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Health Effects due to Air Pollution in China

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Abstract

This paper summarizes the assessment of health effects carried out by Paul Scherrer Institute (PSI) within the China Energy Technology Program (CETP). CETP has been sponsored and coordinated by ABB in conjunction with the Alliance for Global Sustainability (AGS). PSI, together with American (MIT), numerous Chinese, Japanese (Tokyo University) and Swiss (ETHZ and EPFL) partners investigated how the future electricity supply in China could be made more sustainable.

The impacts of outdoor air pollution on health and environment were assessed. The main emphasis has been on the rapidly expanding electricity sector. Most detailed results were obtained for the highly industrialized and energy intensive Shandong Province but a wide spectrum of findings considers the whole China. In accordance with the general objective of CETP “true” costs of electricity generation were estimated, reflecting not only the (internal) production costs but also damages to health and environment. This was done both for the current technologies as well as for candidate technologies that could be implemented within the time horizon of 20 years.

According to the present study air pollution in China currently causes about nine million Years of Life Lost (YOLL) per year. In relative terms sulfates dominate the health impacts and SO₂ is thus indirectly the major contributor, followed by nitrates and primary particulates. The number of YOLL per ton of SO₂ emitted in China is on average almost seven times higher than the average for EU; for Shandong the corresponding factor is about 11. The total (internal plus external) costs of environmentally-friendly electricity supply strategies are significantly lower than those of the seemingly cheaper, but “dirty” and non-sustainable, strategies based on traditional coal technologies. Cost-efficient reduction of health and environmental damage, and of the corresponding external costs, can be achieved by implementation of “clean-coal” technologies, together with fuel diversification, including extended use of natural gas and nuclear energy.

Keywords: Health Risks, Energy Chains, Valuation, Comparative Assessment, External Costs.

1. Introduction

Along with enormous benefits all forms of energy supply have some negative impacts on people and on the environment. In particular, the release of pollutants to air, water and soil can have a profound impact to human health, agricultural crops, natural and man-made environments via different pathways of exposure. Decision-makers around the world are

increasingly aware about the physical and economic consequences to the public health sector and the environment, whose extent depends on their decisions. In practical terms, sustainable energy development means that human health and environmental impacts, resource depletion and intergenerational equity implications should be considered along with traditional economic and

technical issues in the planning and use of energy options.

Many studies have been undertaken in recent years on the health and environmental impacts associated with energy supply. Of particular importance in this context is the ExternE Project of the European Union (European Commission, 1999). A generally accepted framework for comparative assessment of such impacts has been developed and implemented for a number of countries. Recent enhancements and extensions include PSI's work on future systems under Swiss conditions (Hirschberg et al., 2000) and study of impacts in China within the China Energy Technology Program (Hirschberg et al., 2003b). The studies identify, quantify and, to the extent possible, determine the economic value of health and environmental impacts.

2. Health Effects of Normal Operation

The emphasis in the assessment is on air pollutants, whose effects are dominant. Health impacts due to emissions to water have not been analyzed in detail but they are of secondary importance, particularly when energy systems in Western Europe are considered. Furthermore, the assessment concerns impacts on public; occupational damages are normally much less significant and are considered to be by and large internalized, at least in OECD.

2.1 Air pollutants and their health impacts

The following major emissions are addressed in the health effect comparisons covered here:

- *Particulates*. Ambient air pollution particulates are a complex mixture, varying in size and in composition. Many epidemiological studies found evidence of adverse acute health effects of particulate air pollution. There is also strong epidemiological evidence of chronic health effects. Because particulate air pollution is a complex mixture rather than a single substance, there is a lot of diversity in how particulate air pollution is characterized in various epidemiological studies. Internationally, there are many studies showing acute health effects of particulates expressed as PM₁₀ (inhalable particulates), or total suspended particulates (TSP). In Europe, a number of studies refer to black smoke (BS). Some studies, mostly from North America, show the effect of finer fractions such as PM_{2.5} or sulfates. There is some evidence, that these fine fractions are associated with greater risks than PM₁₀. It may also be that the toxicity of particulates is greater according to their acidity, and less according to their solubility. For modelling, we distinguish between "primary particulates" which are emitted directly from the emission sources and the "secondary particulates", i.e. sulfates and nitrates, which are formed in the

atmosphere from SO₂ and NO_x emissions. Secondary particulates are assumed to cause similar health impacts as primary particulates.

- *Sulfur dioxide (SO₂)*. SO₂ is held responsible for a variety of environmental damages, particularly on human health, ecosystems, crops and building materials. As a precursor of sulfates (secondary particulates), sulfur dioxide is indirectly a major contributor to long-term ("chronic") mortality and several morbidity effects. Also evidence of the acute health effects associated with SO₂ is available. SO₂ can cause direct economic damages by reducing crop yields. Acidification resulting from SO₂ emissions is also hazardous to natural ecosystems.

- *Nitrogen oxides (NO_x)*. Currently, the direct effects of NO_x emissions are not being assessed though positive associations between NO_x and daily mortality or respiratory hospital admissions in several European cities have been reported. NO_x is a precursor to nitrates (secondary particulates). The view is supported that the apparent NO_x effects may be due to particulates, or at least, are highly dependent on background particulate levels.

- *Ammonia (NH₃)*. Ammonia emissions play an important role in the chemical transformation of sulfur and nitrogen oxides into hazardous secondary particulates (ammonia sulfates and ammonia nitrates).

- *Radiation*. Impacts on human health and ecosystems can occur when radioactive substances are set free into the environment. During normal operation of nuclear power plants and other facilities in the nuclear fuel cycle, the emissions of radioactivity are at low levels. In relative terms stages in the nuclear fuel cycle such as mining/milling or reprocessing emit more radioactivity than the power plant. The impacts of these emissions are reflected in the comparisons. Health effects related to hypothetical severe nuclear accidents, which might lead to large releases of radioactivity, need to be addressed separately.

2.2 Health impact assessment methodology

The impact pathway approach allows the impact from emission sources within specific energy chains to be estimated. The main features of the approach are as follows:

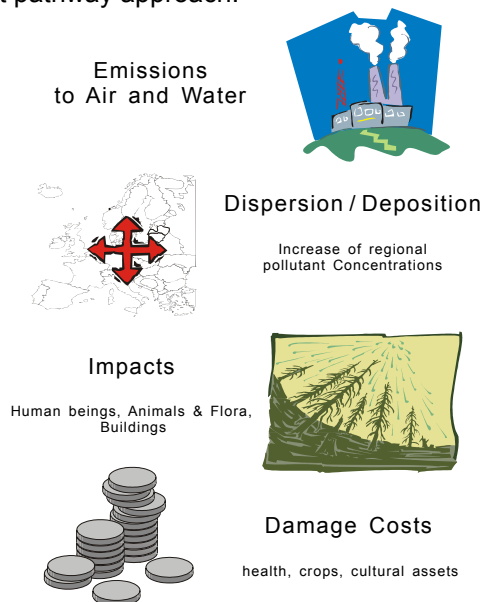
(a) In the full scope analysis, all relevant stages in the various energy chains are covered (extraction, fuel processing, transport, power generation, waste management and storage).

(b) The analysis steps involve technology and site characterization, prioritization of impacts to the environment, quantification of burdens (e.g. emissions), description of the receiving environment, quantification of environmental damage (using, whenever applicable, dispersion models for

atmospheric pollutants and dose-response functions), and, if of interest, economic valuation. Figure 1 shows the analysis steps.

Fig. 1

Impact pathway approach.



The basic tool used for estimation of health and environmental impacts, based on the "impact pathway approach", is the integrated impact assessment model EcoSense, developed by Stuttgart University (European Commission, 1999; Krewitt et al., 2001). The model, earlier developed and used for external cost assessment in Western Europe, was modified for applications to South American conditions (Krewitt et al., 2001), and later to Chinese/Asian (Hirschberg et al., 2003b) and Russian (Droste-Franke et al., 2002) conditions. This involves the development and implementation of application-specific "Reference Environment Databases", covering receptor data, meteorological data and emission data.

EcoSense allows calculations of fuel cycle externalities to be carried out and supports the assessment of damage resulting from the operation of a single point source (e.g. a power plant) at a given location, taking into account pre-defined background conditions. Furthermore, the effects of changes in emissions from specific sectors (e.g. energy, industry, transport, households, etc.) can be assessed on a continental, national, provincial or community level.

In a first step, the emission inventories are organized according to administrative units and sectors. The Windrose Trajectory Model (WTM) employed by EcoSense simulates the long-range atmospheric transport and chemical conversion of air pollutants, resulting in concentrations and deposition fields. The physical impact on health and environment are

calculated by implementing the receptor distributions and the marginal increases of pollutants into the dose-effect models. Finally, to obtain the damage costs, the impact end-effects are multiplied by the monetary unit cost per incident.

For the basic health effect functions, a linear relation between marginal changes of concentrations and health impacts is assumed. The World Health Organization (WHO, 1999) adopted a 'no threshold' position for particulates and ozone. ExternE (European Commission, 1999) recommended to quantify health effects from particulates, SO₂, and ozone on a 'no-threshold' basis.

Acute mortality effects are associated with correlations between short-term (order of days) changes in concentrations of air pollutants and short-term changes in mortality. Chronic mortality refers to long-term (order of years) effects of air pollution. The measure used to quantify mortality effects is the reduction of life expectancy expressed as "Years of Life Lost" (YOLL). The individual YOLL are summed up to total YOLL for the whole affected population. Mortality studies usually measure changes in mortality rates of the population. Non-trivial extra steps are needed to convert mortality rates into YOLL. The slopes of the exposure-response functions used for impact assessment of mortality and morbidity are summarized in Table 1. (The table and the following results refer to the state-of-the-art as of years 2003/2004; research on impact and valuation factors is still ongoing e.g. in European ExternE follow-up projects.) Among the reference sources provided in the table we emphasize the study by Pope et al., (1995), carried out on behalf of American Cancer Society (ACS). More than 500'000 adult individuals in 151 US cities were followed over a period of about 8 years (1982-1989). A clear correlation was found between mortality and air pollution after adjusting for age, sex, race, current cigarette smokers, former cigarette smokers, pipe/cigar smokers, exposure to passive smoking, occupational exposure, education, body-mass index (BMI), and alcohol use. The adjusted mortality rate was about 17% higher for a difference of 24.5 µg/m³ PM_{2.5} between the highest and lowest polluted areas. For sulfates, an increase of mortality of about 15% was associated with an increase of 19.9 µg/m³ SO₄. The strongest associations were observed for cardiopulmonary disease and lung cancer, with insignificant associations with death due to other causes. Results from the ACS study were used in ExternE to derive a dose-effect model. The results for a 16-years follow-up period (1982-1998) confirmed again the clear correlation between ambient fine particulate concentrations and mortality (Pope et al., 2002).

Table 1

Exposure-response functions for the quantification of human health impacts according to (European Commission, 1999) with updates from (Friedrich and Bickel, 2001). The exposure response slope, f_{er} , has units of [cases/(yr-person- $\mu\text{g}/\text{m}^3$)] for morbidity, and [YOLL/(yr-person- $\mu\text{g}/\text{m}^3$)] for mortality.

Receptor	Impact Category	Reference	Pollutant	f_{er}
ASTHMATICS				
Adults	Bronchodilator usage	Dusseldorp <i>et al.</i> , 1995	PM ₁₀	0.163
			Nitrates	0.163
			Sulfates	0.272
Cough	Dusseldorp <i>et al.</i> , 1995	PM ₁₀	0.188	
		Nitrates	0.188	
		Sulfates	0.280	
Lower respiratory symptoms (wheeze)	Dusseldorp <i>et al.</i> , 1995	PM ₁₀	0.061	
		Nitrates	0.061	
		Sulfates	0.101	
children	Bronchodilator usage	Roemer <i>et al.</i> , 1993	PM ₁₀	0.078
			Nitrates	0.078
			Sulfates	0.129
Cough	Pope and Dockery, 1992	PM ₁₀	0.133	
		Nitrates	0.133	
		Sulfates	0.223	
Lower respiratory symptoms (wheeze)	Roemer <i>et al.</i> , 1993	PM ₁₀	0.103	
		Nitrates	0.103	
		Sulfates	0.172	
ELDERLY 65+				
Congestive heart failure	Schwartz and Morris, 1995	PM ₁₀	1.85E-5	
		Nitrates	1.95E-5	
		Sulfates	3.09E-5	
CHILDREN				
Chronic cough	Dockery <i>et al.</i> , 1989	PM ₁₀	2.07E-3	
		Nitrates	2.07E-3	
		Sulfates	3.46E-3	
ADULTS				
Restricted activity days	Ostro, 1987	PM ₁₀	0.025	
		Nitrates	0.025	
		Sulfates	0.042	
Chronic bronchitis	Abbey <i>et al.</i> , 1995	PM ₁₀	2.5E-5	
		Nitrates	2.5E-5	
		Sulfates	3.9E-5	
ENTIRE POPULATION				
Respiratory hospital admissions (RHA)	Dab <i>et al.</i> , 1996	PM ₁₀	2.07E-6	
	Ponce de Leon, 1996	Nitrates	2.07E-6	
		Sulfates	3.46E-6	
		SO ₂	2.04E-6	
Cerebrovascular hospital admissions	Wordley <i>et al.</i> , 1997	PM ₁₀	5.04E-6	
		Nitrates	5.04E-6	
		Sulfates	8.42E-6	
Acute mortality (YOLL)	Anderson <i>et al.</i> , 1996, Touloumi <i>et al.</i> , 1996	SO ₂	5.4E-6	
Chronic mortality (YOLL)	Pope <i>et al.</i> , 1995	PM ₁₀	1.57E-4	
		Nitrates	1.57E-4	
		PM _{2.5}	2.60E-4	
		Sulfates	2.60E-4	

To obtain the damage costs, one multiplies the number of impacts (for example, the number of asthma attacks) by the cost per case (US\$ per asthma attack). For health impacts, the unit costs include the cost of illness, wage and productivity losses, which are market based factors, as well as non-market costs that take into account an individual's willingness-to-pay (WTP) to avoid the risk of pain and suffering. For mortality impacts, one needs to determine the Value of a Life Year Lost (VLYL) or, equivalently, the Value of a Life Year (VOLY), which in turn is based on the so called Value of Statistical Life (VSL), the amount of money that an individual is willing to pay to avoid premature death. The median values for VSL and VLYL (for valuing long-term mortality impacts) in most industrialized

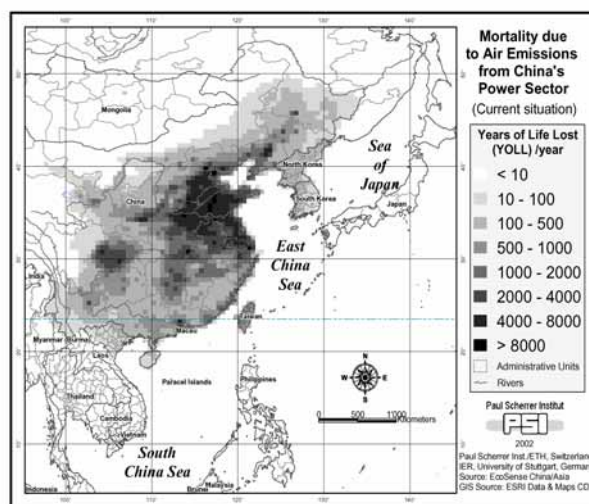
countries (European Commission, 1999) are, respectively, 3.1 million and 110'000 US\$₂₀₀₀ (undiscounted). Adjustments for other countries are based on the assumption that there is an "elasticity" of WTP with respect to real income.

3. Selected assessment results

As an example of assessment results Fig. 2 shows the distribution of mortality due to air-pollutant emissions from China's power sector. There is a large variation of these effects, with the highest damage occurring in areas with intensive industrial activities and high density of population.

Fig. 2

Distribution of mortality due to current emissions of air pollutants from China's power sector (Hirschberg *et al.*, 2003b).



Generally, damages resulting from the emission of a unit of pollutant are high if the number of affected receptors is very large. Table 2 shows factors for the impact "mortality" in terms of Years of Life Lost for different countries and different locations within countries. It can be seen clearly that the specific YOLL factors depend strongly on the location of the emission source.

Table 2

Comparison of different countries and locations – Mortality risk in terms of “Years of Life Lost” (YOLL) resulting from the emission of one kilo-tonne of pollutant (Reference years 1990/1998).

	YOLL per kt of SO ₂ due to exposure to SO ₂	YOLL per kt of SO ₂ due to formation of sulfate aerosols	YOLL per kt of NO _x due to formation of nitrate aerosols	YOLL per kt of PM ₁₀ due to exposure to PM ₁₀	Reference
Zürich	3.3	53.0	77.0	87.0	Own calculations
Bezau (Aargau)	3.4	57.7	75.4	88.2	Own calculations
St.Gallen, countryside	2.7	45.9	64.5	66.1	Own calculations
Austria	2.1	36.8	44.0	56.5	Krewitt et al., 2001
Belgium	3.2	39.2	32.4	92.7	Krewitt et al., 2001
Denmark	0.9	17.0	20.0	22.4	Krewitt et al., 2001
Finland	0.3	7.0	7.8	6.0	Krewitt et al., 2001
France	2.3	40.0	51.4	62.9	Krewitt et al., 2001
Germany	2.2	31.6	27.9	68.6	Krewitt et al., 2001
Greece	0.8	24.3	33.8	32.6	Krewitt et al., 2001
Italy	1.5	27.3	34.6	48.0	Krewitt et al., 2001
Ireland	0.7	12.7	17.8	17.1	Krewitt et al., 2001
Netherlands	2.8	34.9	27.4	61.0	Krewitt et al., 2001
Portugal	0.9	17.4	21.7	24.4	Krewitt et al., 2001
Spain	0.9	21.7	27.8	33.0	Krewitt et al., 2001
Sweden	0.4	9.6	11.5	7.3	Krewitt et al., 2001
UK	1.8	21.1	17.5	40.4	Krewitt et al., 2001
EU-15	1.7	27.0	28.5	56.7	Krewitt et al., 2001
China average	5.2	190.8	148.1	110.3	Hirschberg et al., 2003b
Shandong Province (China)	8.4	312.3	225.2	211.3	Hirschberg et al., 2003b
Shanxi Province (China)	8.3	305.3	181.0	185.9	Hirschberg et al., 2003b
South America average	0.34	4.9	6.8	16.3	Krewitt et al., 2001
Brazil	1.2	13.3	10.9	16.4	Krewitt et al., 2001
State of Sao Paulo	3.9	38.5	52.5	39.9	Krewitt et al., 2001
Colombia	0.33	3.6	6	5.5	Krewitt et al., 2001

For the calculation of external damage costs, the various impacts have to be valued in monetary terms. The contributions from the different impacts resulting from the emissions of various hazardous pollutants are summed up over all affected receptors. All results provided in the following figures include the contributions from the rest of energy chains associated with the considered power plant technologies.

Figure 3 summarizes the current external damage costs due to air pollution from the power sector and from all sectors in Shandong province and in the whole of China. The total external costs are dominated by mortality, followed by morbidity impacts. Compared to the large mortality and morbidity costs, crop losses contribute only marginally to the total damage costs.

Fig. 3

Damage costs due to outdoor air pollution for the reference year 1998 in Shandong Province and in the whole of China (Hirschberg et al., 2003b).

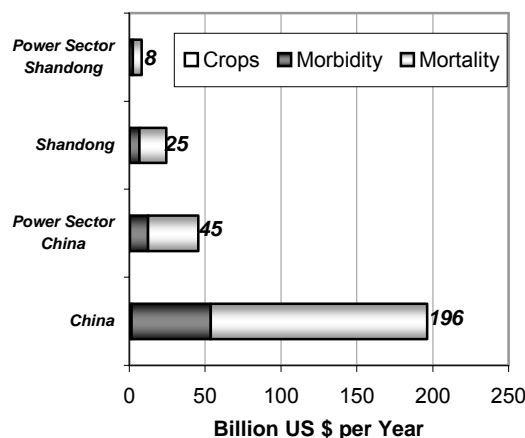


Figure 4 shows the relative contributions of different health impacts to the total morbidity costs. Morbidity costs are dominated by chronic bronchitis and restricted activity days. The figure refers to air pollution from Shandong's power sector, but the relative distribution of morbidity costs is similar for the other air pollution sources considered.

Fig. 4

Distribution of external damage costs of morbidity due to air emissions from Shandong power sector (Hirschberg et al., 2003b).

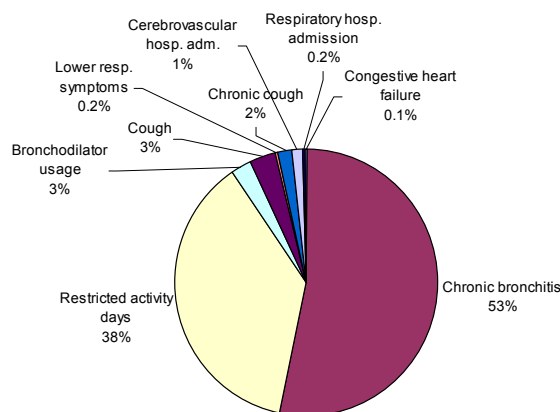
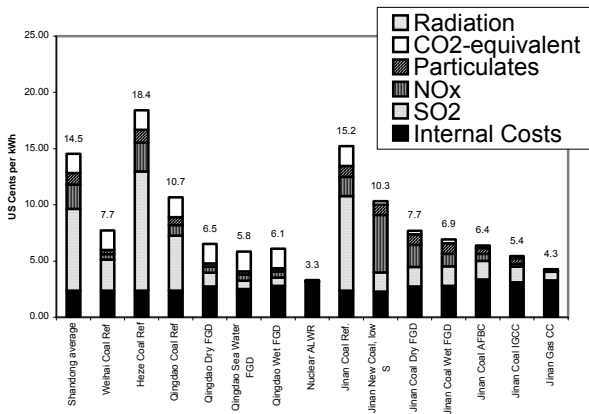


Figure 5 shows the “true” costs of electricity generation in Shandong, a relatively highly industrialized province of China. It should be noted that currently only conventional (reference) coal power plants without Flue Gas Desulfurisation (FGD) are operating in Shandong. The costs are provided for a variety of coal technologies in few selected locations in Shandong, for (possible) natural gas plant

in Jinan and for (possible) nuclear power located on the coast of Shandong. Jinan is the largest city in Shandong, and is located inland. Qingdao is located on the coast. Heze and Weihai are located in the south-western part of the province and in the northern part of the Shandong peninsula, respectively. For comparison, the average external costs for Shandong's power sector are shown.

Fig. 5

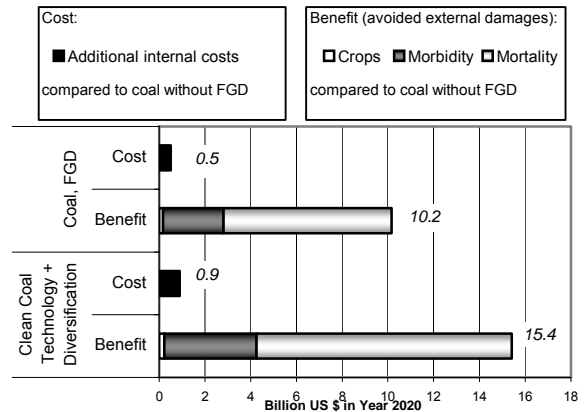
“True” costs of electricity generation by various means in China, Shandong Province; contributions to external costs from major pollutants and global warming (CO₂-equivalent) are shown (Hirschberg et al., 2003b).



Over 18'000 electricity supply scenarios for the years 2000 to 2024 were analyzed for Shandong Province within CETP. External costs were estimated for more than 100 selected scenarios. Figure 6 shows results from a cost-benefit analysis for two selected electricity supply strategies for Shandong Province in the year 2020 in relation to a strategy based on the use of coal without scrubbers (FGD). The two cleaner scenarios shown are: (1) conventional coal with FGD; and (2) improvements of existing generation—retirement of aging units, retrofits (including FGD), coal treatment—together with clean/advanced coal technologies, nuclear and some natural gas. Since the relative difference in internal costs is quite small, the total (internal plus external) costs of much more environmentally friendly strategies are clearly lower than the full costs of seemingly cheap, “dirty”, non-sustainable strategies.

Fig. 6

Cost-benefit analysis of “clean” versus “dirty” strategies of power supply in Shandong Province in year 2020, including LCA contributions. CO₂ damage costs are not considered though their inclusion would further strengthen the benefits of cleaner strategies (Hirschberg et al., 2003b).



Uncertainty analysis of complex integrated models such as those used in the impact pathway approach is a highly demanding task. Not all underlying issues are fully resolved within the current state-of-the-art. An approximate quantitative estimate of uncertainties has been implemented.

The impact pathway analysis is essentially multiplicative. According to the central limit theorem of statistics, the “natural” distribution for multiplicative processes is a lognormal function. For the uncertainty analysis of the impact assessment, two basic measures are important: geometric mean value (or geometric expected value) μ_g and geometric standard deviation σ_g . For a lognormal distribution, multiplicative confidence intervals around the geometric mean can be derived easily from the geometric standard deviation. The 68% confidence interval is approximately $[\mu_g / \sigma_g, \mu_g * \sigma_g]$, and the 95% confidence interval is approximately $[\mu_g / (\sigma_g)^2, \mu_g * (\sigma_g)^2]$. Table 3 summarizes the uncertainties related to the dominant end-point “chronic mortality”.

Table 3

Estimated uncertainties in terms of geometric standard deviations for end-point “chronic mortality”.

	Chronic Mortality ExternE Europe (European Commission, 1999)	Chronic Mortality China (Hirschberg et al., 2003b)
Emission data	1.2	1.5
Atmospheric modeling WTM	2	2
Exposure-response function, original study	1.3	1.3
Transfer of exposure-response function to other region	2	2.3
YOLL calculation from mortality Latency	1.5 1.4	1.8 1.4
Population data	-	1.1
<i>Total (without monetary valuation)</i>	3.2	3.9

4. Conclusions

A systematic comparison of health impacts associated with major energy chains and their normal operation has been carried out. Based on state-of-the-art approaches this paper provides selected results of such comparisons, applicable to China. The following conclusions build on the results presented here and on the full set of findings from the research performed.

Overall Health Impacts – Health impacts associated with air pollution caused by combustion products are most serious. Fossil power plants (primarily coal- and oil-fired), are major contributors to these effects, particularly in developing countries. Air pollution in China has a strongly negative feedback on the rate of economic growth. Health impacts dominate the assessed damages. Outdoor air pollution from all sectors in China resulted in about nine million years of life lost (YOLL) in 1998. The health damages caused by this pollution cost about 6-7 percent of GDP based on the willingness-to-pay method, which is comparable to current growth rates. The power sector contributes about one quarter of the total air pollution damage costs in China.

Health Impacts of Specific Pollutants – The major share of health damage is due to secondary particulates formed by chemical transformation of SO₂ and NO_x into sulfates and nitrates. Sulfates dominate damages, so SO₂ is the major contributor, followed by nitrates and primary particulates. The estimated physical impacts are sufficiently robust to be used for decision-making independently of their monetary value. For the reference Huangtai plant in Shandong, 1998 emissions caused about 25'000 YOLL per year. The average number of YOLL per tonne of SO₂ emitted in China is almost seven times higher than the average for the European Union; for Shandong the corresponding factor is about eleven. Impacts per tonne of pollutant emitted at different

sites in Shandong vary by a factor of four, with the sites located on the coast having the lowest normalized impacts. This is due to the influence of such factors as the density of population, meteorological conditions as well as background concentrations of air constituents.

Mortality Benefits of Alternative Technologies – Taking the Huangtai power plant in Shandong and its associated coal chain as a reference, the use of low sulfur coal reduces mortality (expressed in YOLL per GWh) by a factor of 1.7; and FGD with 95 percent SO₂ removal efficiency by a factor of 4.4. Replacement by AFBC gives a reduction factor of 8; by IGCC a factor of 13; by natural gas CC plant a factor of 52 and by nuclear power plant a factor of 63. The strong dependence of health damages on technology is also reflected in the corresponding reductions of the estimated “true” costs of electricity generated by these technologies.

Total Costs Justify Cleaner Technologies – The external costs of the “clean” Shandong electricity supply scenarios analyzed are typically a factor of three to four lower than for the “dirtiest” ones (depending on whether global warming damages are included or not). The total (internal plus external) costs of environmentally friendly strategies based on clean coal technologies and diversified supply (i.e. natural gas and nuclear power), are significantly lower than the total costs of “dirty” and non-sustainable strategies using conventional pulverized coal generation. Alternative monetization methods, considered inappropriate by the international scientific community, can lead to lower estimates of external costs. However, the damages avoided by cleaner technologies exceed the increase in internal costs in all the sensitivity cases analyzed, demonstrating the robustness of the findings. Reduction of major air pollutant emissions from electricity generation in China/Shandong, and the associated health and environmental damage is feasible, and economically and socially justified.

Along with the impacts of the normal operation of energy systems, treatment of severe accidents should be an integral part of any comprehensive comparative assessment. The assessment of health and other damages caused by severe accidents has been the subject of extensive comparative analyses (Hirschberg et al., 1998; 2003a), not addressed in the present paper. In order to give some perspective on the results we note that the experienced total damages due to severe accidents in the energy sector though widely debated are very small in comparison with natural catastrophes but also when compared with the impacts of air pollution originating from the energy sector. This conclusion is valid also for the extreme case of Chinese coal chain, exhibiting

severe accident fatality rates about 50 times higher than the corresponding rates in OECD. This finding underlines the merits of comprehensive and balanced comparative assessment.

Acknowledgment

Figures 2, 4, 5, 6, and Tables 1 and 3 are reproduced here from (Hirschberg et al. 2003b) with kind permission of Springer Science and Business Media.

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STUDY ON THE EFFECTS OF WATER TREATED WITH DIFFERENT DOSES OF ULTRAVIOLET LIGHT ON CULTURAL PROPERTIES OF BIFIDOBACTERIA, LACTOBACILLI AND BAKERY YEAST

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Abstract

The efficiency of usage of ultraviolet-treated water in cultural media for microorganisms, participated in production of food stuff was studied.. The activity of growth and development and also different properties of lactobacilli, bifidobacteria and bakery yeasts were analyzed. The frequency of genetic transfer of Escherichia coli markers in liquid nutrient media were estimated.

It was shown that under the influence of ultraviolet treated water the propagation of microorganisms, their restoration from liophylised phase is accelerated. The colonies which were grown on the media which contain water, treated by ultraviolet, has increased number of colony forming units. The colonies, which were grown on agarised media, containing modified water, has a tendency of increased production of some enzymes (bacteriocines, beta-lactamase, hemolysin).

Conjugation, performed in the broth based on water, treated by ultraviolet revealed no changes in plasmids transfer frequency. The number of colony forming units of yeasts also depended on ultraviolet-treated water in media, as well as on amount of nutrient substances.

Probably one of the leading mechanisms of acquired modifications of bacterial characteristics, based on modification of electric conductivity in modified media.

The application of ultraviolet-treated water may be recommended for production of foodstuffs in different processes, which are used by microorganisms and nutrient media.

Key Words: Microbial cultures, Growth, Pretreatment by UV, Media

Introduction

It is a well-known fact, that some physical factors cause stimulating effect on biological properties of micro organisms. For example, factors of increased pressure of gaseous medium contribute to activation of Gram-positive micro organisms (1,2). Some evidences confirm that low doses of radiation and changed solar activity cause optimization of cultural activity of a number of micro organisms (3).

Our investigations were aimed at evaluating the growth properties of micro organisms participating in foods production processes (bread-making, brewing and sour milk products manufacturing) - bifidobacteria, lactobacilli and bakery yeast - in conditions of their culturing on media prepared with the use of water pretreated with hard ultraviolet irradiation.

Materials and methods

Water treatment with ultraviolet light

The necessary amount of water was treated with non-filtered light produced by a source of ultraviolet radiation (DRT-400) with a radiant flux that contained no less than 30 % of ultraviolet quanta with a wavelength range of 190 to 250 nm. The luminous flux with a power of 0.4 W/cm² was modeled with the use of electromagnetic field of an auxiliary device. Water processing had been carried out until the internal energy of water increased, according to viscometer readings, two fold.

The following standard culture media were prepared with the use of water treated with ultraviolet light:

- MRS medium for culturing lactobacilli;
- Bactofoc medium for culturing bifidobacteria;
- LB medium for culturing aerobic test cultures;
- meat infusion broth for determining the frequency of plasmids transfer during conjugation and
- wort agar for yeast culturing.

Similar culture media containing water, which had not been treated with ultraviolet light, served as control.

Strains of micro organisms

Collection strains of *Lactobacillus casei*, *Bifidobacterium longum*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus*, *Saccharomyces cerevisiae* obtained from RAS IMBP RF SSRC collection were used in the study.

Study of lactobacilli and bifidobacteria cultures survival in culture media containing water treated with ultraviolet light

Initially, the cultures being tested had been in lyophilized condition. The cultures were rehydrated, 10-fold titrated in culture media and incubated for 48 hours at 37 °C. Cultures survival was evaluated based on the number of grown colonies.

Evaluation of viable cell counts in the colonies of lactobacilli and bifidobacteria grown in the culture media containing water treated with ultraviolet light

Colonies of micro organisms grown in agar were isolated, diluted in sterile physiologic salt solution and titrated in test tubes containing the standard growth medium. Inoculated media were incubated in a thermostat at 37 °C for 24 hours; then, counting of the grown colonies was carried out.

Study of microbial antagonism in culture media containing water treated with ultraviolet light

Culture of the test strain of lactobacilli was grown on the surface of nutrient agar in the form of a macro

colony for 24 hours at 37 °C. After incubation, the macro colony was sterilized with chloroform vapor and covered with semi-liquid agar containing the following cultures:

- *Staphylococcus aureus*;
- *Pseudomonas aeruginosa* (blue pus bacillus);
- *Escherichia coli* (colon bacillus);

The inoculated media were incubated for 24 hours.

After incubation, the antagonistic activity was evaluated based on the diameter of the zone of growth inhibition around the macro colony of the lactobacillus strain being tested.

Study of the frequency of genetic material transfer with liquid culture medium prepared with the use of water treated with ultraviolet light

Fresh agarized cultures of Strain J 5-3 *E. coli* containing pRI plasmids bearing the determinants of resistance to broad-spectrum antibiotics belonging to various chemical groups (ampicillin, carbenicillin, kanamycin), as well as a fresh agarized culture of Strain C-600 *E. coli* sensitive to all antibiotics excluding nalidixic acid, were incubated in water treated with ultraviolet light at a temperature of 37 °C. Incubation in ordinary media at a temperature of 37 °C was used as a control. After incubation, the cultures were re-inoculated on broth and placed in conditions corresponding to preincubation ones for 24 hours. After incubation, conjugation mixtures were prepared as follows: 1 ml of donor culture containing 1x10⁹ CFU/ml were mixed with 1 ml of recipient culture in the same concentration. The following conjugation systems were prepared:

- donors and an R plasmids recipient grown in water treated with ultraviolet light and carrying out the conjugation in water treated with ultraviolet light;
- donors and an R plasmids recipient grown in water treated with ultraviolet light and carrying out the conjugation in ordinary medium;
- donors and an R plasmids recipient grown in ordinary medium and carrying out the conjugation in water treated with ultraviolet;
- donors and an R plasmids recipient grown in ordinary medium and carrying out the conjugation in ordinary medium (control).

After the incubation, the mixtures were plated on culture dishes containing two antibacterial agents (for transconjugants selection) - one of the antibiotics, to which the donor strain had shown resistance, and nalidixic acid at a concentration of 100 µg/ml. After the incubation, transconjugant colonies grown on the dishes were counted using the following formula:

$$N = \frac{A}{B} \text{ (Lg)}$$

N - frequency of plasmids transfer,
 A - number of transconjugant colonies (CFU/ml),
 B - number of viable cells of the recipient in conjugation mixture (CFU/ml).

Enzymatic activity of cultures grown in culture media containing water treated with ultraviolet light

This activity was evaluated based on production of an inducible enzyme (beta-lactamase) and a constitutive enzyme (hemolysin).

Determination of beta-lactamase activity.

Culture of beta-lactamase-producing strain of E. coli was grown in the form of a macro colony on the medium containing ampicillin in a concentration of 60 mg/ml for 24 hours at 37 °C. After the incubation, the macro colony was sterilized with chloroform vapor, and Escherichia coli culture sensitive to ampicillin was poured on the surface of the medium. The inoculated medium was incubated for 24 hours at a temperature of 37 °C. After incubation, beta-lactamase activity was evaluated based on the diameter of the zone of ampicillin-sensitive strain growth around the macro colony of beta-lactamase producing strain.

Determination of hemolysin activity.

Doses of Staphylococcus aureus culture with hemolytic properties were placed on the surface of 5 % blood agar prepared with the use of water treated with ultraviolet light. Blood agar prepared with using the ordinary water served as control. The inoculated medium was incubated for 24 hours at 37 °C. After incubation, activity of hemolysin production was evaluated.

Evaluation of Saccharomyces cerevisiae cultural properties

A strain of bakery yeast Saccharomyces cerevisiae was used in the experiments. A 0.5 g weight of dry yeast was subjected to suspending in 10 ml of physiologic salt solution for 5 to 10 minutes. Then, plating was carried out on culture dishes with Saburo and wort agar nutrient media prepared with the use of distilled water and water treated with ultraviolet light. Inoculated media were incubated in a thermostat at 29 °C for two days. Simultaneously, number of yeast cells in the original suspension was counted. Counting the yeast spores in the suspension was carried out using Goryaev's counting chamber.

Results

Study of lactobacillus and bifidobacterium cultures survival in culture media containing water treated with ultraviolet light

Data on survival of lactobacilli in culture media prepared with the use of water treated with ultraviolet light are presented in Tables 1 to 8. These data show, that the counts of viable lactobacillus colonies increased approximately 100-fold in conditions of culturing in growth media containing water treated with ultraviolet light. This tendency appeared on the first day of culture growth and continued in consecutive days.

Table 1

Survival of lactobacilli in the growth media containing water treated with ultraviolet light.

0.2 % MRS medium prepared with the use of water, which had not been treated with ultraviolet light
$5 \times 10^8 \pm 1 \times 10^8$
0.2 % MRS medium prepared with use of water treated with ultraviolet light
$3 \times 10^{10} \pm 1 \times 10^9$

A strain of lactobacilli, which had been stored in lyophilized condition in an ampoule for 13 years, was successfully revived with the use of the medium containing water treated with ultraviolet light (Table 2).

Table 2

Revivification of Strain K-25 of Lactobacillus casei with the use of growth media containing water treated with ultraviolet light (CFU/ampoule).

0.2 % MRS medium prepared with the use of water, which had not been treated with ultraviolet light
No growth
0.2 % MRS medium prepared with use of water treated with ultraviolet light
3×10^{10}

Evaluation of viable cell counts in lactobacillus and bifidobacterium colonies grown in nutrient media containing water treated with ultraviolet light

Viable cell counts in colonies grown in nutrient media containing water treated with ultraviolet light were greater than the same for ordinary culture media (Tables 3,4).

Table 3

Viable cell counts in colonies grown in nutrient media containing water treated with ultraviolet light (CFU/ml) (Experiment No. 1).

Colonies isolated from MRS medium prepared with the use of water, which had not been treated with ultraviolet light.	$6 \times 10^3 \pm 1 \times 10^4$
Colonies isolated from MRS medium prepared with the use of water treated with ultraviolet light.	$3 \times 10^3 \pm 2 \times 10^3$

Table 4

Viable cell counts in colonies grown in nutrient media containing water treated with ultraviolet light (CFU) (Experiment No. 2).

Colonies isolated from MRS medium prepared with the use of water, which had not been treated with ultraviolet light.	$2.0 \times 10^3 \pm 3 \times 10^3$
Colonies isolated from MRS medium prepared with the use of water treated with ultraviolet light.	$1.4 \times 10^3 \pm 1 \times 10^3$

Meanwhile, the cultures grown on nutrition media containing water treated with ultraviolet light did not reproduce their properties during consecutive passage on ordinary media (Table 5).

Table 5

Survival in ordinary nutrient media of lactobacilli preincubated in growth media containing water treated with ultraviolet light.

Growth on 0.2 % MRS medium prepared with use of water treated with ultraviolet light	
Dilution	6
	$1 \times 10^3 \pm 1 \times 10^3$
Consecutive passage on 0.2 % MRS medium prepared with use of water, which had not been treated with ultraviolet light	
Dilution	6
	$1 \times 10^3 \pm 1 \times 10^3$

Survival of bifidobacteria in the growth media containing water treated with ultraviolet light was evaluated in a similar way (Table 6).

Table 6

Survival of bifidobacteria in the growth media containing water treated with ultraviolet light (CPU)

0.2 % Bactofoc medium prepared with use of water, which had not been treated with ultraviolet light	$2 \times 10^3 \pm 1 \times 10^4$
0.2 % Bactofoc medium prepared with use of water treated with ultraviolet light	$1.4 \times 10^3 \pm 3 \times 10^3$

Study of microbial antagonism in nutrition media containing water treated with ultraviolet light

Antagonism of lactobacilli in relation to colon bacilli, blue pus bacilli and staphylococci also increased in conditions of lactobacilli growing on media prepared with use of water treated with ultraviolet light. Statistically significant difference in activities was noted with respect to staphylococcus and E. coli. As

for blue pus bacilli, difference in activities did not reach the level of statistical significance (Table 7).

Table 7

Microbial antagonism of lactobacilli grown on culture media prepared with use of water treated with ultraviolet light (mm)

Staphylococcus aureus	Water treated with ultraviolet light	2 ± 0.5
	Water, which had not been treated with ultraviolet light	0.7 ± 0.1
Pseudomonas aeruginosa	Water treated with ultraviolet light	1 ± 0.2
	Water, which had not been treated with ultraviolet light	0.8 ± 0.3
Escherichia coli	Water treated with ultraviolet light	1 ± 0.3
	Water, which had not been treated with ultraviolet light	0.5 ± 0.3

Comparative study of the growth properties of lactobacillus cultures in nutrition media containing water treated with ultraviolet light and neutron flux

We evaluated the effect of water, which had been treated with another factor, on biological properties of test cultures; this effect was used as one of controls. For this purpose, we treated the water with a directed flux of thermal neutrons, measuring 0.2 neutrons/cm² per one second in density, for 14 days. This treatment corresponded to parameters of cosmic radiation acting on biologic objects during orbital flight. Results of this study are presented in Table 8.

Table 8

Survival of lactobacilli in growth media containing water treated with directed flux of neutrons

0.2 % MRS medium prepared with use of water, which had not been treated with a flux of neutrons	$1 \times 10^3 \pm 1 \times 10^3$
0.2 % MRS medium prepared with use of water treated with directed flux of neutrons	$1 \times 10^3 \pm 1 \times 10^3$

Data presented in this table are wholly compatible with the data on cultural growth of lactobacilli in nutrient growth media containing water treated with ultraviolet light. Apart from similarity of the data on cultural growth, MRS medium color change from light brown to light green was noted. The same change in color of MRS medium was noted in case of treatment with ultraviolet light. However, consecutive studies revealed differences between properties of lactobacillus colonies grown on media prepared with use of water treated with ultraviolet light and the same properties in cases of water treated with neutrons, with all the rest conditions of culturing being similar. Data on viable cells in colonies grown on both types of media are presented in Table 9 below.

Table 9

Viable cell counts for colonies in growth media containing water treated with different methods

Colonies isolated from MRS medium prepared with use of water treated with ultraviolet light	$8 \times 10^8 \pm 1 \times 10^8$
Colonies isolated from MRS medium prepared with use of water treated with neutron flux	$7 \times 10^8 \pm 1 \times 10^8$

Study of the frequency of genetic material transfer in liquid nutrient medium prepared with use of water treated with ultraviolet light

Frequency of genetic material transfer between mature cells of *E. coli* and integrity of this material did not depend on experimental conditions.

Table 10

Frequency of pRI plasmid transfer in nutrient media containing water treated with ultraviolet light

Water treated with ultraviolet light	$10^{-5} \pm 10^{-7}$
Water, which had not been treated with ultraviolet light	$10^{-5} \pm 10^{-7}$

All isolated clones of their experimental and control series preserved the whole set of phenotypic features controlled by the plasmid.

Study of *Saccharomyces cerevisiae* cultural properties

Primary study of the effects of water treated with ultraviolet light on the counts of viable units of *Saccharomyces cerevisiae* yeast was carried out. Results of this study are presented in Table 11.

Table 11

Study of *Saccharomyces cerevisiae* cultural properties

Determination of yeast counts	Yeast spore counts
Media prepared with use of distilled water (mean value)	3.4×10^8 cells/ml
Media prepared with the use of water treated with ultraviolet light (mean value)	2.5×10^{10} cells/ml

As the presented data show, statistically significant increase in the viable cell counts was noted in case of primary inoculation with yeast spore suspension of medium prepared with use of water treated with ultraviolet light as compared to the same counts for similar inoculation of standard media. Therefore, structure of water subjected to ultraviolet light facilitated the exit from anabiosis of significantly greater number of cells (but not all cells).

Agreement was reached on carrying out the studies evaluating the effects of water treated with ultraviolet light on kinetics of yeast development, with use of the water for primary suspending the dry mass of yeast and use of physiologic salt solution as a control.

Enzymatic activity of cultures grown in nutrient media containing water treated with ultraviolet light

Data presented in the Table 12 show the absence of significant differences in enzymatic activity of cultures grown on nutrient media containing water treated with ultraviolet light as compared to control.

Table 12

Enzymatic activity of cultures grown on media containing water treated with ultraviolet light

Determination of yeast counts	Yeast spore counts
Media prepared with use of distilled water (mean value)	3.4×10^8 cells/ml
Media prepared with the use of water treated with ultraviolet light (mean value)	2.5×10^{10} cells/ml

Study of the effects of modified water on kinetics of *Saccharomyces cerevisiae* yeast development

The first series of preliminary experiments included the studies, which determined the effects of modified water (MW) treated with ultraviolet light on the counts of colony-forming units of yeast during exit from anabiosis.

Procedure and results of the study

A strain of bakery yeast used by Bakery Plant No. 21 was chosen for the experiments.

A 0.5 g weight of dry yeast was subjected to suspending in 10 ml of physiologic salt solution for 5 to 10 minutes. Then, plating was carried out on culture dishes with Saburo and wort agar nutrient media prepared with the use of distilled water and MW. Inoculated media were incubated in a thermostat at 29 °C for two days.

Simultaneously, number of yeast cells in the original suspension was counted. Counting the yeast spores in the suspension was carried out using Goryaev's counting chamber.

Results of the studies, which have been carried out, are shown in Table 13.

Table 13

Survival of bakery yeast in growth media containing water treated with ultraviolet light

Determination of yeast counts	Yeast spore counts
Media prepared with use of distilled water (mean value)	3.4×10^8 cells/ml
Media prepared with the use of water treated with ultraviolet light (mean value)	2.5×10^{10} cells/ml

As the presented data show, statistically significant increase in the viable cell counts was noted in case of primary inoculation with yeast spore suspension of medium prepared with use of MW as compared to the

same counts for similar inoculation of standard media. Therefore, primary inoculation with yeast of nutrient media prepared with use of MW facilitated the exit from anabiosis of significantly greater number of cells (but not all cells).

The second series of experiments included the studies aimed at evaluating the effects of MW on kinetics of yeast development.

Procedure and results of the study

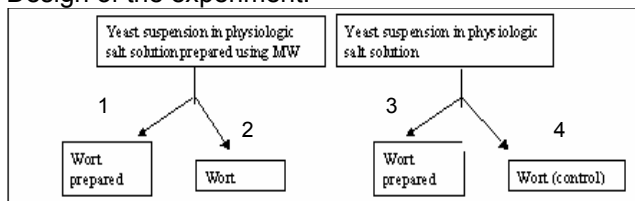
A strain of bakery yeast used in Bakery Plant Ng. 21 was chosen for these experiments.

A 0.2 g weight of dry yeast was subjected to suspending for 15 to 20 minutes.

1 and 2 - in 5 ml of physiologic salt solution prepared with use of MW;

3 and 4 - in 5 ml of ordinary physiologic salt solution.

Design of the experiment:



After this, inoculation of solid and liquid nutrient media was carried out (amount of liquid medium in flasks was 25 ml):

1 and 3 (in 7-6 B) - wort prepared with the use of only MW;

2 and 4 (in 7-6 B) - ordinary wort. Inoculation of solid nutrient media was carried out with the use of serial dilutions of original yeast suspension; triple repetition of plating on dishes was used; inoculation of corresponding media was carried out. Inoculated media were incubated in a thermostat at 29 °C for two days. Number of colony-forming units (CFU) counted for this inoculation corresponded to zero time point of yeast development curve.

One milliliter of yeast suspension containing 1×10^7 to 2×10^7 cells was transferred to liquid media prepared with the use of corresponding solutions (see the diagram). Total number of cells contained in the suspension was counted with the use of Goryaev's chamber. Flasks with liquid media and inoculates were incubated in a thermostat at 29 °C in the course of the whole experiment. Collecting the samples for microscopic examination and inoculation was carried out with obtaining no more than 0.2 ml of material from each flask at each sampling. Inoculation of similar solid media was carried out (see the diagram). Description of inoculation procedure is presented above. Microscopic examination was used for evaluating the condition of yeast culture or monitoring the process of its development by counting the total number of cells. This was done for more accurate

determining the timing of different stages of yeast growth.

As a result of the carried out studies, yeast CFU counts were determined for different conditions and time points of development. Time course of *Saccharomyces cerevisiae* yeast growth in liquid media is presented in Fig. 1.

Three phases of development were clearly demonstrated for all the studied variants: lag phase, logarithmic growth phase and stationary phase.

Phase 1 (lag phase) was a period occupied by adaptation to surrounding medium of the yeast cells introduced by us, as well as their preparation for budding. For all variants, the budding started at four hours. However, the daughter cells had not been mature yet and did not increase the number of CFU.

According to obtained data, this phase of yeast growth, as well as baseline number of cells exiting from anabiosis due to MW and their possible condition, played an important role.

The greatest yeast CFU count during exit from anabiosis was noted in the first variant: in this case, CFU count corresponded to total cell count determined with the use of Goryaev's chamber. Microscopic examination of this suspension carried out in the course of the first two to three hours revealed the yeast cells sized 12 to 14 μm (normal cell size = 6 to 8 (10) μm). Possibly, the membranes of these cells facilitated the intracellular accumulation of substances, whereas the enzymatic systems had insufficient time for switching to synthesis of necessary organelles, which resulted, possibly, in the absence of multiplication in the cells, which were ready for budding. At three to four hours, the nutrient liquid contained only those cells, which were adapted to the given medium, and the budding started.

Phase 2 (logarithmic growth of cells) was a period characterized by highly active multiplication of cells. For all the studied variants, this period lasted for 8 to 10 hours. In the second, third and fourth variants, the rates of multiplication of cells during the initial period of this phase were nearly equal and corresponded to baseline number of cells adapted to experimental conditions. Henceforward, the lagging in formation of new mature generations of cells was noted; this lagging was especially prominent in the second variant.

Maximum growth rate of yeast cells during this period was noted in the fourth variant. The remaining cells adapted to conditions of the experiment started a quick growth and reached their maximum CFU counts at 13 to 14 hours.

Phase 3 (stationary phase) was observed at 13 to 14 hours and corresponded to a virtually stopped new cells formation. Microscopic examination carried out during this period revealed the termination of budding.

Number of cells in diploid stage did not exceed 3 to 2 percent.

By 14 hours of the experiment, number of CFU cells for all variants increased by 3 to 3.5 orders of magnitude (3,000 to 3,500). Therefore, culture media contained roughly equal amounts of nutrients.

Thus, the conducted studies have shown, that:

- use of MW facilitated the exit from anabiosis condition of the greatest number of yeast cells;

- for decreasing the sensitivity of yeast cells to conditions of culturing in case of using the double effect of MW (Variant 4: physiologic salt solution prepared with the use of MW + nutrient medium prepared with use of MW) ensuring the exit from anabiosis of the greatest number of cells, culture medium, temperature, pH, culture medium aeration, etc. shall be selected for their recommending to yeast manufacturers;

- in the studies, which have been carried out, the growth in yeast CFU counts did not depend on the use of MW in culture liquids: it depended only on the amounts of nutrients contained in them.

For using the MW in bread-making and alcohol production, it is necessary to know the following yeast parameters: rising capacity, maltase activity and resistance to thermal effects.

Table 14

Presence of additional growth in experimental and control media in conditions of prolonged lactobacillus cultures exposure.

Week of exposure	Control media	Experimental media
1	-	-
2	-	-
3	-	-
4	-	-
5	+	-
6	+	-
7	+	-
8	+	-

CONCLUSION

The studies, which have been carried out, convincingly showed, that the use of water treated with ultraviolet light in technologies process resulted in increased growth of micro organisms used in foods production biotechnologies. Use of water treated with ultraviolet light increases the probability of micro organisms revivification from expired lyophilized collections and makes it possible to include archive micro organisms in production process quickly and productively, without the need for multiple time-consuming passage steps. This approach results in quick accumulation of biomass. One more positive feature of water treated with ultraviolet light is the absence of reproduction of modified properties by the objects being tested after withdrawal of this water;

that is, the modified properties, obviously, are not the consequences of genetic changes in test objects (the micro organisms being studied). Cultures grown on nutrient media containing water treated with ultraviolet light increased the production of bacteriocin. Therefore, the medium used for growing the objects being tested becomes aggressive with respect to external colonization. This feature was confirmed by results of prolonged bacterial cultures exposure on media prepared with use of water treated with ultraviolet light and on control media (see Table 19). In case of exposure of cultures on media containing water treated with ultraviolet light, contamination with other cultures was absent, whereas the control media showed an additional growth already on the fourth week.

One of the important features of nutrient media prepared with use of water treated with ultraviolet light was stability of their properties: the gap between experiments on survival of lactobacilli was two months, and the break in cultural activity of micro organisms grown in conditions of experiment and control remained unchanged.

Absence of expressed enzymatic activity of experimental and control micro organisms is a disputable result, because other experiments demonstrated an increase in activity of bacteriocin, which, like hemolysin and beta-lactamase, is an exoenzyme. Therefore, these data need verification in the course of implementing the second stage of the agreement.

Frequency of transfer of genetic markers between bacteria did not depend on conditions of culturing.

The following possible places of installation of the units related to the use of culture media and biologic objects for implementing the process being studied can be proposed:

A. Sour milk products manufacturing

1. Block of reconstitution of industrial strains of micro organisms from lyophilized condition;
2. Barm preparing block;
3. Sour milk products preparing block.

B. Bread-making

1. Block of reconstitution of industrial strains of micro organisms from lyophilized condition;
2. Barm preparing block;
3. Dough preparing block.

C. Preparing the beer yeast

1. Block of reconstitution of industrial strains of micro organisms from lyophilized condition;
2. Beer yeast preparing block;
3. Beer preparing block.

D. Preparing the inoculum for biological degradation of food products and physiologic waste

1. Block of reconstituting strains and micro organism associations from lyophilized condition;
2. Block of preparing the inoculum;
3. Fermentation block.

E. Preparation of soil bacteria colonies

1. Block of reconstituting the industrial strains of micro organisms from lyophilized condition;

Conclusion

1. In the process of lactobacillus, bifidobacterium or bakery yeast cultures reconstitution from inactive (lyophilized or dried) condition with the use of culture media containing water treated with ultraviolet light, number of colony-forming cells increased roughly 100 fold.
2. This process was accompanied by an approximately 10-fold increase in the biomass of the colonies.
3. Culturing lactobacilli in the media containing water treated with ultraviolet light was accompanied by increase in bacteriocin production.
4. Carrying out the bacterial conjugation in liquid media prepared with the use of water treated with ultraviolet light was not accompanied by changes in the frequency of plasmids transfer or changes in plasmid segregation stability.
5. The specified features were not reproduced in case of lactobacilli or bifidobacteria passage to

ordinary media after exposure in the media containing water treated with ultraviolet light.

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MIND/BODY MEDICINE AND STRESS MANAGEMENT

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Abstract

The purpose of this review article was to introduce key concepts of psychosomatic medicine or mind/body medicine, and to show the importance of stress management in clinical practice and daily life. According to the Japanese National Survey of Health in 2001, 49.0 % of the Japanese people (> 12 years old, n = 109 million) perceived some psychosocial stress. Such stress was more frequently perceived when they complained of any physical or psychological symptoms. A specific illness can be caused, when the stressors are too intense and persistent, or when persons are vulnerable to the stressors because of their character and ability to adapt. In a clinical population, psychosocial stress is closely related to mind/body symptoms. Our own study has shown that the reporting of somatic symptoms is a good predictor of major depression or depression-related symptoms such as suicidal ideation in outpatients attending Japanese mind/body medicine clinics. Concerning the therapeutic effects of mind/body medicine interventions, relaxation and stress management techniques have been commonly applied for various diseases, such as anxiety disorders, mild and moderate depression, hypertension, insomnia, and irritable bowel syndrome. The relaxation response counteracts the harmful effects of stress in such diseases. Medicine can be seen as a three-legged stool, balanced equally by three healing resources (medication, surgery and self-care).

Key Words: Anxiety, Depression, Mind/body Medicine, Psychosomatic Medicine, Relaxation, Stress Management.

1. Recent epidemics of stress in Japan

Stress is the term used to define the body's physiological and/or psychological reaction to circumstances that require behavioural adjustment. According to the recent Japanese National Survey of Health¹⁾, 49.0 % of the Japanese people perceived stress in their daily lives. In this survey, the subjects answered "yes" if they perceived any of the stressors for 22 life-related categories including work, family, neighborhood relations, as well as living-, social-, financial-, and health related situations. The percentage of those with perceived stress was higher in women (52.6%) than in men (45.1%), and has continued to increase in both sexes. Work-related

problem was the most frequent stressor, followed by health-related problems and financial problems¹⁾.

One of the interesting findings of this survey was that stress was more frequently perceived when patients complained of any physical or psychological symptom; 70.4 % of those with such symptoms (n = 33 million) reported having stress whereas 41.3% of those without symptoms (n = 67 million) reported having stress (p < 0.0001, chi-square test)¹⁾. These results suggest that those perceiving psychosocial stress are likely to complain of mind/body symptoms.

2. Mind/body medicine in Japan

The symptoms related to psychosocial stress are often temporary and would disappear with the relief of

such stress. However, specific illness may be caused when the suffering stressors are too intense and persistent. When people are vulnerable to stress because of their character and ability to adapt, mind/body illness is likely to occur even if the stressors are mild or moderate. For example, diet restriction is a common behaviour especially in young women, but those with eating disorders (e.g. anorexia nervosa and bulimia nervosa) are known to have characteristics such as depression²⁾ or excessive adaptation³⁾.

The Japanese Society of Psychosomatic Medicine defines "psychosomatic illness" as any physical condition with organic or functional damage affected by psychosocial factors in the process of its onset or development⁴⁾. This definition largely corresponds to that of "psychosocial factors affecting general medical conditions (code 316.00)" of the Diagnostic and Statistical Manual of Mental Disorders, Third Edition Revised⁵⁾ or Fourth Edition (DSM-IV)⁶⁾, published by American Psychiatric Association. Because the term of 'psychosomatic' often sounds like something 'neurotic' or 'hypochondriacal', the term 'mind/body' has recently been used to describe the association between mind and body.

Clinicians find the management of mind/body illness difficult, challenging, and time-consuming. Thus, patients with mind/body illness are often referred to mind/body medicine clinics along with patients with specific diagnoses, such as chronic pain, insomnia, and cardiac conditions.

In Japan seven universities as well as a few regional hospitals have separate and independent mind/body medicine departments and almost three thousand physicians and psychotherapists are the members of the Japanese Society of Psychosomatic Medicine. In contrast to Germany⁷⁾, the build-up of the units of mind/body medicine and psychotherapy was not made systematically and they were officially recognized with great effort in 1997.

There are no mind/body medicine clinics in most countries, and therefore the knowledge of mind/body medicine needs to be a part of every day work for all physicians. Also of importance, the organization of stress care programs involving physicians, nurses, psychologists, and other health-care specialists would be beneficial to mind/body medicine activities when the build-up of mind/body medicine clinics is not promising in such countries.

3. Diagnosis of mind/body medicine

Because international criteria of mind/body illness do not exist, not only diagnoses by the International Statistical Classification of Diseases and Related

Health Problems, Tenth Edition (ICD-10)⁸⁾ but the DSM-III-R or DSM-IV diagnoses for psychiatric disorders have been recorded up at the Department of Psychosomatic Medicine, the University of Tokyo School of Medicine⁹⁾, which has been one of the central institutes leading mind/body practice, research and education in Japan.

In this institute, the major physical disorders seen were autonomic nervous dysfunction, irritable bowel syndrome, essential hypertension, and hyperventilation⁹⁾. [Table 1] Eating disorder, anxiety disorder, and depressive episodes were also frequently seen in this institute. Concerning psychiatric diagnoses, the numbers of "somatoform disorders not otherwise specified" were the largest in both the DSM-III-R and DSM-IV groups, followed by bulimia nervosa, depressive disorder not otherwise specified, anorexia nervosa, conversion disorder, major depression or depressive disorder, panic disorder with agoraphobia, and psychological factors affecting the physical or medical condition.

These findings seem to be atypical when compared with the previous studies of Western countries. For example, a study of Italian mind/body clinic showed that the most frequent mind/body diagnostic finding was recorded under the rubric of "psychological factors affecting physical condition", followed by affective illness, anxiety disturbance, and somatoform disorders according to the DSM-III criteria. In our Japanese study⁹⁾, a detailed manual of diagnoses was made and the physicians specializing in mind/body medicine discussed the patients' diagnoses in order to improve the reliability of diagnoses. Thus the results reinforce the belief that both the DSM-III-R and DSM-IV axis I is largely inadequate for describing mind/body phenomena^{10,11)}.

New diagnostic systems for use in mind/body research are now being developed in Japan¹²⁾. One of the most important research areas within mind/body medicine field is to construct the international disease criteria of mind/body illness conditions. This has been attempted in some disorders including irritable bowel syndrome and tension-type headache. For the diagnostic research in mind/body medicine, there are several key concepts. Two psychological concepts, alexithymia and somatosensory amplification, are summarized in the next section.

4. Concepts for the understanding of the mind/body phenomenon

Alexithymia is a personality construct derived from clinical observations of patients with mind/body diseases, characterized by difficulty distinguishing

between emotions and bodily sensations¹³⁾. The Toronto Alexithymia Scale (TAS) and its modified version, the TAS-R and TAS-20 are among the most common questionnaires to measure this construct¹⁴⁾. Somatosensory amplification refers to the tendency to experience somatic sensation as intense, noxious, and disturbing¹⁵⁾. The construct of somatosensory amplitude is helpful in the assessment of the perceptual style of somatization and in the conceptualization of mind/body illness. The Somatosensory Amplification Scale (SSAS) was designed and validated to measure this phenomenon¹⁶⁾.

Evidence has suggested that the tendency to develop functional somatic symptoms is associated with alexithymia¹⁷⁻¹⁹⁾. Our recent study reported that the SSAS was significantly correlated with the part of the TAS, which includes difficulties in identifying and describing emotions in the sample with mind/body illness²⁰⁾. It makes sense that somatosensory amplification is linked to alexithymic characteristics statistically and clinically. The roles of the two psychological concepts in clinical conditions need further study to clarify pathogenesis of mind/body illness in the future.

5. Example of mind/body connection: somatic symptoms and depression

Somatic manifestation of depression may be a good example to show mind/body connections of health conditions. Although depression itself does not meet the criteria of mind/body illness, somatic symptoms are common in depression. In some cases, the affective and cognitive symptoms of depression are hidden behind a variety of somatic complaints in so-called "masked depression" or "mild depression"²¹⁾.

More than 30,000 people commit suicide annually in Japan, and the number has dramatically increased with the Japanese economic recession after 1998²²⁾. Many employees are forced to work hard because of the ongoing business restructuring, and some workers who have committed suicide have been officially acknowledged as victims of depression caused by overwork for the past 5 years. There is little doubt that depression is closely associated with suicide²³⁻²⁵⁾. From the viewpoint of risk management, it is clinically and economically important to detect depression earlier because the natural disease course can be changed by anti-depressive regimens^{26,27)} and because earlier detection of depression reduces the direct costs of prolonged depression, including the costs of medications, hospital cares, and community-based cares; as well

as the indirect costs, such as loss of earning, lost productivity, and unemployment²⁸⁾.

Considering these situations, our group has tried to clarify the relationship between depression and somatic symptoms and to use somatic symptoms for the screening of depression by the reporting of somatic symptoms²⁹⁻³¹⁾. First, the prevalence of somatic symptoms and psychiatric characteristics of major depression were examined in a Japanese mind/body outpatient clinic (n = 2,215)²⁹⁾. In the total sample, 91 outpatients (4.1%) were diagnosed with the DSM-III-R or DSM-IV major depression. Prevalence of fatigue (86%), insomnia (79%), nausea/vomiting (50%), and back pain (36%) as well as the degree of psychosocial stress (DSM-III-R axis IV) were higher (all p<0.05) and scores of global assessment of psychosocial functioning (DSM-III-R/DSM-IV axis V) were lower (p<0.001) in the major depressive patients compared to the remaining outpatients. The most interesting finding of the study was the dose-response relationship between the severity of major depression and the total number of somatic symptoms reported. Although it was not surprising that the scores on Zung's Self-Depression Scale (SDS) increased as the severity of major depression became greater, the total number of somatic symptoms increased with the disease severity as well. [Figure 1] These findings suggest that the level of depression is closely linked to the reporting of somatic symptoms in a mind/body medicine population.

Next, 863 outpatients were studied in the same Japanese mind/body medicine clinic to examine associations of suicidal ideation with somatic symptoms and mood states, using the Cornell Medical Index Questionnaire and the Profile of Mood States (POMS)³⁰⁾. In the study, 266 patients (31%) reported suicidal ideation and the age- and sex-adjusted odds ratios (typically in 1.5-2.5 range) of somatic symptoms for suicide ideation showed statistically significant differences (p < 0.05) for 13 of 15 symptoms. The total number of somatic symptoms and scores on the POMS depression scale predicted suicidal ideation (p<0.05) through a multiple regression analysis. This suggested that an evaluation of somatic symptoms might be important to assess the specific symptom of depression and suicidal ideation in a mind/body medicine population. In addition to these clinical studies on the connection between somatic symptoms and depressive symptoms^{29,30)}, screening practices for detecting major depression were evaluated in workers complaining of somatic symptoms³¹⁾. A total of 1,443 Japanese white-collar employees completed a

medical symptom checklist (major 12 somatic symptoms) and were then diagnosed using the structured clinical interviews of the DSM-IV. There were 42 cases (2.9%) with major depression in the total sample. Concerning the 902 subjects without any somatic symptoms, only one case (0.1%) was identified as having major depression. The prevalence of the disorder was positively associated ($p < 0.001$) with the total number of somatic symptoms, and the area under the receiver operator characteristic (ROC) curve was 0.92 for men and 0.81 for women, which showed the sensitivity and specificity of the total number of somatic symptoms for detecting major depression. Based on the findings of these studies, the number of reported somatic symptoms was found to be a simple and useful predictor of major depression in both clinical and working populations.

6. Mind/body medicine in treatment: biofeedback and hypertension

Clinical effects of biofeedback on hypertension are discussed in this section as an example of a treatment strategy in mind/body medicine. Biofeedback is a kind of relaxation training and is part of a group of non-pharmacological therapeutic procedures that use electronic instruments to measure, process, and provide information to patients regarding their neuromuscular and autonomic nervous system activity in the form of analogue (or binary) and visual (or auditory) signals³²⁻³⁴. Recent technical improvements in blood pressure monitoring and data processing make biofeedback more reliable and comfortable to apply for the treatment of hypertension. For example, our group developed an easy-to-use blood pressure biofeedback system in combination with a continuous blood pressure monitoring device and a personal computer^{35,36}, and reported that the system was useful in treating hypertension including essential hypertension, white-coat hypertension, and mild hypertension without organ damage³⁷⁻³⁹.

Because the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure, Seventh Report (JNC-VII) recommends that hypertension be prevented or managed to reduce morbidity and mortality by the least intrusive means possible⁴⁰, biofeedback has been used as a second-line non-pharmacological treatment for essential hypertension in the early stages^{41,42}. Concerning lifestyle modifications, biofeedback training may help hypertensive patients to become aware of the importance of controlling blood pressure⁴³ and of changing to a health-promoting lifestyle⁴⁴.

To assess treatment effects of biofeedback to lower blood pressure in essential hypertension qualitatively and quantitatively, a meta-analysis of studies conducted between 1966 and 2001 was made⁴⁵. A total of 22 randomized controlled studies with 905 essential hypertensive patients were selected for review. Compared with clinical visits or self-monitoring of blood pressure (non-intervention controls), the reduction in systolic and diastolic blood pressures was significantly greater in the biofeedback intervention by 7.3 [95% confident interval, 2.6, 12.0] and 5.8 [2.9, 8.6] mmHg, respectively. When biofeedback intervention was compared with sham or non-specific behavioral intervention controls, the net changes of systolic and diastolic blood pressures were 3.9 [-0.3 to 8.2] and 3.5 [-0.1, 7.0] mmHg, respectively. The results of multiple regression analysis also indicated that biofeedback intervention decreased systolic and diastolic blood pressure more than non-intervention controls ($P < 0.001$), but not more than sham or non-specific behavioral intervention controls ($P > 0.05$), controlling for the effects of initial blood pressure. When biofeedback intervention types were classified into two types: simple biofeedback group and relaxation-assisted biofeedback group, only the relaxation-assisted biofeedback group significantly decreased ($P < 0.05$) both the systolic and diastolic blood pressures, compared with sham or non-specific behavioral intervention controls⁴⁵. [Figure 2]

The results suggested that biofeedback was more effective in reducing blood pressure for essential hypertension than no intervention. However, this treatment was suggested to be superior to sham or non-specific behavioral intervention in essential hypertension only when combined with other relaxation techniques.

7. General relaxation response

As suggested in the meta-analysis of the biofeedback treatment for hypertension, the relaxation training may be a simple and useful method to calm persistent hyperactivity of the sympathetic nervous system. According to the series of works by Herbert Benson^{33,46,47}, the relaxation response is defined as the physiological and psychological opposite of the arousal or stress response, characterized by decreased metabolism, blood pressure, rate of breathing and heart rate in association with feelings of calmness and control. From traditional Eastern and Western techniques (e.g. pray, zen, yoga, and meditation), four basic components have been proposed to bring forth the relaxation response⁴⁸.

(1) *A quiet environment*: Ideally a quiet room with as few distractions as possible is suitable. The quiet environment contributes to the effectiveness of the repeated word or phrase by making it easier to eliminate distracting thoughts.

(2) *A mental device*: To shift the mind from logical, externally oriented thought, there should be a constant stimulus: a sound, word, or phrase repeated silently or aloud; or fixed gazing at an object. The repetition of the word or phrase is a way to help trainees break distracting thoughts. The eyes are usually closed when making a repeated sound or word. Attention to the normal rhythm of breathing is also useful and enhances the repetition of the sound or the word.

(3) *A passive attitude*: When distracting thoughts occur, they are to be disregarded and attention redirected to the repetition or gazing. It is important to adopt a "let it happen" attitude not to worry how well the technique is performed. The passive attitude is perhaps the most important element in eliciting the relaxation response.

(4) *A comfortable position*: A comfortable posture is important so that there is no undue muscular tension. Some methods call for a sitting position. A few practitioners use the cross-legged position of yoga. Trainees should be comfortable and relaxed.

The subjective feelings that accompany the elicitation of the relaxation response vary among individuals. The majority of people feel a sense of calm and feel very relaxed. Other descriptions involve feelings of pleasure, refreshment, and well-being. Regardless of the subjective feelings, it has been found that the physiological changes, such as decreased oxygen consumption, are taking place⁴⁸⁾.

8. Systematic stress management program

Based on the regular elicitation of the relaxation response, standardized stress management programs have been applied for various diseases at Mind/Body Medical Institute, Harvard Medical School. Subjects were referred from primary care settings located within the hospital as well as from clinics outside the hospital. The Medical Symptom Reduction Program is a 10-week program in which the most outpatients participated⁴⁹⁾. It consists of 9 weekly two-hour sessions and one four-hour session that includes instruction in the elicitation of the relaxation response, cognitive restructuring, coping, stress hardiness, nutrition, and body awareness. To elicit the relaxation response, patients systematically practiced yoga, diaphragmatic breath awareness exercise, emotional imagery, and meditation throughout the program. Using these techniques,

they were instructed to elicit the relaxation response at home each day for 20 minutes or twice a day for 10 minutes.

To identify stressors and corresponding physical sensations and emotions, patients were assigned to complete a diary every day throughout the program. Lectures and group discussions focused on mind/body awareness during the first 5 sessions. Patients were taught cognitive restructuring skills; they learned to recognize autonomic thoughts and cognitive distortions associated with stress-related physical and psychological symptoms. Patients also received handouts about the nature of thoughts and cognitive distortions, and reviewed them at home.

During the latter 5 sessions, lectures and group discussions focused on self-control and coping (problem-, emotion-, and physical-focused coping styles). The lectures included coping with humor, empathetic communication for social support, and relapse prevention strategies. Through a series of lectures together with the relaxation training, patients improved their stress management skills, which resulted in decreased psychological and somatic symptoms.

The treatment effect was examined in 1,312 outpatients attending this program⁴⁹⁾. The Medical Symptom Checklist (12 major symptoms), Symptom Checklist 90 Revised (SCL-90R), Stress Perception Scale, and the Health-Promoting Lifestyle Profile were administered before and after the program. Of the entire sample, 1,012 patients completed the program, and 911 completed the post-treatment assessment. Self-reported frequency of medical symptoms, degree of discomfort, and interference with daily activities were significantly reduced as a result of the program. Anxiety and other psychological distress as measured by the SCL-90R and stress perception scales also showed significant reductions. Furthermore, health-promoting lifestyle functioning significantly improved. High levels of pre-treatment anxiety predicted a decrease in the total number of medical symptoms endorsed. In this study, it was found that these interventions were effective in reducing medical symptoms coinciding with an improvement in anxiety and that high anxiety at program entry may predict better outcome.

The other studies of this program revealed that gender is an important factor in relation to the report of somatic symptoms in stress-related conditions⁵⁰⁾, the program is suitable for the treatment of both physical and psychological symptoms among somatizing patients⁵¹⁾, and the effectiveness of the program was not diminished by a few absences

although depressed or less educated patients are likely to drop out from the intervention⁵²⁾.

9. Summary

As suggested by Herbert Benson⁴⁸⁾, medicine should be as sturdy as a three-legged stool, balanced equally by three healing resources – medications, surgery and other medical procedures, and self-care approaches. Ideally, medicine would be able to call upon self-care for more than half of the everyday problems that patients experience. All three legs are mandatory and we would draw approximately upon the medicines and surgeries whenever necessary. In Japan, the medical expenses have been increasing, and the medical insurance system needs to be reorganized. In this situation, stress management is strongly required for improvement in quality of life both physically and psychologically.

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Table 1

Major ICD-10 diagnoses in a Japanese mind/body medicine clinic

ICD-10 diagnosis	n (%)
Eating disorder	171 (11.9%)
<i>Bulim ia nervosa</i>	97 (6.8%)
<i>Bulim ia nervosa</i>	97 (6.8%)
<i>Anorexia nervosa</i>	74 (5.2%)
Anxiety disorders	108 (7.5%)
Autonomic nervous dysfunction	99 (6.9%)
Somatoform disorder	90 (6.3%)
<i>Neurocirculatory asthenia</i>	34 (2.4%)
Irritable bowel syndrome	73 (5.1%)
Dissociative disorder	70 (4.9%)
Reaction to severe stress	59 (4.1%)
Depressive episode	59 (4.1%)
Essential hypertension	43 (3.0%)
Breathing abnormalities	43 (3.0%)
<i>Hyperventilation</i>	43 (3.0%)
Other ICD-10 diagnoses*	545 (38.1%)
No diagnosis	72 (5.0%)
Total	1,432 (100%)

Data was derived from the Psychosomatic Clinic, Tokyo University Hospital during 1994-1996. Other ICD diagnoses were not specified in the table, because the percentage of each diagnosis was small (< 3.0%).

Figure legends

Figure 1

SDS scores and total number of somatic symptoms in mild (n = 21), moderate (n = 38), and severe major depression (n = 32).

Values are means with standard errors of the scores, and p values are based on the Morrison's multiple comparison method.

Figure 2

A meta-analysis of effects of biofeedback interventions on lowering systolic blood pressure in essential hypertension.

The no intervention control group included self-monitoring of blood pressure and clinical visits. The sham intervention group included sham or non-specific behavioral interventions. Values are the net reductions in systolic blood pressure by biofeedback intervention.

Figure 1

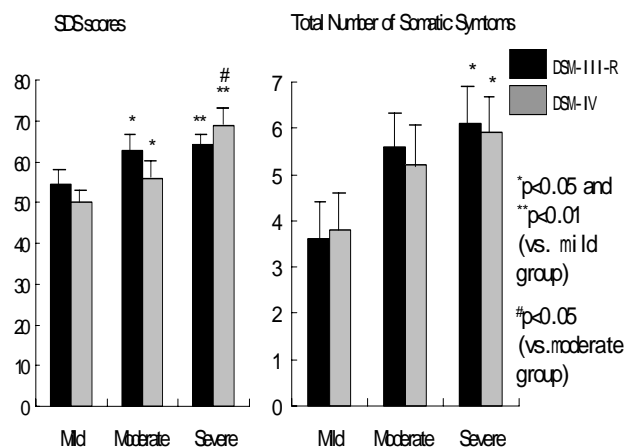
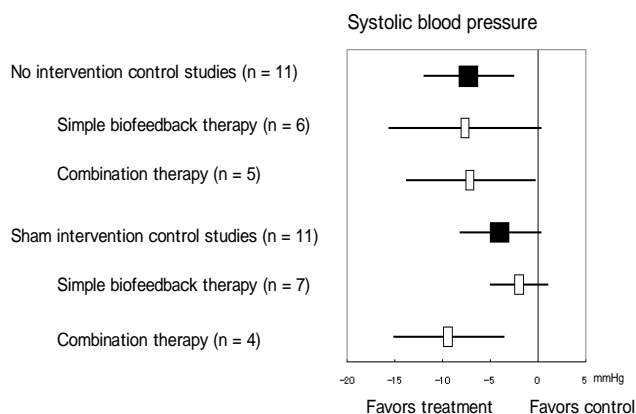


Figure 2



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THE POSSIBILITY TO COMMUNICATE, INTERCHANGE AND SHARE THE HEALTH AND RISK RELATED VIEW AMONG ORDINARY PEOPLE LIVING IN DIFFERENT ASIAN COUNTRIES

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Abstract

For every people, sharing and learning of risk-related realities in daily life is important, and such sharing is seemed to be substantialized in a visible manner in EU member nations and in North America. However, in Asian countries, the situation is far behind. Lots of barriers (such as culture, politics, geographic location, language, etc.) exist to prohibit meaningful sharing and learning even within a country as Japan. In the present paper, the author aimed to develop a new approach for people to communicate, interchange and share the life related view of environment, health and risk.

Keywords: Health education, Risk education, Health promotion, Participation, Educational strategy, Asian perspective

1. What is important as the strategy of health risk education?

Recently, many people understand that our living world is full of risks. Whenever some large scale accidents and/or disasters happen in other parts of world, people recognize that they are not immune to these accidents and/or disasters. Nowadays, people are living in a border-less society in relation to risk. People think that they are able to predict and manipulate their nearest future and such predictability and the sense of manipulation accompanies the notion of risk. However, people's recognition and manipulation of their daily life and related risks are not the same. Some people are under the constant pressure of risks. Some other people can even enjoy their daily risk. Under such diversity of risk related recognition, people are not open to share their risk-related understanding, and such situation is commonly observed in Japan. Therefore, the goal of education of health risk management is not merely a giving of risk related information to avoid health risks. It is more important to empower people to realize, enjoy, participate and challenge the reality of this world by sharing and learning other people's unique daily lives and related views.

2. Limit of traditional health education that focused on a reduction of a specified risk

Before starting to think about the people's empowerment in health risk education, the traditional style of health education will be looked back. The most popular style of health risk education used to focus on some specified risk to improve health status. In Japan, typical examples can be sought in salt-intake-reduction education and non-smoking education. This type of health risk education used to be very popular in Japan during 20th century. Recently, however, health educators are expected to deal with much more topics and/or risk factors. For example, Healthy Japan 21, the Japanese overall health promotion plan¹, declares over 70 pieces of targeted values of health promotion. For most of people, however, a single targeted value, such as decrease of salt intake and/or decrease of smoking, is already enough to offer meaningful challenges toward their healthier life. In this instance, how people are able to face and manipulate over 70 pieces of targeted values instead of a piece of value? Seventy of pieces are too many? This is a typical question that annoys not only people but also health educators in the ongoing Japanese health promotion movement². The reality is that, in stead of accepting meaningful challenges included in Healthy Japan 21,

many people are overwhelmed by too many targeted values. Then, how we will be able to accept multiple targeted values and its accompanying reality without losing our positive and meaningful identity to our life?

3. How to establish sound and meaningful attitude of people toward multiple risks?

Thinking about the present world that is filled with risks, the starting point of health risk education is 1) not to be overwhelmed by multiple risks, and 2) to empower people to recognize and challenge toward their healthier daily life. When people realize the diversity of individual life, the traditional education that value people's uniformity does not work. Promoting one's individuality and one's uniqueness should be the basis. However, how are we able to promote individuality and uniqueness in the stream of risk education? The author focused his research to develop a sensitive inquiry to let people to think about their life related individuality and uniqueness. The forerunner of this research is an inquiry to let children to think about their environment. As the result of this research, the author developed an inquiry called WIFY (what is important for you?)³.

In order to think about the sensitivity of inquiry to touch the life related reality of people, the experience of WIFY will be served as a reference. At the beginning of development, the author tried lots of different inquiries to children about their environment. Suppose that the following two inquiries (A and B) were tested. As an inquiry A, the author asked "what do you image about environment?", and a child replied "Clean water, Dioxin-free foods, and sustainable development". Then, as an inquiry B, the author asked "what do you like about your daily life?" and the same child replied "Watching TV, going to school, playing game, playing soccer". Between these two replies of A and B, reply A refers to important key words of environment. Speaking from the viewpoint of technical knowledge level of environment, reply A sounds more preferable. Further inquiries revealed that the child replied his concerns related to his previous learning at school. In comparison to reply A, reply B does not contain any technical key words regarding environment. All of words in reply B reflect the real concerns of the child in his daily life. Therefore, if the life related reality of subject is valued, attitudes to give this type of reply B should be more encouraged. Then, the author focused on type B reply, tested and elaborated his way of asking inquiries, and finally developed WIFY. Therefore, WIFY is simple and interactive. The basic question of WIFY is as follows: "Name five matters of importance in your life that you would miss if you lost them." This same basic question is asked in each of the following three situations;

(1) "Imagine your daily life beginning in the morning, continuing through into the afternoon and evening."

(2) "Imagine your home, your neighbors, your workplace and your community."

(3) "Imagine your region, your country as a whole, your continent, and the planet earth."

4. Application of WIFY to risk education

After the development of WIFY, the authors started to ask WIFY for people with diversified backgrounds regarding health. During the past 3 years, the author successfully asked WIFY at more than 50 of occasions in Japan, 4 in China, 4 in Thailand and 2 in Korea. Conjoint findings were that, by asking WIFY, people almost always take collaborative attitude and willingly offer their personal views. WIFY itself brought out and enhanced collaborative thinking. As the three years' trials of WIFY, the following five strategies were obtained to nurture the risk related worldview among people with build-in sense of sharing reality.

(1) Encourage to reflect daily life.

Encourage people to imagine and reflect their daily life from one's own view point.

(2) Avoid using the word "risk".

The word "risk" so often triggers the negative and depressive image among people. It further suppresses the creative thinking of people.

(3) Starting from importance and continuing to the loss of importance.

At first, let people to imagine critically important things and/or issues in their daily life. Then, let people to image the loss of important issues. This way of thinking let people to think about the notion of risk without using the word "risk."

(4) Encourage to shift viewpoints systematically.

Encourage people to shift their viewpoints systematically to substantiate and enhance their standing point to think about health and risk holistically.

(5) Share and nurture one's unique views and ideas by learning each other.

5. Conclusion

In Western society, each person's individuality and uniqueness is a basis of health education and promotion. The situation is also true in the area of risk management for preventive medicine. However, in a culture in which group based harmony is much more valued than individuality and uniqueness, rediscovering people's individuality and uniqueness is

an indispensable part in the process toward meaningful preventive medicine activities such as health promotion and risk management. Although "individuality" and/or "uniqueness" are important, they cannot be taught in the usual class room. The present study shows the effectiveness of WIFY to let people rediscover their individual contexts and responsibilities regarding their preventive medicine activities.

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ECOCYTOGENETICS: A NEW APPROACH TO PREVENTIVE MEDICINE IN THE 21ST CENTURY

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Abstract

For the last few decades, evaluating genomic damage from environmental and occupational exposure to clastogenic agents has been performed measuring unstable biomarkers. Genetic toxicology relates to chemical and biodosimetry (FISH) offered tools for detecting lifelong cumulative genomic damage and in correlation with specific cancer development risk. Pressed by the above, a new profession may be warranted that will unify knowledge of cancer related genomic reorganizations and knowledge of the origin and mechanisms of genomic damage. We suggest ecocytogenetics as a new discipline in preventive medicine. Growing database for FISH and cancer registries will provide reliable sources for making cancer risk assessment for general and occupational exposed populations in the near future. Mounting ethical questions combined with societal pressure should cause employers to consider radio- or chemo-sensitive genetic differences between individuals that put them at health risk in the workforce. Methods used to support ecocytogenetics must be accurate and able to analyze large populations. We discuss the accuracy of FISH to measure DNA damage and efforts being made to increase the speed of FISH measurements to routinely accommodate population-monitoring. We shall show how ecocytogenetics may compile and evaluate data to maximize life quality and minimize injury in the living and working environment.

Keywords: genetical toxicology, biodosimetry, clinical cytogenetics, FISH, chromosome aberration, cancer, health risk assessment

Introduction

Numerical and structural chromosome alterations are formed after exposure to clastogenic (chromosome breaking) agents. Such agents are natural and man made radiological isotopes, some chemicals and processes associated with natural ageing (1). Similar chromosomal abnormalities are present in almost all types of tumour cells. The correlation between genome damage and malignancy was described at the beginning of the last century (2). Introduction of methods like chromosome aberrations assay, micronucleus assay, sister chromatid exchange frequency, micronucleus assay, comet assay and

finally fluorescent in situ hybridization (FISH) during the last 30 years facilitated the formation of genetical toxicology and biodosimetry. Both disciplines represent scientific areas using primarily cytogenetics in order to investigate genome damage caused by chemical and physical agents in in vitro models, animal models and humans. In general, these methods use peripheral blood lymphocyte as a target cell for estimation of genome damage. From the beginning of these fields, genetical toxicology and biodosimetry have been related to human population monitoring. The historical problem for these methods to overcome has been monitoring of complex exposures including

inter-individual differences (radio- and chemosensitivity).

The difference between action of clastogens agents, which preferentially damage DNA, and aneugens agents, which preferentially damage mitotic spindle, are now satisfactorily solved by the application of two genotoxicological methods, chromosome aberration assay and micronucleus assay.

About the time that genetical toxicology and biodosimetry were introduced, 30 years ago, clinical cytogenetics flourished thanks to introducing of G banding. G banding facilitated detection of specific structural rearrangements of chromosomes, which were related to specific cancers (or congenital malformations). The analysis is based on detection of several cells with the same genetical alternations that represent clones responsible for disease very often already diagnosed by some other cytological or hematological method. In that way method became a tool for confirming the type of cancer, follow up of therapy results, prognosis of fullcured, analysis of peripheral blood after bone marrow transplantations and regular control of patients in a period between relapses.

However, G banding is very demanding method, time-consuming and clinical cytogenetician has to be extremely experienced to recognize bands translocated from one chromosome to another (3). The critical markers in clinical cytogenetics are contrary to genetical toxicology exclusively translocations, deletions and inversions which are stable in time and which allow viability and division of cells which contains them. Due to difference in staining such alterations are not visible by chromosome aberrations assay. The additional difference between this two methods is that clinical cytogenetics is looking for several cells with typical marker by "reading" of G bands usually analysing up to 50 cells and chromosome aberration assay is looking for dicentric, ring chromosomes and breaks which is much more easily to detect but which are present usually one or few of them in 500 cells. G banding was the only possible methodological approach to accomplish basic aim of genetical toxicology, the exact location of stable transmissible genome damage related with malignancy. For methodological reasons, studies of population exposed to chemical agents or radiation using G bandings are very few (4,5,6,7).

The introduction of fluorescent in situ hybridization (FISH) 15 years ago brought completely new quality in the biodosimetry and genetical toxicology and to clinical cytogenetics as well. Staining of chromosomes with different colors by FISH improve recognition of short inversions and translocations especially in those regions of chromosomes which were by G banding practically excluded from analysis due to homogeneously light or dark coloring. In a short time

clinical cytogenetics was able to detect even genes in interphase cell what was critical in some cases when malignant cells were extremely difficult to cultivate.

The benefit of FISH for biodosimetry was immediately recognized. Dicentrics as unstable markers were replaced with translocations. The large number of cells which could be analysed in a short time by FISH was much less time consuming than G banding. We believe that merging and overlapping of methods in application of clinical cytogenetics, genetical toxicology and biodosimetry, and the lack of knowledge of recognition of non-random markers related to malignancies will force a closer working relationship between experts in biodosimetry and experts in genetical toxicology in order to forge a more united practice of etiology of malignancies due to exposure to agents from environment and preventive measures before appearance of first clinical symptoms in critical populations. Ecocytogenetics, a term suggested by the authors for such new discipline, will put in the same institution/laboratory/department experts which currently divided in completely different areas of medical practice and governmental institutions and making them, unified, significant factor in preventive medicine. The practice at Oncology departments, Departments of prenatal and neonatal diagnostics do not include any information of exposure of children or adult population on occupational exposure, parental exposure or hobbies. Collaboration and common databanks which could be launched at Ecocytogenetic departments will feel a gap between diagnosis of cancer marker by FISH for clinical cytogenetics and measured frequency of translocations at Institutions registered for monitoring of environmental or occupational exposures by the very same method.

Methods

Chromosome aberration assay (CA)

Blood samples for cytogenetic analysis were heparinized. Into 0,5 ml samples of whole blood, 8 ml of F-10 medium (GIPCO) containing 20% calf serum was added. Lymphocytes were incubated for 48h. After 45h colchicine was added. Fixation of cultures and preparation of slides were carried out according to conventional methods (8). Two hundred well-spread and complete metaphases were analysed for each subject. The results are presented as percentages.

Sister chromatid exchange frequency (SCE)

Bromodeoxyuridine in a final concentration of 10 mikrogr/ml was added to the previously described cell culture. The cultures were harvested at 72 h. Fifty second division cells were scored for SCE (9)

Micronucleus assay (MN)

Whole blood was cultured for 44h. Cytochalasin B was added in final concentration of 3 µg/ml. The cells were harvested after the total culture period of 72h. Five hundred binucleated lymphocytes were analysed per subject (10)

Fluorescence in situ hybridization (FISH)

In situ hybridization was performed on slides prepared as for chromosome aberration assay using Chromoprobe-M kit containing labelled whole chromosome painting probes for chromosomes 1,2 and 4 (Cytocell, UK) according to the Chromoprobe in situ hybridization protocol.

Subjects

Twelve hundred subjects were analysed by chromosome and cellular abnormalities between 1998 and 2000. The subjects are occupationally exposed to ionizing radiation (X rays, CS, Sr, Ir, Am, I), chemical substances (vinyl chloride monomer (VCM), antineoplastic drugs, formaldehyde, ethylene oxide and solvents) and unexposed. Non of monitored subjects was accidentally overexposed by ionizing radiation. Film dosimeters showed an annual dose less than 20 mSv per year for all subjects. Subjects exposed to VCM belong to two groups, one exposed to 300 ppm on average for a period of 20 years and the second one exposed to 50 ppm every three months over a period of 10 years. For the ethylene oxide and formaldehyde contaminants subjects were exposed to 2 ppm of both gases.

Results

All subjects exposed to ionizing radiation were analysed by CA. The highest frequency of chromosome aberrations was detected in subjects exposed to ionizing radiation in industrial radiography which is in accordance with literature. This group showed an increase number of chromatid breaks, chromosome breaks, acentrics, dicentrics and ring chromosomes.

In a case of complex exposure to ionizing radiation and ultrasound in a population of medical personnel and industrial radiography it is shown by CA and MN that genome damage is more severe than if subjects are exposure only to ionizing radiation (11,12).

Subjects exposed to ionizing radiation in industrial radiography were analysed by FISH at time when unstable chromosome aberrations were at the level of control values. However, detected increase frequency of translocations confirms significance of this method in evaluation of increased health risk in monitoring. (13).

In subjects occupationally exposed to chemical substances CA, SCE and MN were performed

showing that there is a clear correlation between severity of genome damage and VCM concentration in the working environment. By G banding method it is shown that detected break points are related with those described for hematopoietic malignancies (5,14). In a case of exposure to antineoplastic drugs absence of correlation between SCE and MN, and SCE and CA is clearly shown (14,15).

In all subjects exposed to chemical substances it is shown by SCE the influence of smoking as a synergistic factor.

Discussion

The analysis of 1200 subjects occupationally exposed to low doses of physical and chemical agents supports the necessity of biomonitoring of human population not only after accidental overexposures but also in a case of exposures to low doses. Detection of genome damage before first clinical symptoms is crucial in preventive medicine.

Exposure to polluted environment or to xenobiotics in working environment is not only related with increased incidence of cancer development but also with development of respiratory or cardiovascular diseases. However, still low curability of malignant diseases justify the carcinophobia of mankind and put carcinogens on the top of priority lists.

It is well known that the cancer is a complex multistage process, which is not possible to reduce by the simple presence of detected genome damage like translocation or deletion. Aneuploidy, apoptosis, genome instability, adaptation and interindividual sensitivity (polymorphism of metabolizing enzymes) to environmental agents or age are integrally important.

During last 25 years about 100 genes have been found to be involved in neoplasia-associated chromosomal rearrangements (16) mostly related with haematological disorders while for solid tumours knowledge is very limited and there is still much more to be done. The strong advance of diagnostics in the last decade is based on collaboration between cytogenetics and molecular genetics.

The position of biodosimetry and genetical toxicology is at present, in a lobby of oncology and clinical cytogenetics. Although they exchange data and methodology more than in the past, there is still no feedback mechanism by which all three fields benefit.

As a tool for giving new quality to genetical toxicology, biodosimetry and clinical cytogenetics, we suggest the need for a new field, "ecocytogenetics".

This field will have as a goal to recognize agents from environment which caused genome damage located on certain band related with described neoplasia, detect clones and suggest further preclinical surveillance within preventive medicine.

The aim of ecocytogenetics should be a further refinement of karyotyping in subjects occupationally

exposed to physical and chemical clastogens, disclosing non-random stable aberrations that maybe prepared for construction of new FISH probes to monitor accumulation of rearrangements or detect residual aberrations after overexposures, to evaluate the prognostic significance of chromosome aberration found in exposed person related with development of neoplastic disease and to suggest gene targeted therapy in a near future.

Epidemiology and cancer incidence would be in that way displaced with intermediate cytogenetic markers, predisposing cancer genes (17) and move from retrospective to prospective assessment.

Ecocytogenetics will establish "risk profiles" (18) for individuals and conditions of exposure incorporating interindividual variability. Radio and chemo sensitive subjects will be more easily persuaded to avoid smoking and be targeted for intensive smoking cessation programmes, be part of chemoprevention programmes and be consider as special group for cancer screening programs (18,19).

In detection of marker chromosomes, evaluations should be limited to follow up studies of occupationally or accidentally exposed populations; as only in in vivo conditions effect of additional parameters such as polymorphism of metabolizing genes (especially in the case of chemical agents) and repair capacity are present while in vitro study are reflection of more mechanistic approach.

Contrary to previously used genes in genetical toxicology like hprt gene, aprt gene or HLA genes, which were selected due to elegance of methods, ecocytogenetic will have a set of target genes specifically related to exposure and show a directly relationship to health risk.

Random and non random distribution of genome damage caused by environmental agents are still the matter of numerous discussions (20,21,22,23,24,25,26,27). It is very important in such studies to be critical regarding the number of analysed cells, method and exclusion of those which are based on analysis of cancer patients in order to avoid instability caused by cancer. However for ecocytogenetics the question of random or non-random genome damage is irrelevant if the target break points are determined for certain type of agent(s).

The most frequently detected breakpoints revealed by G banding in the general population and population exposed to low doses of ionizing radiation or chemical agents were detected on 14q11 and 7p13 bands, which are related with malignant lymphomas and leukemias (6,5,28,29). Of especial interest are bands such as 14q32 or 7q35 involved in chronic lymphoproliferative disorders, acute lymphoblastic leukemia and non-Hodgkins lymphoma, and rearrangements of TCR and B-cell immunoglobulin genes (30,31). As a rare example of solid cancers, it

is worth mentioned that a gene at band 1p11-13 is except hematological malignancy also involved in radiation induced meningiomas (32).

Ecocytogenetic will have also strategical importance as it could launch international ecocytogenetic network. The main aim of such network would be collecting cytogenetic data after occupational, accidental or environmental exposure in order to develop critical databanks for reliable prognosis of health risks. The need for such network has been expressed (33)

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DEATH MAY HAVE ITS BENEFITS THE ROLE OF FORENSIC PATHOLOGY IN MEDICAL AUDIT

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Abstract

Background Forensic pathology tends to be perceived as a specialty which deals specifically with sudden, unnatural and violent deaths, in order to serve the administration of justice. However, autopsy findings have profitably been applied to accident prevention, particularly in relation to domestic, industrial and transportation safety.

Proposal It is proposed that the practice of forensic pathology may be extended beyond its traditional confines, so as to contribute to improvements in healthcare and clinical risk management.

Materials and Methods A review of the published and on-going work in support of medical audit, undertaken by the Centre for Forensic Medicine in Singapore, since 1991.

Observations There was a steady increase in the necropsy-incidence of Coroner's perioperative autopsies from 2% to 4.4% ($p < 0.01$) during three successive triennia from 1989 to 1997. During this time, the rate of iatrogenic deaths rose from 15.2% to 28.8% ($p < 0.02$), before falling slightly to 24.4%. From 1995 to 1997, the proportions of such deaths amongst patients subjected to multiple interventions, or elective procedures, were more than twice as high as those undergoing single procedures, and those initially classified as emergencies.¹

Recently, a review of maternal mortality showed a progressive increase in the annual necropsy-based, maternal mortality rate from 1990 to 1999 (range: 0.6-1.9 per 10,000 live-births and still-births). In this study, amniotic fluid embolism (0.33 per 10,000) and pulmonary thromboembolism (0.21 per 10,000) emerged as the most common direct causes of maternal death. A quarter (13/51) were perioperative deaths, of which 4 were overtly iatrogenic in nature. Major diagnostic discrepancies occurred in more than half of the direct (20/33) and indirect (9/16) causes of maternal death.²

Full medico-legal autopsies conducted on 70 traumatic and 166 natural fatalities (out of a total of 481 deaths), which occurred over the duration of 3 years in a major general hospital, revealed proportionally fewer discordant clinical diagnoses in the former than the latter group (2/70 vs 24/166; $p < 0.01$); the difference being accentuated after patients who were dead upon arrival were excluded (2/55 vs 24/96; $p < 0.005$). It was estimated that in approximately a third of the misdiagnosed and undiagnosed natural fatalities, a correct diagnosis might substantially have altered the acute management, resulting in improved patient survival.³

Enlightening "oddities", such as fatal retroperitoneal haemorrhage complicating percutaneous endoscopic gastrostomy (PEG),⁴ or massive hepatocellular necrosis possibly related to the use of Orlistat,⁵ or other unusual adverse drug reactions were also encountered.

Conclusion Considerable benefits might accrue from the forensic examination of post-therapeutic, maternal and in-patient deaths from major trauma, as well as from unsuspected causes, such as pulmonary thromboembolism. The potential of forensic pathology as a tool of medical audit merits serious and systematic exploration.

Key words: Forensic pathology; medical audit; healthcare

Introduction

The very mention of the term "forensic pathology" evokes images of the lifeless and mutilated victims of homicides, suicides, accidents and mass disasters. Not surprisingly, forensic pathologists tend to be cast, in the popular imagination, as medical detectives serving the administration of justice. However, this overlooks the fact that autopsy findings have informed accident prevention, particularly in relation to domestic, industrial and transportation safety.

Looking further afield, or rather, closer to home, one might well ask whether forensic pathology could also inform clinical practice. It is submitted that, in keeping with the adage *mortui vivis praecipiant* (let the dead teach the living), it could certainly be of clinical relevance, as well. Indeed, the increasing medical content of forensic autopsies in some jurisdictions (such as Singapore) has made it imperative for forensic pathologists to provide feedback to clinicians (whether the latter want it or not) on patients on die unexpectedly, in support of medical audit. In doing so, forensic pathologists could make significant contributions to both continuous quality improvement in healthcare and clinical risk management.

Materials and Methods

The Centre for Forensic Medicine (CFM) of the Health Sciences Authority undertakes all coronial casework for the island-republic of Singapore, a city-state with a multi-racial population of circa 4 million. The CFM processes at total of approximately 3,300 sudden, unnatural and violent deaths and conducts over 2,000 medico-legal autopsies, annually. Increasing numbers of post-therapeutic deaths have been observed in recent years.

The published and on-going work undertaken by the CFM, in support of medical audit since 1993, was reviewed and summarised. The salient observations are presented below.

Observations

Perioperative deaths

The systematic collation and review of Coroner's perioperative autopsies began in 1991, resulting in the publication of a series of three triennial reports, which concentrated on deaths following invasive therapeutic and diagnostic procedures.^{1,6,7} There was a steady and statistically significant increase in the necropsy incidence of these deaths during the periods 1989-91, 1992-94 and 1995-97 (2.0% (132/6650), 2.6%(170/6468), 4.4%(270/6074), respectively; $p < 0.001$). During this time, the rate of iatrogenic deaths rose from 15.2% to 28.8% ($p < 0.02$), before falling slightly to 24.4%. Unpublished figures indicate that the necropsy incidence had increased to 6.7% (418/6274) over the past 3 years (2000-02).

During the 1995-97 triennium,¹ a total of 408 procedures were performed, resulting in an average of 1.5 procedures per patient, with 37.4% and 4.4% having undergone ≥ 2 and ≥ 4 procedures, respectively. Most patients (83.3%) were managed by one surgical specialty and a minority by 2 (15.2%) or 3 (1.5%) specialties. Of the 66 (24.4%) iatrogenic deaths identified, almost a third (29.7%) occurred intra-operatively, while 36.2% and 13.7% happened within and after the first post-operative day, respectively. This clearly emphasises the importance of conducting medico-legal autopsies on cases of perioperative death, even if they should have occurred after the first 24 hours of surgery.

Interestingly, during this period, the proportions of iatrogenic deaths amongst patients subjected to multiple interventions, or initial elective procedures, were 2-3 times as high as amongst those undergoing single procedures, as well as those initially classified as emergencies (35.6% vs 16.6% and 33.3% vs 13.2%, respectively; $p < 0.01$). Arguably, the first observations could be taken as evidence that the risk of iatrogenic injury increases (perhaps exponentially) with the number of interventions performed, without

any implied judgement on their indication or necessity. However, that the iatrogenic mortality rate for electives far outnumbered that for emergencies is indeed intriguing and somewhat puzzling, since the former ought to have had a better survival advantage and there was no notable difference in the frequency of multiple interventions between both these groups. However, it remains a possibility that the elective procedures may have been more complex than those performed in emergencies. Where diagnostic accuracy was concerned, minor and major discrepancies between clinical and necropsy-based diagnoses accounted for 21.1% and 1.5% of the 270 cases studied.

Maternal Mortality

Worldwide, well over half a million maternal deaths occur annually, mostly in developing countries. Accordingly, maternal mortality ratios in the latter may be much higher than that in most developed nations (200-1000 vs 10-15 per 100,000 live-births).⁸⁻¹⁰

In Singapore, over the period of two decades (1980-99), the official maternal mortality rates (MMR), published by the Registry of Births and Deaths, were in the narrow range of 0.0-0.1 per 1,000 live-births and still-births, thus implying that maternal deaths were rare to the point of being non-existent in some years. This inference is in stark contrast to earlier studies on maternal mortality, amniotic fluid embolism and pulmonary thromboembolism that have suggested otherwise.¹¹⁻¹³

Accordingly, a necropsy-based study of maternal mortality, arising from coronial casework, was undertaken, recently.² It showed that, over the past decade (1990-99), there were 51 maternal deaths out of 20,854 coronial autopsies, with an increasing necropsy incidence ($p=0.046$ for linear trend) accompanied by a cluster of 24 cases during the last triennium (1997-99). This was mirrored by a similar trend in the necropsy-based, estimated MMR ($p=0.048$), which was, in most years, considerably higher than the MMR calculated from the published figures (0.4-1.9 vs 0.2-1.4 per 10,000 live-births and still-births).

Direct causes of maternal mortality accounted for just over half (51%) of all deaths; the leading causes being amniotic fluid embolism (16/51; 0.33 per 10,000) and pulmonary thromboembolism (0.21 per 10,000), while post-partum haemorrhage (0.06 per 10,000), ectopic pregnancy (0.04 per 10,000), eclampsia and molar pregnancy (0.02 per 10,000, each), comprised the rest of this category. This would imply that mortality from amniotic fluid embolism is at least 4-8 times higher than that reported in the United Kingdom, with pulmonary thromboembolism making an equivalent contribution.¹⁴ While most of the indirect causes (17/51; 0.35 per 10,000) were

cardiopulmonary in nature, there were also 3 suicides (0.08 per 10,000).

It was observed that the occurrence of fatal amniotic fluid embolism was evenly distributed throughout the 10-year period. In contrast, maternal deaths from pulmonary thromboembolism mirrored the overall trend in the necropsy incidence, which rose steadily from 1990-95, to peak at 1.56% over 2 consecutive years (1995-96), before decreasing from 1997 onwards. Indeed, amniotic fluid embolism had a tendency to afflict older women, as compared to those who died from other causes (mean age: 35.1 vs 32.2 (95% CI for difference: 0.4-5.8) years; $p=0.006$) and that the age difference was particularly marked when compared to fatalities from pulmonary thromboembolism (35.1 vs 29.8 (2.9-7.7) years; $p<0.001$).

In addition, there were 4 iatrogenic deaths (out of a total of 13 perioperative deaths). These comprised 2 cases of post-partum haemorrhage from utero-vaginal rupture, associated with forceps-assisted deliveries; and 2 cases of resuscitative liver lacerations that occurred against the background of pulmonary thromboembolism, with pulmonary thromboembolism having been performed in one of these.¹⁵ Significantly, major diagnostic discrepancies were rife, with correct clinical diagnoses being obtained in only two-thirds (20/33) and half (9/16, excluding a case of suicidal hanging) of the cases of direct and indirect maternal deaths, respectively. Again, this serves to highlight the need for full medico-legal autopsies in most cases of maternal death.

Emergency Medicine

A collaborative study with the emergency department of a major hospital³ revealed that of 481 deaths, which occurred over a 3-year period (1992-94), 89% were referred to the Coroner. Of the latter, full medico-legal autopsies were conducted on 236 (55.1%) cases. The clinical diagnostic accuracy for traumatic deaths was considerably higher than that for natural deaths (44/70 vs 36/166; $p<0.01$); an observation which was rendered all the more poignant after patients who were dead on arrival were excluded (44/55 vs 36/96; $p<0.005$).

It was further determined that the impact of the inaccurate diagnoses upon the traumatic deaths would probably have been negligible, as the Injury Severity Scores (ISS) of these victims were mostly in the range of 30-75 (where $ISS \geq 16$ denotes a poor prognosis, while a maximum score of 75 is considered to be incompatible with life). On the other hand, in about a third (18/55) of the natural deaths, a correct diagnosis may have substantially altered the acute management and improved patient survival.

These results have, in fact, prompted the emergency department in question (to which the author is a visiting consultant), to devise measures aimed at improving its management of non-traumatic emergencies.

Medico-legal Vignettes

The following are illustrations of how forensic pathology could contribute directly to clinical risk management through the elucidation of the causes of unexpected post-therapeutic deaths:

*Fatal retroperitoneal haemorrhage complicating percutaneous endoscopic gastrostomy (PEG)*⁴

A 93-year-old lady with dementia, neurological dysphagia and aspiration pneumonia, died from massive retroperitoneal haemorrhage after PEG, performed for feeding purposes. The initial, unsuccessful attempt at needle puncture of the stomach, under endoscopic guidance, resulted in iatrogenic perforation and laceration of the splenic and superior mesenteric veins close to their confluence with the portal vein. It is likely that the dense fibrous adhesions between the pyloro-antral region of the stomach and the posterior hepatic surface had altered the immediate anatomical relations of the stomach in such a manner as to have predisposed to these events.

*Massive hepatocellular necrosis possibly caused by Orlistat*⁵

Orlistat (tetrahydrolipostatin) is a lipase inhibitor which is used, in conjunction with appropriate dietary control for the treatment of obesity. It is generally deemed to be a safe drug, as it mainly exerts a topical action on the stomach and small bowel, with negligible systemic absorption and oral bioavailability. Nevertheless, there have been published reports of non-fatal hepatitis and systemic hypertension associated with its use. Latterly, there has been a report of a 62-year-old male who died from massive hepatocellular necrosis, consistent with drug-induced, fulminant hepatitis, associated with the use of oral Orlistat, presumably taken at the recommended daily dose of 360 mg. It is postulated that this may represent an idiosyncratic reaction to the drug.

*Sudden maternal death associated with resuscitative liver injury*¹⁵

A pregnant lady suffered massive pulmonary thromboembolism whilst undergoing pelvic ultrasonography. She was vigorously resuscitated for almost 2 hours and later underwent emergency pulmonary embolectomy. At the time of surgery, some 2 litres of blood, emanating from lacerations of the right hepatic lobe, were found in the peritoneal

cavity. Despite heroic measures, she died intraoperatively, having developed disseminated intravascular coagulation. Autopsy demonstrated the presence of multiple liver lacerations, believed to have been caused by protracted external cardiac massage. In addition, the recently gravid uterus was found to contain an intrauterine device (an indication of contraceptive failure).

Discussion

The application of forensic pathology to medical audit, arguably a keystone of clinical risk management and preventive medicine, can be a most fascinating process. Indeed, it is not limited to reviews and retrospective, clinico-pathological surveys. Accordingly, the CFM is currently, or will be, collaborating with clinical departments on interventional and prospective studies. These include (a) empiric platelet inhibition in cardiac arrest, involving a randomized controlled trial to assess the efficacy of thrombolysis with Abciximab (a glycoprotein IIb/IIIa inhibitor) in cases of out-of-hospital cardiac arrest (OHCA); and (b) cardiac arrest and resuscitation epidemiology in Singapore, designed to elucidate the epidemiology of pre-hospital cardiac arrest and treatment in the city state.

Moreover, there has, for some years now, been ongoing collaboration in medical audit and risk management activities with various clinical departments, comprising participation in monthly mortality and morbidity rounds (emergency medicine); weekly surgical intensive care rounds (multi-disciplinary dialogue and consultation); and trauma audit and medical assurance committees, in addition to advising health administrators on matters of clinical quality (as reflected by coronial casework).

Naturally, not all of this is smooth sailing and there is no shortage of pitfalls, which include the following:

1. The clinical records may be in a mess, at least from time to time.
2. The clinical records may be voluminous and time consuming to review in some instances.
3. The attending pathologist would have to contend with an ever expanding lexicon of therapeutic abbreviations, eg CRRT, CVVH, PICC, BIVAD, MARS, IABP, VATS, PTCA, etc.
4. The attending surgeon or clinician (of the deceased patient) is often absent at the autopsy (and there is only so much that one can glean from the case notes).
5. A post-therapeutic autopsy can take several hours to complete (a real imposition on a busy day).
6. The requisite autopsy report may also take hours to write.
7. Important information critical to the conduct of a meaningful autopsy may be missing.

8. The evaluation of a putative case of fatal adverse drug reaction (ADR) is by no means easy, if only on account of polypharmacy and extensive comorbidity, which frequently feature in such cases. Unpublished data from the CFM, over a recent 5-year period (1996-2000), showed that of the 22 cases of fatal ADR subjected to Coroner's autopsies, 12 patients had taken ≥ 5 types of medication, while the majority (15) had a variable combination of ischaemic and hypertensive heart disease, congestive cardiac failure, end-stage renal failure, peripheral vascular disease, diabetic nephropathy, cerebrovascular disease, bronchogenic carcinoma and idiopathic pulmonary fibrosis, just to mention a few.

Conclusion

There can be little doubt that considerable benefits might accrue from the forensic examination of perioperative and iatrogenic deaths, maternal deaths, and in-patient deaths from major trauma, as well as a wide range of post-therapeutic deaths. The potential of forensic pathology as a tool of medical audit certainly merits serious and systematic exploration. This, of course, raises the question of who is to audit the auditors. Perhaps this could be topic of another international conference. For the present, we might simply be content to close with a quotation from Charles Dickens:

Dead, your majesty.

Dead, my lords and gentlemen.

Dead, right reverends and wrong reverends of every order.

Dead, good men and women everywhere, born with heavenly compassion in your hearts

And dying thus around us everyday.

Bleak House, 1952-53

Mortui vivis praecipiant

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HEALTH PROMOTION, HEALTH EDUCATION AND RISK MANAGEMENT: ASIAN PERSPECTIVES

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SHORT RUNNING HEAD: Health Promotion in Asia

Abstract

By virtue of technological innovations and advances in diagnosis and treatment of common conditions, development of effective immunizations and control of many infectious diseases, and steady declines in infant mortality, medical science and public health have made great strides in achieving reductions in morbidity and mortality. Yet, despite these accomplishments and advances, the health burden imposed by unhealthy behaviours (such as improper diet, sedentary lifestyle, and use and abuse of drugs, tobacco and alcohol) as well as by preventable illnesses, injuries, and disability remains substantial, especially in Asian countries. As a result, patients, physicians, other health care professionals, and the public have increasingly recognized the importance of effective strategies for health promotion, health protection, and risk reduction as being essential to protect, promote, and improve the health of all. This paper seeks to highlight the health promotion/education and risk management/education endeavours adopted by the Asian countries to promote healthy lifestyles, combat communicable diseases, confront non-communicable diseases, sustain healthy environment and strengthen health care system.

Keywords: Health promotion, health education, risk management, Asia.

Introduction

Health promotion is a comprehensive social, educational and political action for health development. It enhances public awareness of health, fosters healthy lifestyles and community action and empowers people to increase control over the determinants of health and thereby improve their health.

The general strategies and approaches required to successfully confront the worldwide deterioration of health were outlined in the First International Health Conference on Health Promotion (Ottawa Charter, 1986) and in subsequent conferences (Adelaide, 1988; Sundsvall, Sweden, 1991; Jakarta, 1997; Mexico, 2000). The Ottawa Charter¹ identifies three basic strategies for health promotion, viz. advocacy for health to promote the essential conditions for health, enabling all people to achieve the final health

potential and mediating between the different interests in society in the pursuit of health.

This paper seeks to highlight the health promotion/education and risk management/education endeavours adopted by the Asian countries to promote healthy lifestyles, combat communicable diseases, confront non-communicable diseases, sustain healthy environment and strengthen health care system.

Health status in Developing countries

According to World Bank (2003) about 66% of the Asia countries are either in "low-income economy" (GNI: \$745 or less) or in "lower-middle-income economy" (GNI: \$746 - \$2,975)², and both groups altogether constitute developing countries. There is a widening of gap between needs and resources for health development in these countries - while these countries have 75% of the world's population, they

have only 17% of the world's GNP, 5% share of science and technology, 15% of energy consumption, 11% of spending on education, 18% of export earnings, 8% of industry and 6% of world's expenditure on health³.

Developing countries are now experiencing "risk transition" and "demographic transition" along with a double burden of diseases – the combination of long-established infectious diseases and newer trends of chronic, non-communicable diseases. Of the 4.4 billion people in developing countries -

- nearly three-fifths lack basic sanitation
- one-third have no access to clean water
- one-quarter lack adequate housing
- one-fifth have no access to modern health services.

About 1.7 million deaths a year worldwide are attributed to unsafe water, sanitation, and hygiene, through infectious diarrhoea. Nine out of ten such deaths are in children, and virtually all of the deaths are in developing countries⁴.

In the *World Health Report 2002* of World Health Organization (WHO)⁴, ten leading risk factors, in terms of the burden of disease they cause, are identified: underweight; unsafe sex; high blood pressure; tobacco consumption; alcohol consumption; unsafe water, sanitation and hygiene; iron deficiency; indoor smoke from solid fuels; high cholesterol; and obesity. Together, these account for more than one-third of all deaths worldwide and most of these deaths occur in developing countries.

Asia: Different Context, Different Needs

Asia is the largest continent and also most heterogeneous of any world's regions. Cultural, political systems, religions, climates and life styles are different among the countries. In recent years, a number of demographic, socio-economic, environmental, technology and health trends observed in Asia (Box – 1).

The state of health in developing countries are greatly affected by a number of external forces:

threats from super power, global warming, undue influences of international donor agencies, war and conflicts, and economic boom or bust. Internal factors, which are responsible for lowering of the status of the health, are political systems of the countries, political uncertainties and conflicts, natural disasters, poor economic management, empowerment and community participation, human rights, high national expenditure on defense, international blacklisting of the countries and development plans giving less priority to health development.

The South-East Asia region accounts for 5% of the global land mass and 25% of the world's population. The region bears the largest portion of the global

burden of many communicable diseases, which include tuberculosis, poliomyelitis, malaria and leprosy. Adding a new dimension to the already challenging health situation, is the rising trend in the prevalence of non-communicable diseases, such as cardiovascular and cerebrovascular diseases, cancer and diabetes mellitus, as well as in the number of accidents and injuries. The health situation of the region is outlined in Box 2.

A society in which human rights are promoted and protected, and in which human dignity is respected, is a healthy society. Human rights in Asia are affected by a number of factors, which directly or indirectly affect health of the population: military governments, nuclear war between bitter rivals, "War on terror", civil wars, refugees and internally displaced persons, religious minorities, violence and discrimination against women and children.

Health Education and Health promotion: Asian Perspectives

Health education is recognized as the first of the eight elements of primary health care (PHC) in Alma-Ata Conference in 1978⁵. Since then health education bureaus under ministry of health are formed in most of the countries which were equipped with core trained staff and equipment, and strengthened further in response to global initiatives by international organizations i.e. UNICEF. A number of initiatives have been taken to strengthen the health education programs i.e. institutional training on health education, development of core human resource development, community mobilization, utilization of the media, recruitment of multipurpose voluntary cadre and intersectoral collaboration.

Health promotion is one of the most viable processes to ensure equitable health development. It can be a very effective preventive measure for a large number of human illnesses, whether it is mental health, cancers or others. In Asia, health promotion movement was catalyzed by Ottawa Conference in 1986¹ and almost all countries incorporated essential elements of health promotion into various primary health care and health educational programs. Necessary national budgetary allocation was made to intensify focus on "healthy settings approach" and partnership with other government sectors, NGOs and the private sectors were established.

Fourth International Conference on Health Promotion was held in Asia at Jakarta, Indonesia in July 1997⁶ and the theme was: "*Health Promotion: New Players for a New Era -- Leading Health Promotion into the 21st Century*". This is the first conference held in a developing country and also in Asia and first to involve private sectors. Conference adopted "*The Jakarta Declaration*" which identified five priority

areas, especially aimed at developing countries and suitable for Asian countries:

- Promoting social responsibility for health
- Increasing investments for health development
- Expanding partnerships for health promotion
- Increasing community capacity and empowering individual
- Securing an infrastructure for health promotion.

Health Promotion Experiences in Asia

Improving knowledge and understanding of health is an indispensable step in promoting health-supportive actions. Creating social, economic, and environmental conditions that are conducive to health is also essential. Policy-makers, politicians, professionals, community leaders and general public should have awareness about health matters. WHO¹ set out three principal strategies for promoting healthy lifestyles:

- Advocacy for health and healthy policies
- Empowering people for health action
- Developing support systems and building alliances

The health promotion experiences in Asia can be grouped under the abovementioned headings. Advocacy is a key word in health promotion. In Asia, initiatives are taken by government, community, NGO, media, universities and research institutes and international agencies to encourage public policies that are supportive to health. The main aims of involvement of these stakeholders were to compile health policy with adequate allocation of resources, heightened public awareness and community support, to search for active and equal partners for achieving health goals, to create public awareness and bringing about action for health, to provide service, training and research on priority health issues and to render manpower, technical and logistic support.

People have the need for and the right to information on how to maintain, protect and promote health. The strategies of empowerment equip individuals, families and communities with right knowledge and skills to take positive action for health and make sound health choices. Information, communication and health education are at the heart of empowerment process. Strategies undertaken by government and other organizations to empower people in Asia to promote health are outlined below:

- Reaching communities
 - For prevention, early diagnosis and control of diseases
 - Motivation about family planning, nutrition, water, sanitation, breast feeding, maternal care, eating habits etc.
- Empowering specific population groups

- Women, young people, school-age children, workers, religious leaders, disadvantage communities to take control of their own health

- Using media
 - Promote social marketing/public relation
 - Using posters, radio spots and documentaries, stories, folk drama, songs, street plays, puppet show etc.

Adequate knowledge and desirable attitudes about health do not necessarily lead to appropriate practices. The gap between knowledge and practice is well recognized. To reduce this gap, social support was sought from community and religious leaders, family members, professionals who have an important role in making decisions and in supporting behaviour patterns conducive to health. Establishment of support systems and building grand alliances between and network with groups and agencies were targeted.

Concerns and challenges for health in Asia

Health education, health promotion and social actions for health in Asian countries are not achieved as targeted. WHO's Health for All (HFA) strategy was not realized fully in many countries, as health was not considered to be an integral part of the social and economic development. Social justice and human rights for women, children, workers and minority groups are not maintained adequately. The concerns and challenges relating to health promotion and health education are listed in Box 3.

Despite the significant achievements in the control of communicable diseases and improvements in drinking water supply and sanitation, Asian countries are facing an unparalleled challenge of new and emerging infectious diseases⁴. HIV/AIDS, drug-resistant malaria and tuberculosis are major causes for concern. The other challenge concerns non-communicable diseases and the upsurge in cancer and cardiovascular diseases and other lifestyle-related diseases, such as diabetes, high blood pressure, mental depression and suicide. In this context, the increase in tobacco consumption is a cause for added concern. The link between tobacco use and cardio-vascular diseases and cancer is well established.

Control of non-communicable diseases (NCD) is somewhat patchy and dependent on special efforts and interests of some individuals e.g. diabetes control in Bangladesh, control of cancers in some part of India, control of rheumatic diseases in Indonesia and CVD control in Myanmar. Only India, Indonesia and Thailand have some progress towards implementation of integrated NCD prevention approach.

The newer health problems in Asia are associated with disruption to traditional practices in food and

nutrition due to the rapid urbanization and globalization, which initiated changing patterns of consumption⁷. Presence of under-nutrition and over-nutrition is observed within many nations and within subgroups of those nations. The rapidly growing epidemic of non-communicable diseases, already responsible for some 60% of world's deaths, is clearly related to changes in global dietary patterns and increased consumption of industrially processed fatty, salty and sugary foods⁴. In Japan, alterations in health practices, such as decreasing the intake of salty foods and strict management of hypertension, reduces cerebrovascular diseases⁸. On the other hand, bladder and colon cancer in Japanese are on the rise due to adoption of Western foods and cooking styles⁹. The magnitude of changing patterns of consumption can be assessed by the number of the McDonalds' Restaurants in some of the countries in Asia (Box- 4).

Globalization increases the smoking rates in Asia. Sustained campaign, conducted since early 1980s by USA trade officials to open markets for American tobacco in Japan, South Korea, Taiwan and Thailand, is also responsible for explosion of smoking rates across the region. Other causes responsible for such deadly practice include: US intervention to government regulations, multinational corporations and Western advertising images and governments consideration of tobacco as a revenue source^{7,9}.

In Bangladesh and some parts of the India, arsenic poisoning in drinking water is a burning health problem. More than 90% of people of Bangladesh depend on tube wells whereas these are contaminated in 59 of the 64 districts causing 35-75 million people to be affected.

Promoting health in Asia: Future Directions

Health Promotion: Making healthy choices easy, early and exciting.....everywhere. (WHO, WPRO)

To promote healthy lifestyles in Asia, focused policy direction for the development of intensified, innovative, well-coordinated and effective health promotion movement is necessary to build national capacities of the countries. It has been identified that WHO's main efforts to improve health are towards medical & public health initiatives rather than social directions of the Ottawa Charter¹. The strategies for social action as outlined by WHO¹ are as follows:

(i) Advocacy for health to generate public demand, place health issues high on public agenda and convince policy-makers and decision-makers

(ii) Social support for health by involving community organizations and institutions and health care and other related services; and

(iii) Empower most vulnerable to take control of their own and thereby improve their health.

Specific strategies for promoting health in Asia are outlined in Box – 5.

The result of reducing risks and promoting healthy life will have a wide and lasting social value, even beyond preventing death and disability, for each country. In his address to the Fifty-second World Health Assembly, the Nobel laureate, Dr Amartya Sen mentioned that "even with low income levels, health and life expectancy could be improved through appropriate social support, such as health care, education, etc". The level of health and well-being in a community is largely determined by the way of life and behaviour of its members. Health promotion, by fostering healthy lifestyles and community action in support of health, offers a sound strategy for protection and improving public health. It should be a fundamental component of every health service based on primary health care in both developed and developing countries.

Health Promotion is everybody's job, as mentioned by Gro Harlem Brundtland, Director General, WHO³: "Reducing risks to health is the responsibility of governments- but not only of governments. It rightly remains a vital preoccupation of all people, in all populations, and of all those who serve them". Let's seize the time! The sooner we get on with it the better.

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Box – 1

Recent Trends affecting Health in Asia

- Disproportionate global disease burden
- Socio-economic changes
 - Globalization
 - Environmental degradation
 - Unplanned urbanization
- Demographic transition
 - Increased ageing population
- Technology advances
- Extensive privatization and commercialization
 - Poor accessibility of health services for marginalized population.

Box – 2

Health profile of Asia

- 30% of the under-five deaths (1995-2000)
- 33% of the infant deaths (1995-2000)
- 33% of the blind persons (1997)
- 33% of the estimated cases of diabetes mellitus (2000)
- 38% of the estimated cases of tuberculosis (1997)
- 40% of the maternal deaths (1990)
- 41% of the deaths due to infectious diseases (1995)
- 67% of the estimated cases of hepatitis E (1995)
- 75% of the polio cases (1998)
- 78% of the reported cases of leprosy (1999)

Box – 3

Concerns and challenges of health promotion in Asia

- Negative lifestyles
 - Smoking and alcohol use
- Sedentary lifestyles & risk taking behaviours
 - Non-communicable diseases
- Poor health of most vulnerable
 - Women and poor
- Emerging infectious diseases
 - HIV/AIDS
 - Drug-resistant malaria and
 - Tuberculosis
 - DHF
- Arsenic Poisoning
- Widespread malnutrition, poverty and illiteracy

Box – 4

Number of McDonalds' Restaurants in Asian countries [2000]

- Japan : 3,598
- Taiwan : 338
- China : 326
- South Korea : 243
- Philippines : 235
- Hong Kong : 177
- Malaysia : 139
- Singapore : 121
- Thailand : 88
- Indonesia : 75

Box – 5

Specific strategies for promoting health in Asia

- Strengthening health systems
- Combating communicable diseases
- Confronting non-communicable diseases
- Promoting healthy lifestyles
- Sustaining a healthy environment
- Ensuring women's health
- Protecting children's health
- Improving nutrition
- Health promotion financing
- Research- evidence-based demonstration

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Place: University of Costa Rica
Date: August 25-27, 2004
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By: Vsevolod Shakin
Place: Moscow, Russia
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