies targeted to changing symptom profiles (7-9)
  - Choice of medication based on symptom profiles, side effects and response
  - Education about benefits and problems
  - Adherence training and maintenance
  - Side effects prevention and minimization
  - Early warning signs of exacerbation
- Education of patients and informal carers in stress management strategies (10,11)
  - Education to enhance understanding of the nature of psychotic disorders and their clinical treatments
  - Training in effective interpersonal communication and structured problem solving to achieve personal goals and manage life stresses
- Assertive case-management (12)
  - Development and maintenance of effective social support - housing, finances, health and safety
  - Early detection and intensive care to resolve clinical and social crises in the settings most conducive to full and rapid recovery
- Goal-oriented social and occupational skills training (9,13)
  - Training patients and informal carers in the skills they need to achieve their personal goals for friendships, close relationships, work and recreational activities
  - Supporting patients to access the full range of social and occupational opportunities available in their communities
- Specific pharmacological and/or psychological strategies for residual or emerging symptoms (8,14-17)
  - Coping with persistent psychosis
  - Managing negative symptoms
  - Coping with anxiety and panic
  - Coping with mood swings, dysphoria and suicidal thoughts
  - Managing substance misuse
  - Managing anger and frustration
  - Managing sleep disorders
  - Managing nutritional problems

project. Patients with a DSM-IV diagnosis of a schizophrenic disorder were selected. Clinical diagnoses were based on standardised interviews. These included the Structured Clinical Interview for DSM-IV (SCID-I, 18), the Schedules for Clinical Assessment in Neuropsychiatry (SCAN, 19) or the Current Psychiatric State, 50-item version (CPS-50, 20). No specific exclusion criteria were used: in particular, cases with comorbid psychiatric, neurological, physical or substance misuse problems were included so that the sample represented typical clinical cases. Cases entered the study once they were stabilised from any recent exacerbations. In four centres (Ankara, Gothenburg, Trondheim and Benevento), cases were randomly assigned to OTP or routine case management.

A core battery of global measures was used in each centre. These included: a) the Mental Functions Impairment Scale (MFIS, based on 21), a 7-point scale which measures the proportion of time each day the subject experiences impairment in mental functioning as a result of all types of symptoms; b) the Disability Index (DI, based on 22), a 7-point scale which measures limitations of subjects' ability to perform interpersonal and social functions in accordance with their cultural expectations; c) the Global Carer Stress (GCS, 23), a 5-point scale which measures the subjective stress experienced by the key caregiver associated with the patient's mental disorder. Ratings were translated, and at each centre two or more raters who were independent of the clinical teams were trained to apply the scales to a high level of reliability (intraclass correlation coefficient > 0.90). The ratings were made at 3-month intervals by the clinical teams, and at least at baseline and at 12 and 24 months by the independent assessors. Ratings were made after interviews with both the patient and his or her key caregiver, with supplemental information available from charts and case managers when necessary. Background information on residence, work and social functioning was also collected by the independent raters at 3 month intervals. In addition to these core measures, several centres used other standardised clinical, social, economic and neuropsychological assessments. A manual describing the assessment battery and its standardisation was produced (20).

Paired t-tests were used to assess the changes in the cohorts from before treatment to 24 months of treatment. Cohen's d was used to calculate effect sizes (24).

RESULTS

At the end of 2002, 1012 cases had entered the project, with 603 having completed at least two years of 'optimal treatment'. Table 2 summarises the background characteristics of this cohort. Complete data was available on 594 cases, 99% of the sample. Included in this cohort were 58 cases that had withdrawn partially or fully from participation in the clinical protocol of the project but were evaluated at 24 months. Thus the analysis was conducted on an intention-to-treat basis. A further 9 cases were unavailable for evaluation at 24 months. Thus, a total of 67 cases, or 11%, could be considered project drop-outs.

Fidelity in applying all the evidence-based strategies was examined on a random selection of cases at each service. This usually ranged from good to excellent, with fidelity tending to improve the longer services participated in the program. The most common problems involved applying pharmacotherapy according to the project guidelines, that aimed to target specific symptoms, to maximise adherence and to minimise side effects. Other problems included engaging families and other informal caregivers in services where routine contact previously had been rare, and applying supportive goal-oriented methods to assist patients to enhance their social networks and to gain constructive occupation. Further training and supervision usually remedied these deficits.

Table 3 shows the results on the clinical, social and carer indices. Significant improvements occurred on all measures over the 24 months. These benefits appeared to have clinical significance, with average percentage changes of 41% on the impairment index, 39% on disability and 48% less stress on carers. The cases assigned to continue their routine case management showed similar improvements, but these appeared to have less clinical significance: impairment 12%, disability 13% and carer stress 15%.

Table 2 Characteristics of cohorts at each centre

Centre	N (% total)	Age: years (SD)	Sex: male (%)	Marital status: unmarried (%)	First episode (%)	Duration of illness >10 years (%)	Optimal treatment (%)
Trondheim	49 (8)	25.2 (4.6)	28 (57)	46 (94)	49 (100)	0 (0)	29 (59)
Auckland	24 (4)	27.1 (8.3)	15 (63)	21 (88)	22 (92)	2 (8)	24 (100)
Tokyo	19 (3)	36.1 (7.7)	12 (63)	11 (58)	0 (0)	4 (21)	19 (100)
Valencia	102 (17)	26.3 (6.0)	69 (68)	91 (89)	18 (18)	14 (14)	102 (100)
Athens	51 (9)	35.4 (6.9)	25 (49)	46 (90)	0 (0)	51 (100)	51 (100)
Bonn	18 (3)	33.6 (6.3)	11 (61)	10 (56)	0 (0)	6 (33)	18 (100)
West Sweden	88 (15)	38.3 (8.3)	55 (63)	80 (91)	0 (0)	53 (60)	56 (64)
Hungary	35 (6)	33.4 (10.4)	14 (40)	25 (72)	8 (23)	7 (20)	35 (100)
Benevento	24 (4)	30.0 (2.0)	19 (79)	23 (96)	0 (0)	0 (0)	12 (50)
Ankara	100 (17)	28.9 (7.0)	66 (66)	55 (55)	19 (19)	13 (13)	50 (50)
Como	93 (15)	61.0 (8.8)	52 (56)	90 (93)	0 (0)	93 (100)	47 (51)
TOTAL	603 (100)	35.7 (13.8)	366 (61)	501 (83)	120 (20)	243 (40)	443 (73)

The direct comparison between cases randomly assigned to OTP (n=146) or routine case management (n=114) in the centres of Ankara, Trondheim, Benevento and Gothenburg showed an even greater contrast between the two treatment approaches, with OTP cases presenting more than twice the benefits observed by blind, independent raters on routine case management. The Cohen's d for impairment was 1.49 for OTP (48% improvement) vs. 0.56 for routine case management (21% improvement). The corresponding figures for disability were 1.41 (53% improvement) vs. 0.56 (16% improvement), and those for carer stress were 1.22 (63% improvement) vs. 0.33 (15% improvement).

An analysis of the rates of recovery (full = no significant impairment or disability; partial = substantial improvement in impairment and disability) showed that 35% of OTP cases met the criteria of full recovery at 24 months vs. 10% of those on routine case management. When the recent-onset group (onset of psychotic symptoms within 10 years) was considered separately, 43% had made a full recovery vs. 6% in the contrast group. However, a very similar proportion of both groups (74 vs. 73%) showed patterns of substantial recovery from impairment and disability, with similar proportions making little or no progress (26 vs. 27%). This would appear to suggest that the rate of recovery with OTP was more rapid and complete than with routine case management.

DISCUSSION

This interim report of a five-year international field trial supports the hypothesis that consistent benefits are derived from evidence-based treatment strategies when

Table 3 Clinical impairment, social disability and carer stress at start of project and after 24 months

	Number of cases	Impairment mean (SD)	Disability Index mean (SD)	Carer Stress mean (SD)
At start of 'optimal treatment'	434	3.57 (1.57)	3.16 (1.32)	2.29 (1.34)
After 24 months of 'optimal treatment'	434	2.12 (1.46) d = 1.04	1.94 (1.25) d = 0.92	1.09 (1.14) d = 1.10
At start of continued current treatment	160	3.79 (1.89)	3.78 (1.53)	2.76 (1.29)
After 24 months of continued current treatment	160	3.32 (1.58) d = 0.25	3.29 (1.46) d = 0.32	2.34 (1.17) d = 0.33

d = Cohen's effect size

they are applied in a systematic way for schizophrenic disorders. It may be concluded that the combination of pharmacological and psychosocial strategies that have proven efficacious in controlled trials can be applied and evaluated in routine practice without additional resources, apart from the obvious need to ensure adequate training and monitoring of the fidelity of the strategies. The effect sizes and percentage improvements indicate that the clinical and social benefits associated with two years of optimal treatment are substantial, and with a clear trend towards recovery from clinical impairment and social disability.

In common with most field trials, this study can be criticised for its lack of methodological rigour. The lack of random allocation of all cases to a standardised comparative treatment approach with blind ratings should be set against the completeness of the data gathering and the broad range of cases sampled across a range of cultures with widely differing health care delivery systems. It is commonly observed that efforts to improve the scientific methodology of trials result in a reduction in the estimates of specific benefits that are associated with more naturalistic studies. In contrast, in this project the sub-sample of centres that provided a random controlled comparison between the evidence-based approach and more traditional case management programmes showed greater benefits on all core measures than those treating consecutive cases without a randomly controlled comparison.

It should be noted that significant improvements on all measures were observed when the traditional case management approach that was used as the control condition was provided over the 24-month period, reflecting the high clinical standards of the centres that entered the project. However, the lower effect sizes suggest that these benefits were less clinically significant and did not lead to the major improvements achieved from the attempts to adhere to the evidence-based protocol.

The OTP project provides further strong evidence for a change in the prognosis of schizophrenic disorders. In recent years there has been much speculation about the origins of the apparent improved outlook for patients diagnosed with these disorders (25,26). Biomedical and psychosocial factors have been implicated. Until now there has been little evidence that treatment has contributed to anything more than stabilising the course of the acute episodes of the disorder, without enhancing the rate or extent of recovery (2,27,28). On the basis of these preliminary results, it could now be hypothesised that integrated optimal pharmacotherapy and psychosocial treatment programmes may play a major role in expediting recovery from these disorders. Almost half the cases that began evidence-based treatment within 10 years of onset of their disorders showed a pattern of excellent recovery after two years. This apparently dramatic benefit should be interpreted with caution. Not all these cases were totally free of all psychiatric symptoms or social disability, nor does this interim report indicate that this recovery was stable. Residual symptoms of anxiety and depression, cognitive and learning difficulties, and the unavailability of social and occupational opportunities for patients were often more distressing and handicapping than the psychotic and deficit symptoms specific to the schizophrenic syndromes. The services that participated in the project were trained in the application of a broad range of evidence-based psychological strategies for drug-resistant psychotic and deficit symptoms, as well as strategies for managing anxiety, depression, suicidal ideation, anger, sleep and nutritional problems. Many of these strategies have not been tested specifically for residual symptoms and problems of patients with a first line diagnosis of schizophrenia (14,17). However, as in other branches of medicine, the goal/problem oriented approach to case management suggests that both pharmacological and psychosocial approaches may be effective when targeted to specific problems rather than merely to the core symptoms of each diagnostic category. The single-case evaluation that is necessary to establish the validity of the treatment plan for every case would appear to be a key component in the application of the wide range of treatment strategies over the entire course of a disorder. This approach was an integral part of optimal clinical management of cases in this project and may have contributed to the better than expected outcome of many cases, including many of those with disorders of long duration (29).

While the positive outcomes were striking, it is important to note that one in four cases of recent onset and first episode cases, and 40% of chronic cases showed no improvement after two years of optimal treatment. This substantial minority represents a significant challenge to clinicians and researchers. Although worthwhile advances have been made in pharmacotherapy and psychosocial treatments, there is much work still to be done. However, this lack of effectiveness of new strategies for *all* cases of schizophrenia should not excuse services from providing the full range of evidence-based strategies in a competent and optimistic manner to all cases.

The 5-year outcome data from this project will help establish whether the benefits from these methods are stable and continue to accrue. Unfortunately during the course of this project it has become very clear that few mental health services are provided with the resources to deliver continued optimal treatment programmes of this kind. Relatively short-term intensive treatment that produces worthwhile but incomplete improvement is still considered ethical in the mental health field. This acceptance of inadequate treatment led to most of the centres of excellence that began this OTP withdrawing because they were unable to ensure continued comprehensive treatment beyond the first year. The evidence gathered from this project is that two years of comprehensive evidence-based treatment is not sufficient for at least half the cases and that progress continues far beyond this point. To aim to achieve full and lasting recovery from mental disorders

should not be considered idealistic, but rather a societal necessity, and we should all fight to ensure that the resources are provided to implement optimal treatment for all disorders until this objective is met.

In addition to the core methodological weaknesses already discussed, this project suffered several other limitations. First, although every effort was made to include all cases of schizophrenic disorders within specific catchment areas, this was achieved in few centres. In almost all centres individual psychiatrists maintained personal control over the treatment programme provided to patients assigned to their care, and most were unwilling to follow an evidence-based protocol for a large proportion of their cases. This included an unwillingness to adhere to the principles of pharmacological practice, to discuss aspects of diagnosis and treatment rationales with patients and their informal carers, or to consider psychological strategies as adjuncts to pharmacotherapy for persisting and residual symptoms. Thus, the cohort included in the field trial may not be representative of schizophrenic disorders in the community. In particular, cases who showed rapid and full recovery after relatively brief psychotic episodes were seldom considered to need any psychosocial strategies in order to ensure full and lasting recovery of clinical and social functions and to prevent future episodes, despite the fact that such interventions could be brief and tailored to the individual strengths and weaknesses of patients and their carers. However, the multi-centred, cross-cultural nature of this project adds strength to the conclusion that an evidence-based approach applied within a individualised goal and problem oriented framework may be effective in routine clinical practice for both recent-onset and long-term cases of schizophrenia.

The relationship between clinical and social benefits and specific treatment strategies was not clearly defined. Although we attempted to ensure that all cases adhered to the treatment protocols, this was not always evident. It was clear that poor adherence to the treatment methods was not only due to poor compliance by the patient, but frequently to poor compliance by the professionals in applying the treatment strategies. Attempts to increase the flexibility of structured treatment methods beyond the parameters established under controlled trial conditions all too frequently become a license to implement methods in a highly idiosyncratic way, providing only part of the strategy, delaying implementation or avoid using those approaches that are clearly indicated in favour of those that are more convenient or those supported by marketing incentives. Careful and assertive monitoring that maximises adhesion to protocols in controlled trials appears just as necessary in routine practice if similar benefits are to be achieved.

Finally, it is important to note again that this is a report of work in progress and that the final results after five years of continued optimal treatment may show a different picture to that reported here. Prognostic factors and random effects that had less influence on the outcomes at two years may have greater impact on the course of the disorders after five years. The advent of improved medicines or psychological strategies may improve the outcomes, while new problems, such as a further reduction in the capacity of services to maintain fidelity to treatment protocols, may emerge to limit the benefits of treatment strategies that have proven effective in the short term.

Appendix

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Mental disorders among the Borana semi-nomadic community in Southern Ethiopia

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This study aimed to estimate the lifetime prevalence and socio-demographic correlates of psychiatric disorders among the Borana semi-nomadic community of the Oromia region of Ethiopia. 1854 people of both sexes, aged 15 years and above, were interviewed during the survey. The households were selected by using a cluster sampling method proportionate to population size. The interviews were conducted by trained high school graduates using the Oromiffa version of the Composite International Diagnostic Interview (CIDI). The lifetime prevalence of ICD-10 mental disorders, including substance abuse, was 21.6%. Affective disorders were found in 1.7% of the study population, whereas neurotic and somatoform disorders constituted 14%. No cases of schizophrenia were detected. The prevalence of substance use was 10.1%. Studies using other methods, including interview by clinicians, might shed more light on the nature of mental illness in this unique community.

Key words: Borana, semi-nomadic community, mental disorders, prevalence

Mental illness is now being recognized as a major public health problem throughout the world. Prevalence studies highlight the gravity of the problem and thereby challenge policy makers to take appropriate action.

There are few prevalence studies done on isolated population groups. One is the Amish study, which reported a preponderance of affective disorders among cases of mental illness (1). Other similar studies were done on Formosan aborigines in Taiwan (2) and among the Hutterites, a unique religious group in North America (3,4). Both studies reported a low prevalence of schizophrenia and bipolar disorder. There are no published studies of mental disorders in a nomadic community in Africa.

The objective of this study was to estimate the prevalence of psychiatric disorders and their socio-demographic correlates among the Borana semi-nomadic community, in the Oromia region of southern Ethiopia.

The Borana Oromo is a distinct group among the Oromo peoples of Ethiopia. The Borana, which are believed to be the ancestors of all of the Oromo ethnic groups, are among the few nomadic groups existing today. They live in seven districts of the zone extending over a Savannah grassland area of more than 500 km diameter in the southern part of the country bordering Kenya. The Borana move from place to place in search of grazing land and water for their cattle, especially during the severe periodic drought seasons, which occur as frequently as every 2 to 3 years. They mostly live on milk and meat.

It is important to study unique and isolated communities like the semi-nomadic community in Borana to see whether the pattern of mental illness there has any peculiarity, and what aspects, if any, can be attributed to the unique environment and living conditions.

METHODS

The study, which is a cross-sectional survey, was conducted in three areas of the Borana zone (Didara, Didi Yabello, and Megado) between mid-June and mid-August 2000 and in August 2001.

The study population was selected from the three areas by a cluster sampling method proportionate to size. Information regarding the population in the area was obtained from the respective local registries. The list of the villages and their populations was used as a sampling frame. Cumulative population and sampling intervals (cumulative total population/number of clusters) were calculated. After a random identification of an initial village, 30 villages were systematically selected. A systematic sample of households from each village was taken after identifying an initial starting household by a random number method. All members of the selected household aged 15 and above were included in the study. The same procedure was repeated for all three areas in which the survey was conducted.

The Borana dialect Oromiffa version of the Composite International Diagnostic Interview (CIDI, 5) was used in the survey. The section on eating disorders was left out of the interview, because the condition was not regarded as a problem in the region. Questions were read to the study subjects. If a question was not clear, the interviewers were instructed to read the question again but not to attempt to modify it or give any clarification. Each answer was coded and the interviewers circled the appropriate code (a number) corresponding to the response of the subject. The questionnaire was pre-tested in a similar community outside the sampled population before the survey was launched.

Twenty-three high school graduates were recruited as interviewers from the towns near the study sites. The recruits were given two weeks of training in CIDI interview techniques and instructions on completing the questionnaire.

Officials in various levels of administration in the area

were contacted before the launching of the study to inform them of the purpose of the study. Guides were provided to the survey team by the officials to direct the interviewers to the various villages. A field supervisor, who was employed by the study project from the area, gathered village elders before every visit to a village, to introduce the interviewers to them and to inform them of the purpose of the study.

Approaching a house that was selected for the study, the interviewers first introduced themselves and then identified household members aged 15 and above. They then asked each interviewee for his/her consent to participate in the study. All interviews were conducted in private. Male interviewers interviewed male respondents, and female interviewers interviewed female respondents because of cultural sensitivities. If the individuals in the selected households were not available for the interview, a maximum of three visits to that particular household were made by the data collectors. All the questionnaires were edited for proper completion on a daily basis by a research assistant and by the field supervisor. Interviewers were sent back to households to have incomplete questionnaires completed.

The CIDI Data Entry Program version 3.0 was used for data entry. The ICD-10 diagnoses were generated by the CIDI computer algorithms, which were then used for analysis. The EPI-INFO version 6 was used for descriptive analysis. The Statistical Package for the Social Sciences (SPSS) version 10.0 was used for bivariate and multivariate analysis.

The study was approved by the ethical review committees of the Amanuel Psychiatric Hospital and the Ethiopian Science and Technology Commission.

RESULTS

The total study population consisted of 1,854 subjects. 1,067 (57.6%) were females. Fifty-seven percent were under the age of 40, 66.8% were married, 87.7% were working at the time of the survey, and 92.2% had no prior formal education.

The lifetime prevalence of all psychiatric disorders, including substance abuse, was 21.6%. That of mental disorders excluding substance abuse was 14.6%. Subjects with only one diagnosis were 10.8%, while the rest of the cases had two or more diagnoses. Neurotic and somatoform disorders were the most frequent disorders, with a lifetime prevalence of 14%. The prevalence of affective disorders was 1.7%. Alcohol dependence was found in 1.6% of the study population and tobacco dependence in 3.6%. No cases of schizophrenia were detected in this study (Table 1).

The prevalence of neurotic and somatoform disorders was strongly associated with female sex. The odds of the disorder among females was almost twice that in males (odds ratio, OR = 1.84; 95% confidence interval, CI = 1.31-2.60, p = 0.02). There was also a higher prevalence of these disorders among the age groups 40-59 and 60 years and above as compared to the age group of 15-24 (OR = 1.77, 95% CI = 1.12-2.80, and OR = 1.82, 95% CI = 1.11-3.00, respectively; p = 0.02 in both cases). Marital status, current working status, and the status of formal education were not significantly associated with neurotic and somatoform disorders.

The odds of females having affective disorders was more than twice that of males (OR = 2.67, 95% CI = 1.0-7.34, p = 0.05). The prevalence of these disorders increased with increasing age in such a way that the odds among those who were 60 years old and above was 10 times that of the age group of 15-24 (OR = 9.96, 95% CI = 1.67 - 59.5, p = 0.01). Marital status, current working status, and formal education were not significantly associated with affective disorders.

Tobacco use was found to be more frequent in both sexes among psychiatric cases as compared to non-cases (21.4 % vs. 6.5 %, $p < 0.0001$). Alcohol dependence was higher among males in cases compared to non-cases (4.7 % vs. 3.6%) but the difference was not significant. There was a strong association between tobacco use and phobia in males (p = 0.006) and between tobacco use and affective disorders in females ($p < 0.0001$). There was only one female detected with alcohol dependence in this study.

DISCUSSION

The lifetime prevalence of mental disorders, excluding substance abuse, found in our study is similar to that reported in two studies from Addis Ababa (respectively, 13.1% and 14.3%) (6,7). It is, however, lower than the 26.7% lifetime psychiatric morbidity rate reported by Awas et al from Butajira in southern Ethiopia (8). Other studies from elsewhere in Africa (9,10) and the rest of the world (11-13) also reported a higher lifetime prevalence of mental disorders. In our study, women had a higher prevalence of mental disorders when substance use was excluded. However, there was no difference between the sexes in the overall prevalence of mental disorders when substance use was included.

The lifetime prevalence of affective disorders in this study, which was 1.7%, is lower than that reported from elsewhere in Ethiopia. A study in Addis Ababa (14) detected a lifetime prevalence of 5%, and another one in Butajira (a rural setting in Ethiopia) (8) reported a lifetime prevalence of 6.2%. The prevalence found in our study is also lower than that reported from other countries such as the Netherlands (12) and Canada (15). The low prevalence in our study may accurately reflect the situation in this nomadic community. However, queries have also been raised about some CIDI questions that connect the diagnosis of a major depressive disorder with visiting a health professional. As individuals in this community rarely visit health professionals for any sort of illness, their

Table 1 Lifetime prevalence of mental disorders among the Borana, southern Ethiopia

Diagnosis	Number (%)		
	Total	Male	Female
Number of diagnoses			
None	1,578 (85.1)	702 (89.2)	876 (82.1)
One	200 (10.8)	75 (9.5)	125 (11.7)
Two or more	40 (2.2)	4 (0.5)	36 (3.4)
Three or more	36 (1.9)	6 (0.8)	30 (2.8)
Any diagnosis (excluding substance use)	276 (14.9)	85 (10.8)	191 (17.9)
Any diagnosis (including substance use)	401 (21.6)	170 (21.6)	401 (21.6)
Substance use (F10-F19)	188 (10.1)	108 (13.7)	80 (7.5)
Alcohol use (F10.1-F10.2)	30 (1.6)	29 (3.7)	1 (0.1)
Alcohol dependence (F10.2)	30 (1.6)	29 (3.7)	1 (0.1)
Tobacco use (F17.1-F17.2)	161 (8.7)	82 (10.4)	79 (7.4)
Tobacco dependence (F17.2)	67 (3.6)	30 (3.8)	37 (3.5)
Stimulant use (F15.1)	5 (0.3)	5 (0.6)	-
Stimulant dependence (F15.2)	4 (0.2)	4 (0.5)	-
Psychoses (F20-F29)	-	-	-
Schizophrenia (F20)	-	-	-
Delusional disorders (F22)	-	-	-
Psychosis not otherwise specified (F23)	-	-	-
Schizoaffective disorders (F25)	-	-	-
Affective disorders (F30-F34)	32 (1.7)	7 (0.9)	25 (2.3)
Bipolar disorder (F30-F31)	2 (0.1)	1 (0.1)	1 (0.1)
Major depression (F32-F33)	9 (0.5)	1 (0.1)	8 (0.7)
Dysthymia (F34)	22 (1.2)	6 (0.8)	16 (1.5)
Neurotic and somatoform disorders (F40-F45)	260 (14.0)	80 (89.8)	887 (83.1)
Phobias (F40)	40 (2.2)	8 (1.0)	32 (3.0)
Generalized anxiety disorder/Panic disorder (F41)	13 (0.7)	3 (0.4)	10 (0.9)
Obsessive-compulsive disorder (F42)	6 (0.3)	1 (0.1)	5 (0.5)
Post-traumatic stress disorder (F43)	-	-	-
Dissociative disorders (F44)	49 (2.6)	9 (1.1)	40 (3.7)
Somatisation disorder (F45)	180 (9.8)	63 (8.1)	117 (11.1)
Persistent pain disorder (F45.4)	180 (9.7)	63 (8.1)	117 (11.1)

responses to such questions might have lowered the prevalence of affective disorders. Further studies are needed to confirm this.

The strong association of female sex with affective disorders is consistent with other studies from Ethiopia (8) and elsewhere (12,13,15). Our finding of an increase in the prevalence of affective disorders with increasing age is also consistent with reports from other studies in Ethiopia (8,14). The prevalence of affective disorders was higher in the middle aged and the elderly when compared to younger age groups in our study, in contrast to reports from the developed world, where younger age groups are often reported as more susceptible to these disorders (12,15). This may reflect the difficult environment in which elders live in this nomadic population, in contrast to the better care given to the elderly in developed nations.

Marital status was not found to be associated with affective disorders in our study. This is in line with a study done in Addis Ababa (14) but contrasts with other studies that have reported a higher prevalence of mood disorders among divorced, separated and widowed persons (15,16). This could be a reflection of the smaller number of the separated, divorced, or widowed in our study population, thereby affecting statistical significance. Cultural factors, which often discourage divorce or separation, might also have played a role, in that couples stay together in spite of the fact that one of them becomes mentally ill. There was also no significant association between current working status and affective disorders in our study. This differs from studies done in Ethiopia (14) and elsewhere (17) and could be because the demarcation between unemployed and employed is not sharply drawn in this semi-nomadic community. The smaller number of those who identified themselves as not working might have also affected statistical significance in the analysis.

We have reported an overall prevalence of 14% for neurotic and somatoform disorders. This is lower than the 22% reported from rural Ethiopia (8) and the 25.1% reported from Baltimore in the Epidemiologic Catchment Area (ECA) study (11). The disorders were strongly associated with female sex and increasing age. The association with female sex is in line with studies from elsewhere in Ethiopia (8,18) and the developed world (15).

The association of neurotic and somatoform disorders with age in our study agrees with earlier findings in rural

Ethiopia (8), but is not consistent with reports from an urban setting in Ethiopia (18) or the developed world (12,19). This may be due to the less optimal care the elderly receive in terms of their physical care in the underprivileged communities of rural Ethiopia.

The prevalence of substance use was 10.1% among our study population. The substances considered were alcohol, tobacco, and a local stimulant, khat. The prevalence of 5.5% of substance dependence in general in our study is in agreement with a study in rural Ethiopia, which reported a 5.1% prevalence (8), although much higher findings have been reported from Europe and North America (11,12,15). We reported a prevalence of alcohol dependence of 1.6%. This is in broad agreement with studies from elsewhere in Ethiopia, that used the CIDI and reported prevalences of 1.1% and 1.0% (8,20). However, these figures are much lower than those reported from the developed world (11,12,15). This may be explained by the stronger social and family relationships that exist in less developed societies such as the Borana study population, which may not permit excesses in alcohol use. The male predominance in alcohol dependence is to be expected, as it is in conformity with almost all available reports. Tobacco use and alcohol dependence generally declined after reaching a peak in the 35-44 age group. One notable exception, however, is female tobacco use, which continues to increase after the mid 50s.

We did not detect a single case of schizophrenia among the study population. This is in sharp contrast to two studies from other areas in Ethiopia, that reported a prevalence of schizophrenia of 4.7 to 9 per thousand (6,21). However, a survey among an isolated island community in Ethiopia identified 31 cases of bipolar disorder and only a single case of schizophrenia in the adult population (n = 1691) (22). A low prevalence of schizophrenia has also been reported from some population groups elsewhere in the world. For example, among a collective population of Formosan aborigines, Rin and Lin found the prevalence of schizophrenia to be significantly lower than among the immigrant Chinese population (0.9 per 1000 and 2.1 per 1000, respectively). Among one of the four tribes of the Formosan aborigines they studied, the Saisiat (n = 1302), they found no case of schizophrenia (2). Re-diagnosing Eaton and Weil's study of the Hutterites by using DSM-III criteria, Torrey (3) confirmed the low prevalence of schizophrenia and bipolar disorder among this unique religious group in North America. Re-diagnosing the same study using DSM-IV criteria, Nimgaonkar et al (4) later reported a similarly lower prevalence of schizophrenia and bipolar disorder. Lower prevalences of schizophrenia have also been reported among the Amish in the United States (23) and in New Zealand (24) and Hong Kong (25). Some studies in Africa have also reported a lower prevalence of schizophrenia. For example, Sikanartey and Eaton (26) reported an overall prevalence of 1.09 per 1000 among a population of 15 years old and above in Ghana. A point prevalence study in Nigeria (27) also reported a lower prevalence of psychosis (0.36 per 1000).

The CIDI was shown to be less effective in detecting cases of schizophrenia and psychosis in general when compared to other methods (28), and Jablensky (29) has described the validity of the CIDI in identifying cases of psychosis as problematic and its capacity for valid detection of psychotic disorders in community respondents as limited. Another possible explanation is probably a high case fatality rate for schizophrenia in the area, as a mobile population living in harsh environmental conditions may not be a good milieu for sufferers of chronic conditions. More studies in similar communities are, however, needed to confirm our finding.

In conclusion, the prevalence of mental disorders in this nomadic community looks somewhat different from other communities in Ethiopia and elsewhere around the world. The CIDI's validity in detecting cases of psychosis notwithstanding, our findings suggest a possible lower prevalence of psychosis and/or schizophrenia in the study population. That is consistent with Torrey's assertion (23) that "the impression remains, however, that there are some areas in the world where schizophrenia is uncommon. These areas are tropical… and there is the suggestion of a possible north-south gradient in the disease's distribution…".

We recommend the use of other methods, including interviews by clinicians and the use of key informants, to find more about the prevalence and nature of mental illness in this unique community. The use of the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) following administration of the CIDI might shed more light in finding out whether the lower prevalence of major mental disorders found in this community reflects the true situation in the community. More studies are also needed in similar communities within Ethiopia to confirm our findings.

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The Global Mental Health Assessment Tool - Primary Care Version (GMHAT/PC). Development, reliability and validity

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The Global Mental Health Assessment Tool – Primary Care Version (GMHAT/PC) is a computerised clinical assessment tool developed to assess and identify a wide range of mental health problems in primary care. It generates a computer diagnosis, a symptom rating, a self-harm risk assessment, and a referral letter. Patients from primary care and community psychiatric outpatient clinics and a small sample of inpatients were interviewed for a period of two months using the GMHAT/PC. A proportion of patients were simultaneously rated by a psychiatrist and a general practitioner for inter-rater reliability. All patients also completed the Hospital Anxiety and Depression Scale (HAD). To conduct the interview was easy in all settings and took 10-15 minutes for patients who had psychiatric symptoms. Inter-rater agreement on mental state symptom groups ranged from 0.49 to 1 (kappa). The computer diagnosis correlated highly with the clinical diagnosis and there was a good level of agreement between HAD ratings and GMHAT/PC ratings. These data suggest that the GMHAT/PC is an easy to administer computerised tool which can be used in primary care for the standardised assessment of mental health problems.

Key words: Psychiatric interview, mental health assessment, mental health in primary care, interview schedule, standardized assessment

There is a growing recognition both in developed and developing countries that comprehensive mental health services cannot be provided without the active involvement of primary care health teams (1). The role of primary care health professionals is crucial in: a) early detection of mental disorders, including psychotic illness; b) management of common mental disorders such as depression; c) getting advice on diagnosis and management of patients with mental illness from specialists; and d) providing care (specially for physical health) to people with severe and enduring mental illness in close liaison with specialist mental health professionals/teams. A proper assessment and identification of mental health problems at primary care level is, therefore, essential in providing appropriate care to people suffering from mental disorders in any community.

In the UK, National Health Service (NHS) general practitioners are expected to identify and assess the mental health needs of their patients, as well as manage common mental disorders within primary care. Standard 2 of the National Service Framework for Mental Health (2) specifies that "any service user who contacts their primary health care team with a common mental health problem should have their mental health needs identified and assessed." In its vision for mental health care (3,4), the government proposes that by 2004 five hundred new "gateway workers" will work with general practitioners and primary care teams. Any such additional resource is a welcome move, but only an efficient use of existing and new resources will make any demonstrable impact on mental health services in primary care (5).

The World Health Report 2001 (6) states that the advantages of integrating mental health services with the primary care include easy access, reduced stigmatisation, and early detection and treatment of mental disorders. This integration also has an advantage of efficient management of resources through shared administrative infrastructure with a potential to provide universal coverage of mental health care.

Primary care physicians throughout the world have limited time and, in many instances, limited training and experience of assessing mental health needs (1,7). Other health workers such as mental health nurses or primary care nurses with training in mental health could therefore be of great value in providing mental health assessment in primary care.

The self-assessment scales and interview schedules currently available have limited value in day-to-day clinical practice. Most were developed for research purposes; many require extensive training prior to use. They predominantly cover only a limited range of clinical problems such as anxiety and depression.

There are a few clinical tools that have been developed more specifically for primary care physicians, such as the Primary Care Evaluation of Mental Disorders (8) and the Symptom Driven Diagnostic System for Primary Care (SDDS/PC) (9). Both are aimed at detecting only common mental disorders. A self-administered scale based on hand-held computers, the Quick Psycho Diagnostic Panel (QDP) (10), also covers a similarly narrow range of disorders. None of these tools helps in detecting psychotic or organic disorders. A structured assessment of long-term

mentally ill patients by their general practitioners increased their involvement in patients' psychiatric care, but was not found to be feasible for use in routine surgery appointments (11).

The Global Mental Health Assessment Tool - Primary Care Version (GMHAT/PC) has the following characteristics: a) it is easy to use in day-to-day clinical practice by general practitioners or other health care staff; b) it is able to detect common psychiatric disorders, yet not neglecting more serious conditions; c) it produces automatically a referral letter to local community psychiatric services.

The aim of the present study was to assess the feasibility of GMHAT use in primary care, to assess the inter-rater reliability between a psychiatrist and a general practitioner, to compare computerised diagnosis against clinical diagnosis, and to compare symptom ratings using GMHAT/PC against an existing standardised rating scale.

METHODS

Description of the GMHAT/PC

The GMHAT/PC is a computerised clinical assessment tool developed to assess and identify mental health problems in primary care. The first screen is for patient information and administration of the program. The assessment program starts with basic instructions giving details of how to use the tool and rate the symptoms. The introductory screens facilitate inputting of descriptive information in the following fields: presenting symptoms, and relevant past, family, and personal problems. If preferred, these details can be dictated and later typed by the practice secretary following the assessment. The following screens consist of a series of questions leading to a comprehensive yet quick mental state assessment focusing sequentially on the following symptoms or problems: worries; anxiety and panic attacks; concentration; depressed mood, including suicidal risk; sleep; appetite; eating disorders; hypochondriasis; obsessions and compulsions; phobia; mania/hypomania; thought disorder; psychotic symptoms (delusions and hallucinations); disorientation; memory impairment; alcohol misuse; drug misuse; personality problems; stressors. One question at a time appears from these respective subsections. The questions proceed in clinical order along a tree-branch structure. For each of the major clinical disorders there are one or two screening questions. If the patient does not have symptoms based on the first one or two items of a subsection, the interview moves on to the next subsection, thus saving much valuable time. Most of the questions are based on the well established interview schedule GMS-AGECAT (12).

At the end of the interview the tool suggests a diagnosis and two final screens appear: one for insertion of the names of currently prescribed psychotropic medication(s), the other for the rater's clinical diagnosis. The screen then proceeds to a menu showing the following items: a) rating scores and computer diagnosis; b) referral letter; c) care pathways. The main symptom groups on which the rating scores are based are anxiety, depression, concentration, eating disorder, hypochondriasis, phobias, obsessions, mania, psychosis, memory impairment, and disorientation. In addition, there are sections for alcohol and other drug misuse, stressful events and personality difficulties. The main computer diagnosis is derived using a hierarchical model and designed around ICD-10. The diagnostic program takes account of severity of symptoms (moderate to severe). It also generates alternative diagnoses based on presence of symptoms of other disorders.

The referral letter option prints out a letter of assessment with details of problems, symptoms with severity, and clinical diagnosis. In addition, it includes an assessment of risk of self-harm. The pathway of care option gives guidelines for care provision (developed for the Cheshire and Wirral Partnership NHS Trust) (13).

The program is based on the Delphi (Borland) System and does not need any other software programming support.

Study procedures

We interviewed patients from primary care and community psychiatric outpatient clinics, although a small number of inpatients were added to reflect both the range and severity of mental disorders seen in routine practice. All patients were asked to complete the Hospital Anxiety and Depression Scale (HAD) (14) prior to the clinical computerised assessment. All patients gave informed consent for participation in the study.

The patients in the primary care sample came from the list of a local general practitioner (AC). They were interviewed by the general practitioner in the primary care set-

Table 1 Inter-rater reliability based on symptom scores between a psychiatrist and a general practitioner using the GMHAT/PC (N=56)

Symptoms	Kappa coefficient
Alcohol misuse	1.00
Anxiety	0.79
Concentration	0.59
Depression	0.82
Disorientation	0.49
Drug misuse	1.00
Eating disorder	0.66
Hypochondriasis	Not computed
Mania	Not computed
Memory	Not computed
Obsessive-compulsive disorder	0.56
Phobia	0.83
Psychosis	0.78

Table 2 Agreement between clinical diagnosis and GMHAT/PC diagnosis

Clinical diagnosis	Computer Diagnosis								
	No mental disorder	Depression	Schizophrenia	Anxiety	Obsessive-compulsive	Organic	Alcohol	Other	Total
No mental disorder	19			2					21
Depression	2	32		6			1	3	44
Schizophrenia	1		25	2					28
Anxiety				18					18
Obsessive-compulsive					2				2
Organic									
Alcohol							2		2
Other								4	4
Total	22	32	25	28	2		3	7	119

ting (in his surgery) using the GMHAT/PC. Another investigator (PL) rated at the same time observing the interview live.

The second sample consisted of consecutive outpatients attending the Mental Health Resource Centre of the Victoria Central Hospital. They were interviewed by two psychiatrists (PL and VKS) using the GMHAT/PC. A subsample was also rated simultaneously for inter-rater reliability by a general practitioner registrar who had no prior psychiatric training. In addition, consecutive admissions to the inpatient unit at the Department of Community Psychiatry of the same hospital were similarly assessed over a period of two months.

Inter-rater reliability was assessed by the Cohen's kappa coefficient. Correlations between HAD and GMHAT/PC scores were tested by the Pearson's coefficient.

RESULTS

We interviewed a total of 119 patients: 29 (24.4%) in primary care, 80 (67.2%) in psychiatric outpatient clinics and 10 (8.4%) in an inpatient unit. The age range was 19-64 years, and the mean age was 38. Sixty-one patients (51.3%) were women and 58 (48.7%) men.

The computer-assisted interview was easy to conduct in all settings, especially in primary care. The duration of the interview ranged from 7 to 25 minutes, with a mean duration of 13 minutes. The interview was well accepted by all patients. Many patients were very pleased that the doctor asked about every aspect of their mental health. The general practitioner investigator carried on using the GMHAT/PC in his routine practice, and reported that he identified patients with some mental disorders by using the instrument, that he would have otherwise missed.

The inter-rater reliability assessment was made on 56 patients (29 in primary care and 27 in outpatient clinics). They were concurrently rated by a psychiatrist (consultant or specialist registrar) and a general practitioner (principal or general practitioner registrar). The general practitioner and the psychiatrist interviewed the patients alternately. The patients' clinical diagnosis was depression in 28 cases, anxiety disorder in 11, psychotic disorder in 7, mania in one, eating disorder in one, and obsessive-compulsive disorder in one. Seven cases had no significant mental disorder. The inter-rater reliability based on symptom scores ranged from 0.49 to 1 (kappa). The numbers of cases with symptoms of hypochondriasis, mania and memory impairment were too few to be computed for inter-rater reliability (Table 1).

Table 2 gives cross-tabulation of clinical diagnosis (ICD-10) and GMHAT/PC diagnosis. The agreement was high, except in cases of depression, where about 27% of the cases with a clinical diagnosis of depression had computer diagnoses of other disorders, mainly anxiety disorders. Two out of 44 cases were not considered as mentally ill by the computer, as they had insufficient symptoms at the time of the interview. One hundred and two cases (86%) had the same clinical and computer diagnosis.

The correlation between HAD and GMHAT anxiety scores was 0.74. The correlation between HAD and GMHAT depression scores was 0.62 (Pearson's coefficient).

DISCUSSION

General practitioners are the first line of contact for most patients with mental health problems, yet they fail to recognise a sizable number of sufferers of mental disorders (15,16). In the UK the National Service Framework for mental health expects that general practitioners and other members of the primary healthcare team will provide acceptable, relevant and informed services to their patients, including proper and early mental health assessment and management of their patients. However, an independent policy review reported gaps in implementing the National Service Framework, particularly with refer-

ence to primary care (7). We believe that the GMHAT/PC will assist this process of implementation. Our study has demonstrated the feasibility of using this method in primary care. Patients on the whole received the GMHAT/PC assessment well and said they found it helpful as it covered more aspects of their mental health than the usual consultation. Coverage of a wide range of mental disorders including psychoses and organic disorders is necessary for their early and accurate detection. The value of early detection and intervention, particularly in psychotic disorders, is well documented (17).

The format of GMHAT/PC is simple to administer as questions appearing on the screen cover only one aspect of the mental state at a time. The interviewer is expected to have some background experience of assessing mental health problems but does not require specific training to use the schedule. A satisfactory level of agreement between psychiatrist and general practitioner ratings in this study indicates that general practitioners can make reliable mental health assessments using this method, although it will require testing on a larger sample. This may become even more useful to the gateway workers in primary care as they may have somewhat more time with patients than general practitioners in their busy surgeries. Cooper (18), in a very recent editorial, highlighted the importance of processes of patient–general practitioner consultation. By contrast, a randomised study (19) of the impact of ICD-10 Primary Health Care (PHC) diagnosis and management guidelines on detection and outcome of mental health problems in primary care patients found that attempts to influence clinician behaviour through a process of adaptation and extension of guidelines were unlikely to change detection rates or outcomes. One study reported that general practitioners could routinely diagnose mental disorders if patients have severe symptoms (for example depression) (20). In another study, general practitioners' ability to detect depression bore no relationship to their observed clinical behaviour (21). A multifaceted approach is needed to improve the quality of consultation interview by using diagnostic aids (15) and interview techniques (22) to detect mental disorders. Incorporation of GMHAT/PC into the existing general practitioner desktop would further facilitate this process, not only by the general practitioners but also by practice nurses and other staff.

The computer-assisted diagnosis, which is based on symptom complexes present at the time of interview, is a useful aid in routine practice but is not intended to replace the clinical diagnosis, although the high level of agreement between the psychiatrist's clinical diagnosis and the computer-assisted diagnosis of the patients in the study is encouraging. The only serious disagreement was in cases with a clinical diagnosis of depression, as many of them were diagnosed as cases of anxiety and other disorders on the GMHAT/PC. Two of them were considered as not suffering from any mental disorder. This discrepancy was largely due to the absence of significant depressive symptoms at the time of the interview, whereas the clinical diagnosis did take historical data into account. As most cases in primary care seek help when they are symptomatic, the GMHAT/PC computer-assisted diagnosis is more likely to be accurate. The standardised method of assessment will give some consistency in diagnosis, which will be very useful for regional and national comparisons.

The other outputs from the GMHAT/PC, such as ratings of symptoms and automated referral letter, are designed for maintaining electronic patient information as well as in communicating with the specialist teams.

The correlation between HAD anxiety scores and GMHAT anxiety scores was good. The correlation for depression scores was not as high. We discovered that the discrepancy between HAD depression scores and GMHAT depression scores was largely in patients suffering from schizophrenia. It is possible that the negative symptoms of schizophrenia may have influenced the self-ratings for depression on the HAD scale.

Regular use of GMHAT/PC in primary care will certainly enhance general practitioners' and primary care workers' skills in assessing mental health problems of their patients. The GMHAT/PC ratings could also be helpful in determining outcome of their patients. Routine outcome measures are rarely used in ordinary clinical practice (23).

There is an interest in using the GMHAT/PC in other countries. It has already been translated into German. Our next step is to evaluate its use by primary care physicians in their routine practice as well as its use by the nurses in the primary care setting.

The GMHAT full version has also been developed for a more comprehensive clinical assessment in routine practice in secondary care settings.

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Mental health epidemiological research in South America: recent findings

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This paper aims to review the recent mental health epidemiological research conducted in South America. The Latin American and the Caribbean (LILACS) database was searched from 1999 to 2003 using a specific strategy for identification of cohort, case-control and cross-sectional population-based studies in South America. The authors screened references and identified relevant studies. Further studies were obtained contacting local experts in epidemiology. 140 references were identified, and 12 studies were selected. Most selected studies explored the prevalence and risk factors for common mental disorders, and several of them used sophisticated methods of sample selection and analysis. There is a need for improving the quality of psychiatric journals in Latin America, and for increasing the distribution and access to research data. Regionally relevant problems such as violence and substance abuse should be considered in designing future investigations in this area.

Key words: Epidemiology, mental health, South America, cross-sectional studies, case-control studies

Epidemiological research in mental health has been systematically conducted in South America in the last few decades, alongside the global increase of population-based studies after the advent of the DSM-III. Data derived from these studies provide a broader picture of the distribution and risk factors of mental disorders in the South American region. Such information is relevant, since regional factors, such as ethnic, sociocultural and political variables, may influence both the prevalence and related risk/prognosis factors. In addition, locally collected information can be a more acceptable and valid basis for the decision-making process involving the recognition and treatment of mental disorders in the region. This paper aims to provide a summary of the main epidemiological studies conducted in South America in the past five years, giving priority to those investigations in which more rigorous methodologies were adopted.

METHODS

An electronic search of Latin America and the Caribbean (LILACS) database was performed. This database indexes regional literature from more than 640 journals, and contains around 300,000 citations of literature published since 1982, and abstracts in English, Portuguese, and Spanish.

We selected only population based papers which met the following criteria: a) random methods in the selection of the sample, aiming to maximise representativeness; b) sample size calculation, with pre-defined levels of statistical significance and power; c) clear criteria of inclusion/exclusion; d) explicit methods of analysis; e) adequate report of attrition rates.

RESULTS

Our search strategy generated 140 references for the period of 1999 to 2003, and 12 papers were selected (Table 1). Most of them were prevalence studies. The prevalence of minor psychiatric disorders in South America studies was found to be 20-25%, with the exception of a Chilean study which found a prevalence of 36%. The prevalence of alcohol abuse/dependence ranged from 4 to 12%. The main risk factors found in these surveys were low level of education (completed years in school), low income, old age, and female gender. We found no cohort study published in LILACS indexed journals.

Cross-sectional studies

There are many similarities in terms of design, sampling procedures, and results across studies. Three surveys (two in Brazil and one in Chile) were country multicentre studies, which aimed to provide information on mental disorders for the whole population. Their results suggest that depression, anxiety, and substance use disorders are the most prevalent disorders in the region. There are concerns about the use of psychotropic drugs among adolescents and adults, and the Chilean survey also highlighted the burden of violence against children.

One study conducted in the northeast of Brazil investigated the psychological impact of many hours of daily work, a common situation in developing countries, in 460 women aged 18 to 70 years. Having a paid job in addition to the house work and working more than 10 hours per day were risk factors for minor psychological disorders for these women. Another study focusing on women's mental health reported that 27% of an adult sample from Santiago, Chile, had a depressive disorder, and the main related factors were being a wife in charge of house work, including taking care of children and cooking and cleaning, low education level, and marital separation.

Table 1 Main recent mental health epidemiological studies in South America

Study	Country/ Year	Population	Main results
Almeida-Filho et al (1)	Brazil/ 1997	Representative sample of the adult population living in three Brazilian urban centers, N=6476	Age-adjusted prevalence of cases potentially in need of care ranged from 19% to 34%. Most prevalent disorders: anxiety (up to 18%); alcoholism (around 8%); depression (up to 10%)
Lima et al (2,3)	Brazil/ 1996	Representative sample of the adult urban population of Pelotas, N=1277	Prevalence of minor psychiatric disorders: 22.3%, higher in the lower social class, elderly, women; use of psychotropics in the previous two weeks: 11.9%; prevalence of alcohol dependence: 4.2%
Costa et al (4)	Brazil/ 2002	Representative urban sample of Pelotas, N=1967	The prevalence of minor psychiatric disorders was higher in people with lower social status and lower income, aged 40 or older, and for females
Parada et al (5)	Chile/ 2002	Representative sample of individuals from four Chilean provinces, N=2978	36% lifetime prevalence of psychiatric disorders (11% agoraphobia, 9% major depression, 8% dysthymia, 6% alcohol dependence). 49% of those with a psychiatric disorder sought medical care
Santana et al (6)	Brazil/ 2001	Random sample of females aged 18 to 70 years in Salvador, Northeast of Brazil, N=460	Being positive on the Adult Psychiatric Morbidity Questionnaire (>7 symptoms) was associated with having a paid job in addition to house work and working more than 10 hours per day
Rojas et al (7)	Chile/ 1999	Representative sample of adult women of Santiago aged 15 to 65 years, N=1188	27% had depression (1.9% severe, 12.5% moderate). Associated factors: low education level, marital separation and house keeping
Kohn et al (8)	Uruguay/ 2001	Two randomly chosen population-based samples of children aged 5 to 15 years (urban and rural), N=115	53% of children had some behavioural or emotional problem. Psychological disorder of the mother was related to a higher risk of problems for the child
Vizcarra et al (9)	Chile/ 2001	Population-based survey; women interviewed in Temuco (Chile), N=422	Psychological aggression by mothers or fathers: 17.5% and 6.8%, respectively. Associated factors: mother impaired mental health, child abuse in parents, parents' alcohol abuse and child emotional problems
Anicama et al (10)	Peru/ 1999	Random sample of Lima metropolitan area population, N=3590	35.4% suffered psychological violence from their partners, 17.4% physical violence. 36.2% of parents psychologically abused their children. 18.6% of mothers had depression during pregnancy
Carlini et al (11)	Brazil/ 2002	Population-based survey (age range 12-65), including the 107 Brazilian cities, N=8589	Alcoholism: 11.2%, higher in men between 18 and 29 years, lower in older subjects. 19.4% used illicit drugs: 9% marijuana, 5.8% inhalants, and 2.3% cocaine/crack
Gonzáles et al (12)	Chile/ 2001	Representative sample of the population of Santiago, aged 15 to 64 years	Lifetime prevalence of use of marijuana: 19%; cocaine 4.5%; crack 2.2%. Last month prevalence: 3.2%, 0.7%, and 0.3%, respectively
Lopes et al (13)	Brazil/ 1999	Case control study: untreated cocaine users and matched controls, N=208	Alcohol dependence increased risk of cocaine abuse/dependence

Case-control study

One case-control study published in a local Brazilian journal evaluated the role of psychiatric disorders as possible risk factors for cocaine abuse/dependence. A history of alcohol dependence was the only diagnosis associated with an increased risk of cocaine abuse/dependence (relative risk as high as 15). This result is relevant for planning programs directed towards the treatment and prevention of cocaine abuse.

DISCUSSION

Population-based surveys provide useful estimates of the prevalence of mental disorders, which are useful for planning health actions and for decision-making process. During the five years period of this review, only a few studies from the South American literature were population based; most of the studies were conducted in treatment settings, with unrepresentative samples. Such data are difficult to generalize to the population as a whole, and are not particularly useful for evaluating risk and prognostic factors or design population-based interventions. There is a lack of longitudinal (cohort) studies, which can generate data on the natural history of the disorders and on prognostic factors.

In South America there has been a significant growth in scientific publications in the last five years compared to the past five year periods from 1981 (14). However,

the quality of the scientific production has not increased significantly. Local journals should have more restrictive criteria for accepting papers for publication and a competent peer-review process.

Moreover, an attempt should be made to publish in international journals, which are more widely disseminated. It is notable that some leading South American journals, such as the Brazilian Journal of Psychiatry and Public Health Reports (a Brazilian journal), have published papers in English on a regular basis for several years and are now indexed in MEDLINE.

Results of cross-sectional studies lead to the conclusion that the general practitioner (or a non-specialized physician) is the most active professional in mental health in South America. This epidemiological evidence has as yet not been translated into major or substantial changes in graduate education. It is vital that general medical training enable physicians to identify and deal with the more frequent mental disorders found in general practice and in primary care units.

The change in demographic profiles, in particular the move from the rural setting to the urban environments in the last few decades, with a majority of the population living in cities that have populations of over half a million inhabitants, could explain in part the excess of minor psychiatric disorders (mainly anxiety states) observed in population-based studies. This migration has resulted in an aggravation of the precarious living conditions, employment insecurity, lack of leisure, and violence arising because of social inequities. It is important to carry out research and develop policies to care for mental health in the more deprived urban centers.

In conclusion, epidemiological research in South America has experienced a significant improvement in terms of the number of published papers, although the quality of research conducted has not increased satisfactorily. Future research should consider local needs, cultural/ethnic features of the populations and current relevant issues such as crime, violence, and substance misuse. Rather than increasing the number of journals, actions regarding the quality and regularity of publication and the distribution of published reports among mental health workers should have priority.

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The Jean Delay Prize, the Okasha Award for Developing Countries and the Geneva Prize for Human Rights in Psychiatry

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President, World Psychiatric Association

During the 13th World Congress of Psychiatry in Cairo, three prizes will be awarded. The Jean Delay Prize and the Okasha Award for Developing Countries will be awarded during the opening ceremony; the Geneva Prize for Human Rights in Psychiatry will be awarded during the closing ceremony.

The Jean Delay Prize

The Jean Delay Prize is the most important award of the WPA (somebody calls it the 'Nobel Prize' of the Association). It bears the name of the first WPA President, who was also the President of the first World Congress of Psychiatry (Paris, 1950). Jean Delay is one of the most important psychiatrists of the 20th century: he introduced chlorpromazine in the treatment of psychotic disorders and described for the first time the antidepressant effect of isoniazide.

The Jean Delay Prize is awarded to an individual who has made a major contribution in the field of biological, psychological or social aspects of psychiatry or tried to build bridges between them. The Prize consists of a diploma, a medal and a check for the amount of 40,000 Euros. The previous winners were Sir David Goldberg (UK) in 1999 and Hagop Akiskal (USA) in 2002.

The nomination form can be downloaded from the website of the Cairo Congress (www.wpa-cairo2005.com). This award is supported by an unrestricted grant from Servier.

The Okasha Award for Developing Countries

The Okasha Award recognizes the contribution of two young psychiatrists or neuroscientists, below the age of 40, whose research efforts have best served psychiatry and mental health in a developing country.

The following criteria will be considered by the members of the jury: a) research of high quality in psychiatry, preferably on topics related to mental health in developing countries; b) strengthening international collaboration in the field of psychiatry; c) training and education in psychiatry in developing countries; d) development of new strategies to build new and efficient institutions taking into account the social and cultural specificities as well as the financial constraints of developing countries.

The Okasha Award includes a diploma, a medal and a donation of 15,000 US$.

The nomination form can be downloaded from the website of the Cairo Congress (www.wpa-cairo2005.com). This Award is supported by an unrestricted grant from Apex Pharma, an Egyptian stock company in the field of psychotropic drugs.

The Geneva Prize for Human Rights in Psychiatry

The Geneva Prize, awarded by the Geneva Foundation for Human Rights, is intended to acknowledge an individual or an organization, or an institution with governmental or non-governmental status, for exceptional achievement at regional, national or international level in promoting equity and the humane qualities of care for people with mental illness; reducing the negative discrimination of the mentally ill; defending the rights of people with mental illness and promoting the application of ethical principles in psychiatric services.

The Prize consists of a diploma and a monetary award of 20,000 Swiss francs.

Nominations for the Prize can be made by individuals, associations or institutions. Self-nominations will not be accepted. The deadline is December 15, 2004. Please address all correspondence to: The Prize of the Geneva Foundation for Human Rights in Psychiatry c/o Professor Norman Sartorius, 14, Chemin Colladon, CH-1209 Geneva, Switzerland.

The WPA International Congress 'Treatments in Psychiatry: An Update'

MARIO MAJ
Chairman, Organizing Committee

This Congress, which will take place in Florence from 10 to 13 November 2004, is designed to provide a comprehensive and high-quality update on all evidence-based treatments currently available for the various mental disorders. Many of the most renowned experts in the various treatment areas will be among the speakers. More than 5000 participants are expected. Simultaneous translation into Spanish will be provided for special and update lectures and part of the symposia. CME credits will be provided by the WPA, the American Medical Association and the relevant European and Italian bodies. The abstracts of all accepted presentations will be published in a supplement to World Psychiatry. An extremely attractive social programme has been organized for participants and accompanying persons.

We provide here an outline of some

ingredients of the Congress which have been already finalized. Further information can be found on the website of the Congress (www.wpa2004florence.org).

Special Lectures

1. Current treatment in psychosis: did it change the outcome? (A. Okasha)
2. Comprehensive diagnosis as a basis for integrated treatment and health promotion (J. Mezzich)

Update Lectures

1. The context of treatment in psychiatry (N. Sartorius)
2. Building up therapeutic alliance in psychiatric practice (A. Tasman)
3. The comprehensive management of schizophrenia (N. Schooler)
4. Early psychosis: detection and interventions (P. McGorry)
5. The comprehensive management of recurrent and chronic major depression (G.A. Fava)
6. Comprehensive long-term management of bipolar disorder (M. Thase)
7. Understanding and managing the consequences of violence and trauma (A. McFarlane)
8. Integrating pharmacotherapy and psychotherapy in the management of anxiety disorders (J. Gorman)
9. Evidence based management of dementia (A. Burns)
10. The multimodal treatment of eating disorders (K. Halmi)
11. The principles and practice of cognitive-behavioural psychotherapy (P. Salkovskis)
12. Psychodynamic psychotherapies: evidence-based and clinical wisdom (P. Fonagy)
13. Integration of services in community mental health care (G. Thornicroft)
14. The challenge of primary prevention in psychiatry (S. Saxena)

Interactive Symposia

1. The current management of personality disorders (Facilitator: P.J. Tyrer)
2. The contribution of neuroimaging research to clinical psychiatry (Facilitator: N.C. Andreasen)
3. Partnerships in mental health care (Facilitator: B. Saraceno)
4. The present and future of consultation-liaison psychiatry (Facilitator: F. Creed)
5. The evaluation of psychiatric treatments (Facilitator: M. Tansella)
6. Recent advances in pharmacogenomics (Facilitator: M. Ackenheil)
7. Epidemiology and prevention of suicide (Facilitator: J. Bertolote)
8. The future of pharmacotherapy for schizophrenia (Facilitator: W.W. Fleischhacker)
9. Prevention and management of substance abuse (Facilitator: A.H. Ghodse)
10. The future of psychotherapies (Facilitator: S. Bloch)
11. Psychotropic drugs and cognitive functions (Facilitator: A. David)
12. The present and future of rehabilitation in psychiatry (Facilitator: M. Farkas)
13. Advances in the diagnosis and treatment of bipolar disorder (Facilitator: H. S. Akiskal)
14. The management of somatoform disorders and medically unexplained physical symptoms (Facilitator: M. Sharpe)
15. Understanding and managing 'comorbidity' in psychiatry (Facilitator: G.B. Cassano)
16. The future of pharmacotherapy for mood and anxiety disorders (Facilitator: D. Baldwin)
17. Current approaches to autism (Facilitator: F. Volkmar)
18. New strategies in the management of sexual disorders (Facilitator: S.B. Levine)
19. Management of alcohol-related problems (Facilitator: K. Mann)
20. Cultural issues in mental health care (Facilitator: L.J. Kirmayer)
21. The current management of obsessive-compulsive disorder (Facilitator: J. Zohar)
22. Family interventions for mental disorders (Facilitator: I.R.H. Falloon)
23. The current management of panic disorder and generalized anxiety disorder (Facilitator: C. Faravelli)
24. Gender-related issues in psychiatric treatments (Facilitator: D. Stewart)
25. Current approaches to sleep disorders (Facilitator: C.R. Soldatos)
26. Molecular genetics and genomics of psychiatric disorders: identification of novel drug targets (Facilitator: G. Racagni)
27. Management of mental disorders in old age (Facilitator: E. Chiu)
28. Diagnosis and treatment of attention-deficit/hyperactivity disorder (ADHD) (Facilitator: C.E. Berganza)
29. Ethical and legal aspects of treatments in psychiatry (Facilitator: D. Moussaoui)
30. Assessment and management of social anxiety disorder (Facilitator: D.J. Stein)
31. Combining medications in psychiatry: advantages and risks (Facilitator: H.-J. Möller)
32. Economic aspects of mental health care (Facilitator: M. Moscarelli)
33. 'Difficult' children and adolescents: underdiagnosis and overdiagnosis of mental disorder and relevant treatment issues (Facilitator: S. Tyano)
34. New strategies for the care of the mentally retarded (Facilitator: N. Bouras)
35. The management of non-schizophrenic psychotic disorders (Facilitator: W. Gaebel)
36. Non-pharmacological somatic therapies in psychiatry (Facilitator: M. Fink)

Advanced Courses

1. How to organize a comprehensive community mental health service (Directors: G. Thornicroft, M. Tansella)
2. The psychiatrist in court (Director: J.E. Arboleda-Florez)
3. Management of the suicidal patient (Director: D. Wasserman)
4. Management of patients with a severe mental disorder and substance abuse (Director: R.E. Drake)
5. Treatment of mental disorders during pregnancy and post-par-

tum (Director: I.F. Brockington)
6. The management of acute psychotic agitation (Director: D. Naber)
7. Implementing a cooperative or other enterprise run by psychiatric patients (Director: G.P. Harnois)
8. Ethical and legal issues concerning psychiatric treatment (Director: A. Carmi)
9. The principles and practice of interpersonal psychotherapy (Director: J.C. Markowitz)
10. Fighting stigma related to schizophrenia (Director: N. Sartorius)
11. Managing HIV-related neuropsychiatric and psychosocial problems (Director: F. Cournos)
12. Assessment of cognitive dysfunction in schizophrenia (Directors: S. Galderisi, M. Davidson)
13. Relevance of phenomenological/anthropological psychiatry to clinical practice (Directors: M.A. Schwartz, O.P. Wiggins)
14. The management of the 'difficult' child (Director: S. Tyano)

Forums

1. Training to psychotherapies: problems and perspectives (Coordinator: B. Martindale)
2. Interacting with the media about psychiatric treatment issues (Coordinator: H. Herrman)
3. The role of non-psychiatric professions in mental health care (Coordinator: J. Leff)
4. The organization of forensic psychiatric services (Coordinator: J.E. Arboleda-Florez)
5. The role of advocacy groups in supporting effective treatments in psychiatry (Coordinator: P.L. Morselli)
6. Resources for mental health care in low and middle income countries (Coordinator: S. Saxena)

Section Symposia

1. The educational challenge of improving the quality of psychiatric treatment (Section on Education in Psychiatry)
2. Conceptual and ethical issues in early diagnosis and treatment (Section on Humanities in Psychiatry and Section on Classification, Diagnostic Assessment and Nomenclature)
3. Predictors of response to therapies for eating disorders (Section on Eating Disorders)
4. Management of first episode schizophrenia (Section on Schizophrenia)
5. Current questions in the treatment of bipolar disorders (Section on Pharmacopsychiatry)
6. Hormones as treatments of affective disorders (Section on Interdisciplinary Collaboration and Section on Affective Disorders)
7. Diagnosing personality disorders: does it matter for treatment? (Section on Personality Disorders)
8. Attention-deficit/hyperactivity disorder in primary care (Section on Psychiatry, Medicine and Primary Care)
9. Treatment research on eating disorders (Section on Eating Disorders)
10. Stress, depression and cardiac events (Section on Conflict Management and Resolution and Sections on Women's Mental Health; Psychiatry, Medicine and Primary Care; and Occupational Psychiatry)
11. Intervention strategies for mental retardation: an integrative approach (Section on Mental Retardation)
12. Childhood sexual abuse: what to do now? (Section on Psychiatry and Human Sexuality)
13. Psychiatric issues in psycho-oncology: a challenge for the new millennium (Section on Psycho-oncology)
14. Spirituality, treatment and health (Section on Religion, Spirituality and Psychiatry)
15. The use of psychoanalysis in today's urban mental health settings (Section on Urban Mental Health and Section on Psychoanalysis)
16. The role of the psychiatrist in the HIV/AIDS epidemic (Section on Urban Mental Health and American Psychiatric Association)
17. Developing and implementing training in old age psychiatry (Section on Old Age Psychiatry)
18. Treatment of eating disorders in psychoanalytically informed psychiatry (Section on Psychoanalysis in Psychiatry)
19. Family functioning and family interventions in Axis I and Axis III disorders (Section on Family Research and Intervention)
20. Settings and techniques of intervention in emergency psychiatry: a comparison of different models (Section on Emergency Psychiatry)
21. The effect of disability pension policy on outcome from mental illness (Section on Public Policy and Psychiatry)
22. Psychopathology and treatment (Section on Clinical Psychopathology and Section on Psychopathology of the European Psychiatric Association)
23. Access to care impediments: African, American and European experiences (Section on Conflict Management and Resolution and Sections on Women's Mental Health; Psychiatry, Medicine and Primary Care; and Occupational Psychiatry)
24. Psychosis: meaning, mechanism and interpersonal consequences (Section on Psychoanalysis in Psychiatry and International Society for the Psychological Treatment of Schizophrenia and other Psychoses)
25. The relevance of neuropsychophysiological research to psychiatric treatment (Section on Psychophysiology)
26. Quality improvement: practice guidelines and suicide prevention (Section on Quality Assurance in Psychiatry)
27. Rehabilitation of torture victims and the problems of these victims from the psychiatrist's viewpoint (Section on Psychological Consequences of Torture and Persecution)
28. Substance abuse and the family (Section on Addiction Psychiatry)
29. Violence against women (Section on Women's Mental Health)
30. Labour, law and disability (Section on Forensic Psychiatry)
31. Ecological changes, mental distress and therapeutic perspectives (Section on Ecology, Psychiatry and

Mental Health and Section on Mass Media and Mental Health)
32. Depression associated with medical conditions in primary care and other settings (Section on Psychiatry, Medicine and Primary Care)
33. Psychiatry, law and ethics (Section on Psychiatry, Law and Ethics)
34. Well-being and quality of life in the 21st century (Section on Mass Media and Mental Health)
35. Updating suicidology (Section on Suicidology)
36. Violence: a man made disaster (Section on Psychological Consequences of Torture and Persecution)
37. Psychophysiological characterization of mental disorders: therapeutic implications (Section on Psychoneurobiology)
38. Topics of prevention: evidence and research (Section on Preventive Psychiatry)
39. Transcultural psychiatry in Europe: something is going on (Section on Transcultural Psychiatry)
40. Sexual health educational programme: an update (Section on Psychiatry and Human Sexuality)
41. Art and therapeutic communication (Section on Art and Psychiatry)
42. Psychoimmunology: evidence and perspectives (Section on Immunology and Psychiatry)
43. European psychiatry from 1800 to 2004: institutions, concepts and policies (Section on History of Psychiatry)
44. Positive and negative impact of new technologies in psychiatric sciences (Section on Informatics and Telecommunications in Psychiatry)
45. Biological correlates of disturbed sleep (Section on Psychiatry and Sleep Wakefulness Disorders)
46. Hormonal treatment of menopausal women (Section on Interdisciplinary Collaboration)
47. Common mental disorders in private practice (Section on Private Practice)

Zonal Symposia

1. Perspectives on psychotherapy from the US (United States of America Zone)
2. Shared care for mental services (Canada Zone)
3. Administration of health services and educational programs in Latin America (Northern South America Zone and Mexico, Central America and Caribbean Zone)
4. Mental health and psychiatry in Latin America (Southern South America Zone)
5. The European Union and its significance for psychiatric organizations (Western Europe Zone and Northern Europe Zone)
6. Interdisciplinary approaches to treatment of mental disorders: the experience of Eastern Europe (Eastern Europe Zone)
7. Psychiatry in Central European countries within the process of affiliation to the European Union (Central Europe Zone)
8. Community psychiatry in the Mediterranean region and the role of psychiatric associations (Southern Europe Zone)
9. Mental health services in North Africa (Northern Africa Zone)
10. Partnership in mental health care in Africa (Southern and Eastern Africa Zone)
11. Modern and traditional treatments in the context of a developing country (Western and Central Africa Zone)

The WPA Sections

George Christodoulou
WPA Secretary for Sections

This short presentation aims at familiarizing the reader with some aspects of the functioning and activities of the WPA Scientific Sections, often referred to as the 'scientific backbone' of the WPA.

Role of the Scientific Sections

The Scientific Sections of the WPA enjoy a semi-autonomous status and they are under the guidance of the Secretary for Sections, who is assisted by the Operational Committee on Sections, composed of five members and a consultant. There are, presently, as many as 55 scientific sections in the WPA, each covering a specific scientific area.

The Sections' work is not usually manifest, because they contribute to the work of the other WPA components (e.g., education, publications, meetings, World Congresses) without being particularly visible. Visibility is not so important as long as the work of the WPA as a whole is carried out. However, the Sections invariably provide the backing for most WPA activities and should receive credit for this. It should be noted that within the Yokohama World Congress of 2002 practically every single Section contributed at least one Symposium to the Congress.

Inter-sectional communication

Inter-sectional communication in joint educational and research activities is greatly encouraged. Paradigms of such joint activities are: a) the Panel Discussion on Psychiatric Prevention that involved five sections (Yokohama World Congress, 2002); b) the Disasters Day organized in Yokohama by two WPA Sections, the Section on Military and Disaster Psychiatry and the Section on Anxiety Disorders and Obsessive-Compulsive Disorder; c) the Panel Discussion that involved ten sections during the WPA Regional Congress on Prevention, February 1999, Athens; d) the research activities of the Section on Classification and Diagnostic Assessment in collaboration with other Sections; e) the volume Advances in Psychiatry, produced with the collaboration of 32 Sections; f) the WPA Regional and Intersectional Congress to be held in Athens in March 2005, where all WPA Sections are expected to participate and collaborate in the production of the second volume of Advances in Psychiatry.

The WPA Sections' Bulletin

All WPA components receive Science and Care, the WPA Sections'

Bulletin, edited four times a year. The main targets of the Bulletin are provision of information on the activities and the perspectives of the Sections and inter-sectional communication.

Promotion of interaction between Sections and Member Societies

This is achieved by periodic correspondence of the Secretary for Sections with Member Societies, via distribution of the WPA Sections' Bulletin, the WPA Forum, the WPA Electronic Bulletin etc. In the course of the WPA International Congress of Caracas, held in October 2003, a special meeting of the Secretary for Sections and the Operational Committee for Sections with the Presidents of WPA Member Societies was held. The scope was to enhance collaboration and more specifically to ask the Presidents to encourage the chairs of the Sections of the Member Societies to join the WPA Sections. Better coordination of activities and more productive collaboration is expected as a result of this initiative.

Publications by the Sections

In addition to publications produced by the Secretariat for Sections (Advances in Psychiatry and Science and Care) the sections produce journals (some indexed), bulletins, newsletters, books and chapters in books edited by the WPA. As many as 20 Sections produce periodic publications. As many as 14 Sections have produced books and more than 40 Sections have produced chapters in books edited by the WPA.

Consensus and position statements

Periodically the Sections prepare consensus or position statements on important issues within the scientific area they represent. Twelve Sections have produced such statements. Many of these statements are very useful for the guidance of the psychiatric community on issues with which familiarity is limited. Some of these statements are produced with the collaboration of many Sections (e.g. the recent position statement on physicians' impairment).

Educational programs

The Sections play a major role in education by organizing special educational activities within scientific meetings and by preparing educational programs pertaining to their area of expertise. More than ten Sections have prepared such programs.

Scientific meetings

The WPA Sections have a very active participation in scientific meetings organized by the WPA, but also by other scientific organizations. Additionally, they organize independent scientific meetings or inter-sectional ones. A meeting in which most of the 55 Scientific Sections will be expected to participate and collaborate is the Regional and Intersectional WPA Congress to be held in Athens in March 2005. As mentioned earlier, practically all Sections have organized one or more symposia within the 12th World Congress of Psychiatry held in Yokohama and similar performance is expected in Cairo in September 2005.

The WPA-Sponsored Symposium 'Harmonizing Perspectives and Experiences in Psychiatric Training'

Levent Küey
WPA Zone Representative, Southern Europe

A WPA-sponsored symposium entitled 'Harmonizing perspectives and experiences in psychiatric training' was held on October 15, 2003 in Antalya, Turkey, during the 39th National Psychiatry Congress of Turkey. The experiences of various international organizations and of Turkish psychiatrists and the perspectives of different experts in psychiatric training were discussed in three sessions. The idea of enhancing training and education in psychiatry across the world, while at the same time respecting the realities and differences that exist in the various regions and in different cultural contexts, was once more emphasized.

In his presentation, Juan E. Mezzich, President Elect of the WPA, outlined the objectives and main components of the WPA Institutional Program to Promote the Professional Development of Young Psychiatrists, which reflects WPA's commitment to the future of our field. This Institutional Program includes, among other activities, a Fellowship Program for WPA World and International Congresses, awards to promote scientific contributions from young colleagues, special networks for young psychiatrists, and the recently established WPA Young Psychiatrists Council.

Mario Maj, President of the European Psychiatric Association (AEP) and Secretary for Publications of the WPA, emphasizing the importance of continuing medical education (CME) in psychiatry, described a programme of itinerant courses launched by the AEP in collaboration with twenty-two national psychiatric societies in Europe. The programme includes 12 courses, dealing with the management of the most prevalent mental disorders and delivered by the most renowned experts in the relevant fields. The courses are taking place within the congresses of the national psychiatric societies.

Levent Küey, WPA Zone Representative for Southern Europe, outlined

the aims, development and main features of the WPA Core Training Curriculum for Psychiatry, which was published in 2002. The idea behind this programme is to share educational expertise while maintaining recognition of the realities that exist in different regions of the world. The main goal is to construct the core elements of a graduate training curriculum in psychiatry in order to ensure high quality of psychiatric services via the creation of competent psychiatrists in all areas of the world.

Anne Lindhardt, President of the Section of Psychiatry of the European Union of Medical Specialists (UEMS), described the recent recommendations for psychiatric training agreed upon by all member countries, with a special focus on training in psychotherapy.

Marianne Kastrup, WPA Zone Representative for Northern Europe, discussed the content of a culture sensitive psychiatric curriculum and the strategies to implement it. Taking the Northern European Region and Denmark as examples, new challenges related to the immigrant population were described.

Valery Krasnov, WPA Zone Representative for Eastern Europe, discussed the problems of psychiatric training in that region, where, like many other processes, the system of professional education is undergoing a transition period. Postgraduate professional education in Russia, Belarus and Ukraine is carried out in internships (one year program) and in clinical 'ordinature' (two years program). It goes without saying that over the course of two years it is difficult to properly prepare a specialist in psychiatry. Recent attempts to improve postgraduate education by special additional courses were described.

Petr Smolik, WPA Zone Representative for Central Europe, described the very new and sensitive situation created in that region by the affiliation of some countries to the European Union. The diversification of Central European countries according to the level of this process will induce very probably various specific problems, especially in such fragile social structures as health care and system of education. Very active and efficacious ways of prevention of these problems should be prepared.

The standpoint of psychiatric trainees was presented by Dominique Mathis, Past-President of the European Federation of Psychiatric Trainees (EFPT). This is the umbrella organization for national European psychiatric trainees' associations. Sixteen European countries are currently full members.

The CME accreditation and continuing professional development (CPD) activities of the Turkish Medical Association (TMA), which started in 1994, were described by Iskender Sayek, Chair of the Section on Training and CME of the TMA and Dean of Hacettepe Medical School. Rasit Tükel, Chair of the Section on Psychiatric Training of the Psychiatric Association of Turkey (PAT), outlined the development of the Psychiatric Board of Turkey. Hamdullah Aydin, President of the Commission for Psychiatric Training and Curriculum of Turkey, explained the principles and the process of preparation of the Training Curriculum for Psychiatry in Turkey. Defne Turhan, President Elect of EFPT, focused on psychiatric training in Turkey from the perspective of trainees. M. Orhan Öztürk, Past President of PAT, underlined the need to establish close collaboration and exchange of trainers and trainees between psychiatric centers.

The symposium was closed by the chairs, Savas Kültür, President of PAT, and Levent Küey, who expressed their wish that improved psychiatric training helps psychiatrists all over the world to gain higher scientific, ethical and humanistic standards.

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