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FOREWORD BY THE DEAN

Welcome to the first issue of the Khon Kaen Public Health Forum (KKPHF). The intention of this on-line magazine about public health is to communicate with friends and supporters of the Faculty of Public Health of Khon Kaen University far and near on a wide spectrum of topics of interest for students, alumni and academics in the field of public health and related sciences. This publication will not be another on-line scientific journal but more a magazine that you would like to open at times when you want to relax by reading about some interesting features which widen your horizon in matters of public health and general academic issues. The intention is also to give some inside view into what happened here at the Faculty in terms of new developments and achievements. We hope that we will have plenty of feedback from all of you here in Khon Kaen and other locations in Thailand, and from our friends in neighbouring countries and faraway places overseas. Please don’t hesitate to provide us with letters and manuscripts which will fit with the general layout of this magazine so that our vision will be achieved by this publication turning into a lively platform of exchange of different views and experiences in the field of public health and related sciences.

Enjoy reading the first issue of this magazine cum newsletter.

Assoc. Prof. Dr. Somsak Pitaksanurat
Dean, Faculty of Public Health, Khon Kaen University, Thailand
Dear Reader,
Hardly one day goes by when there is no invitation to submit a manuscript to a newly launched online journal. This online publication is different! It does not intend to publish original research results, but would like to be a forum to introduce and discuss public health issues of wide scope and general interest. It also could become a forum for exchanging opinions and experiences made in various fields of public health, not necessarily based on academic research, but also on practical field work in the community. The intention is not only to publish some sort of newsletter related to public health where the Faculty of Public Health of the Khon Kaen University and other public health institutions are invited to draw attention to their developments and successes. The purpose of the Khon Kaen Public Health Forum will also be to address various topics of general academic and public health interest. This might include the history of public health and medicine as well as drawing attention to new research fields and developments. Each issue will have a section called ‘Journal Club’ where a publication of particular interest will be introduced and reviewed. All readers are invited to make the editor of this communication aware of a paper published in an international journal where she or he is one of the authors and which is thought to be suitable for a review in the ‘Forum’. It is hoped that a wide range of readers including students, alumni, staff of public health institutions and academics will be interested in this magazine. Articles in the ‘Forum’ should therefore also address the particular problems of students and field workers. Of course, you can read the ‘Forum’ free of charge, and we will be very grateful for all feedback from any source. We intend to publish the journal at least two or three times a year, and we will keep you informed of every new issue by e-mail if you provide us with your e-mail address.

With our very best regards,

The Editorial Board

Khon Kaen, May 2014
HISTORY OF MEDICINE

Is it worthwhile to think of Hippocrates* as the forefather of medicine and, if so, is this of relevance for public health?

There is no doubt, that curative medicine can claim Hippocrates as the father of medicine, but this is also especially true for public health.

‘Thai wisdom’ and development of Western medicine in Thailand

As far as Thailand is concerned, the history of Western medicine in Thailand is connected with Prince Mahidol, the father of His Majesty the King. Prince Mahidol studied medicine in the United States of America and greatly supported the development of Western medicine in Thailand. One of the leading universities in the country, having its roots in medicine, was named ‘Mahidol University’ in honour of the achievements of the Prince. The University displays a banner on the opening page of its website, referring to ‘Thai wisdom’, which could be understood as a reminder of the background of healing and medical practice in Thailand in the past up to the present day. The wording has now been changed to ‘wisdom of the land’. As far as health is concerned this ‘wisdom’ seems to refer, among other issues, to the use of herbs and traditional medicine and is to a great extent integrated into the teaching of medicine in many universities, even as a special curriculum. The patients in some hospitals can choose between attending specialties of Western medicine or departments of traditional medicine.

What has Hippocrates, a healer in ancient Greece, to do with Thailand or Asian countries in general?

Isn’t it enough for Thailand that sufficient justice has been done to medical history by remembering and integrating healing practiced for hundreds of years into modern medicine? So, why refer to someone like Hippocrates, born some 2500 years ago on an island in Greece, thousands of kilometers away from Thailand, as an important figure in the history of medicine? However, without questioning the benefit of ‘Thai wisdom’ and the inclusion of traditional medicine in present-day medical practice in Thailand, one might still have a better grasp of what dealing with health and illness is all about by reflecting the history of what is nowadays termed, ‘Western medicine’.

The culture and history of Asian countries differ considerably from those in Europe, and instinctively one would like to refer also to matters of the history of medicine more closely related to the Asian continent. In fact, similar considerations have been discussed at length by historians in the context of continents other than Asia, and the final conclusion to these attempts was nicely expressed by Elisabeth Fee in the introduction to George Rosen’s ‘A History of Public Health’ (1):

In part, the fragmentation of public health history reflects the fragmentation of social history in general. Critical scholarship has demolished many of the old assumptions and structures of belief without erecting secure new ones in their place. From a contemporary point of view, for example, the traditional framework of western civilization, a history that begins with the Greeks and the Romans, and ends with twentieth-century America, seems Eurocentric, old-fashioned, and limited. Yet, despite the fact that this framework is no longer persuasive, we do not have a clear alternative. In recent years, scholars have produced a growing body of work on public health in countries other than western Europe and the United States, but, while this has both fragmented and enriched our historical understanding, it has not yet led to a new synthetic view or a global history of public health.
What is said here in the context of the history of public health also refers to a great extent to the history of medicine in particular. As far as George Rosen is concerned, while he was one of the leading historians of medicine in the United States, he studied the history of medicine in the first half of the last century at Berlin University in Germany and married the daughter of a German physician (2). Political developments in Germany forced him to return to America. Rosen took a special interest in the history of public health within the overall framework of the history of medicine, and the cover of his book (displayed below) relates very well to one of the major public health fields of interest, namely a clean environment as a precaution against one of the serious plagues of mankind throughout centuries - cholera.

**Is Hippocrates the ‘father of medicine’ also the ‘father of public health’?**

The history of public health requires a consideration of distinctive aspects of health and disease when compared with curative medicine. The question therefore arises as to whether Hippocrates, who is proudly claimed as the ‘father of medicine’ by the curative sector, might also be of special importance for public health in that he showed that public health, as it is known today, has its roots in ancient times and goes back to his teaching and his school.

It might be even argued that the teaching of Hippocrates is still highly relevant for public health but less so for curative medicine. For instance, the Hippocratic Oath, the fundamental basis of ethics in medical practice, might not have been formulated by him, but may well have been written after his death (3). At the time Hippocrates was alive, there was a conflict between two different schools of thought about medical practice: the Knidians based their management of patients on the diagnosis of diseases, while the Koans, to which Hippocrates belonged, had a more general approach to diagnosis and focused on passive treatments. Modern medicine is entirely based on the principle that diagnosis of a disease comes first and appropriate treatment can only be based on a diagnosis. Of course, at the time of ancient Greece it was almost impossible to come to a correct diagnosis, and that is why Hippocrates might have leaned towards the Koans. Clinical practice nowadays hardly resembles what Hippocrates taught, but this is not the case when it comes to public health.

The achievements of Hippocrates were valid for both curative medicine and public health due to his teaching that diseases are not caused by superstitions or the interference of gods, but have natural causes (3). Whether curative medicine, as far as the laymen is concerned, is entirely free of superstitions might be questioned, but it is difficult to blame public health for having to deal with superstition when it comes to manage and solve public health problems. He also stressed the necessity of observation and documentation. His aim was to observe the patient and
record the findings. This can also be counted as a fundamental principle of the public health approach.

The ‘Hippocratic Corpus’ and public health

For historians the ‘Hippocratic Corpus’ is an important source of investigation and interpretation about the teaching of Hippocrates. It consists of about seventy scripts written in Ionic Greek and probably assembled during the 3rd century BC in Alexandria (3). Among those scripts is the one, ‘On Airs, Water and Places’. The fact that all the work compiled in the Hippocratic Corpus could be the original work of only one man and whether the treaty about ‘On Airs, Water and Places’ was truly written by Hippocrates is questionable, but its importance is that all this work reflects the teaching and principles of Hippocrates. An important part for public health in the treatise about ‘Airs, Water and Places’ reads as follows (4):

‘Whoever wishes to investigate medicine properly, should proceed thus: in the first place to consider the seasons of the year, and what effects each of them produces for they are not at all alike, but differ much from themselves in regard to their changes. Then the winds, the hot and the cold, especially such as are common to all countries, and then such as are peculiar to each locality. We must also consider the qualities of the waters, for as they differ from one another in taste and weight, so also do they differ much in their qualities. In the same manner, when one comes into a city to which he is a stranger, he ought to consider its situation, how it lies as to the winds and the rising of the sun; for its influence is not the same whether it lies to the north or the south, to the rising or to the setting sun. These things one ought to consider most attentively, and concerning the waters which the inhabitants use, whether they be marshy and soft, or hard, and running from elevated and rocky situations, and then if saltish and unfit for cooking; and the ground, whether it be naked and deficient in water, or wooded and well watered, and whether it lies in a hollow, confined situation, or is elevated and cold; and the mode in which the inhabitants live, and what are their pursuits, whether they are fond of drinking and eating to excess, and given to indolence, or are fond of exercise and labor, and not given to excess in eating and drinking.’

The text contains a treasure trove of hints related to environmental conditions which up to the present day we can associate with factors influencing health and disease of populations and are relevant to public health. There are numerous infectious diseases, mainly due to the life cycles of their vectors, which are dependent on annual changes in climate. Hippocrates might have observed the increase in the number of patients suffering from severe spells of fever which might have been caused by malaria and reach a peak incidence in many endemic locations at the second half of the rainy season. In many locations the common cold in children quite frequently occurs during the change from the rainy season to the cold season. The importance of clean water for preventing diarrhea is now commonly known, and we now realize that the condition of soil determines the quality of food and in some instances even the micronutrients: one example
of this is the iodine content of soil and the occurrence of iodine deficiency disorder (IDD). Hippocrates could not have known all this, but he observed the consequences of such conditions and clearly pointed towards the environment as the underlying reason for certain diseases. One of the most astonishing foresights of the Hippocrates era is the suggested relationship between people’s behaviour and illness and health. Who in our times cannot recognise the importance of this statement, when thinking about chronic conditions such as cardiovascular diseases and type 2 diabetes . . . . ‘and the mode in which the inhabitants live, and what are their pursuits, whether they are fond of drinking and eating to excess, and given to idleness, or are fond of exercise and labor, and not given to excess in eating and drinking.’

Returning to the title of this article! There is no doubt, that curative medicine can claim Hippocrates as the father of medicine, but this is also especially true for public health. In fact, important aspects of the teaching of Hippocrates are still very modern, which is an observation that cannot always be made regarding his statements about curative medicine.

*Born ca. 460 BC at Kos Island, Ancient Greece; died ca. 370 BC, Larissa, Ancient Greece

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The importance of epigenetic for public health

*Epigenetic was originally defined as the interaction between genetics and environment. A more accurate definition refers to gene functionality which is not encoded into the DNA sequence, but can be hereditary. The important aspect is that the function of the gene is modified by environmental influences. Of particular interest for public health might be the epigenetic features in embryogenesis and postnatal developments related to gestational diabetes and efforts to prevent non-communicable diseases in later life within the framework of mother and child health services.*

A German medical student dared to accuse his examiner of giving him a too easy question while going through the final state exam. The candidate thought that the stupid question was much below his intellectual capacity. He was asked to discuss the so called ‘epidemiological triangle’ (Figure 1) and was expected to refer to environmental factors in disease occurrence. In addition he should have discussed why the model is more suitable for infectious diseases than for chronic diseases. Generally, not only medical students but also medical doctors tend to focus on curative medicine concentrating on the disease and the direct relation of the causative agent to the patient, giving them the opportunity to apply, in case of an infectious disease, an appropriate antibiotic. According to the model, this means that the connection between the causative agent and the patient is blocked. The opportunity for treatment let the student to more or less neglect the upper corner of the triangle – namely, the environment. Only when it comes to thinking about prevention of infectious diseases does the consideration of the environment becomes essential. The model helps to search for the appropriate ways and means to prevent the spread of the disease.

**To look into environmental factors causing diseases is the duty of public health**

A medical doctor is not to be blamed for ignoring where and why the patient got malaria in the first place while fighting for the life of the patient infected with *P. falciparum*, but it is the
The duty of the public health sector to look into the environmental conditions of an epidemic area of malaria and to find ways and means of eradicating the breeding places of the vector.

The application of the model of the ‘epidemiological triangle’ to chronic diseases is possible but not advisable because of the multiple factors linked to the causation of most chronic diseases and particularly because of the long time-span after exposure to the risk factors before the final clinical occurrence of the disease. So, for chronic diseases the ‘risk factor model’ is a better choice for looking into disease causing factors. Nowadays, by applying sophisticated statistical models, all categories of environmental factors such as socio-demographic features and behavioral aspects can be added into the search for causative factors of a given disease. It can be safely stated that the environment is one of the important aspects in the determination of disease occurrence and public health. However, besides environmental factors, genetic determinations also play a role (Figure 2).

**Chronic diseases, behavior, genetics and epigenetic**

Chronic diseases, especially, are due to behavioural factors which are determined by the cultural- and socio-economic environment. Prevention usually starts with attempts to influence these factors: if smoking was entirely unknown, if alcohol was consumed in only very modest quantities, and if everybody observed the national nutritional guidelines for food intake, a substantial number of curative facilities and medical doctors would be superfluous. Genetic conditions are less easy to influence: for example, it is difficult to change the fact that one is a male or a female (even some people try hard to do exactly that), and it is difficult to work against the fact that middle-aged females have a greater risk of suffering from cancer than men and on the other hand middle-aged men have a greater risk of experiencing cardio-vascular diseases. The strict distinction between environmental and genetic factors is no longer possible, at least not as far as the phenotype is concerned. One of a fast developing field of research now is about the question of how the environment interacts with genetics to determine the phenotype (1). This field is called ‘epigenetic’.

Epigenetic is actually not an entirely new issue, but it is given a lot of attention nowadays. One of the earliest hints of an interaction between environment and genetics was expressed by Neel who published the ‘thrifty gene’ hypothesis in 1962 (2). According to the hypothesis, ‘certain genes evolved to regulate efficient intake and utilization of fuel stores’. As far as type 2 diabetes mellitus (T2DM) is concerned, this means that insulin resistance and insulin deficiency delay the metabolism of glucose and that, while this is beneficial during
periods of starvation, it will turn into a problem once food is again available in abundance. Epigenetic should not be confused with genes linked to the genetic risk of developing diseases which are then heritable (3). A better understanding to what epigenetic is all about can be derived from the Agouti mouse model (4). The agouti gene in general with its alleles determines hair colour. The Agouti mouse has a yellow coat because of its special agouti gene alleles. The animal is, however, not only special in the colour of its coat, but it is also fat and tends to develop cancer and diabetes. The animals shown in the picture below are genetically identical, approximately 1 year old females. The phenotype differs in size and coat colour because of the difference in the epigenome. The mother of the animal on the left side was fed a normal mouse diet, but the mother of the mouse on the right side received a diet supplemented with methyl donors, i.e. choline, folic acid, betaine, and vitamin B12. Feeding a pregnant female mouse with the methyl supplements changed the phenotype of the offspring in that the offspring is of normal size and has a brown coloured coat (Figure 3).

The animal model nicely demonstrates an epigenetic effect in that the nutritional environment changes the phenotype of the offspring. This phenomenon was originally described as the interaction between genetics and environment (5). A more accurate definition refers to gene functionality that is not encoded into the DNA sequence but can be hereditary (6). The important issue is that the function of the gene is modified by environmental influences. A definition, which is shorter, but less clear to those who not very familiar with genetics, refers to a ‘mitotically heritable alteration in gene expression potential’ (7).

Epigenetic modifications are attributed at present to three main mechanisms: these are DNA methylation of the DNA base of cytosine, chromatin remodeling and micro-RNAs modeling gene expression (8).

Basic genetics

To obtain a better understanding of what all this means it is necessary to recall some long forgotten high school knowledge. It is useful to remember that nucleotides are letters of DNA and RNA, that complimentary base pairs of DNA are formed through hydrogen bonds, that guanine binds with cytosine, adenine with thymine and uracil instead of thymine as far as RNA is concerned, that histones are small DNA binding proteins consisting mainly of lysine and argentine and are the fundamental protein components of nucleosomes. The information of the genetic code stored in the DNA is translated by RNA into protein. Transcription of RNA results in mature RNA which is channeled out of the nucleus, and translation occurs at the ribosome.
where, by the action of tRNA, amino acids are finally formed into proteins (Figure 4). The control of the activities of genes at the cellular level is summarised in Figure 5.

There are numerous codes stored on a DNA strand. Without an efficient control of gene activities the system would not work. One of the major control mechanisms related to epigenetic is linked to DNA methylation. A methyl group at the 5\textsuperscript{th} carbon of the cytosine base is added into a CpG dinucleotide pair (Figure 6). Transcription along a DNA strand is initiated by a promoter which enables transcription.

Chromatin, which is genomic DNA in eukaryotic cells, is attached together with proteins named histones, located within the cell’s nucleolus, interacts with the promoter to reduce transcription and, in a highly methylated state, heterochromatin is silenced.

Epigenetic phenomena also can be triggered by chromatin remodeling. In this case, an originally blocked promoter region is freed up for transcription because specific nucleosomes (Figure 7) act at times of cell differentiations and developments.

How epigenetic works is not yet entirely clear and what is known is much more complex than is described here. However, to go deeper into the molecular and genetic mechanisms is beyond the aim of this article, which is intended just to give a broad overview of what epigenetic is all about and why public health academics should be interested in the topic.

When it comes to T2DM and obesity, it is still true that major risk factors are a sedative lifestyle and an oversupply of energy intake, particularly in the form of carbohydrates. Recent interest in the genetic background of T2DM and obesity has so far revealed about 150 genetic loci, but only 5 – 10\% of the variance in the development of T2DM and obesity has been attributed to genetic loci and only about to 2\% of the variance in body mass index (BMI).
In addition to the environmental factors usually linked to behaviour, a mother or father having T2DM as well as epigenetic mechanisms contribute to the present spread of T2DM through the population (3). The following figure (Figure 8) illustrates the relationship between environment, genetics and epigenetic.

In addition to the environmental factors usually linked to behaviour, a mother or father having T2DM as well as epigenetic mechanisms contribute to the present spread of T2DM through the population (3). The following figure (Figure 8) illustrates the relationship between environment, genetics and epigenetic.

**Examples of epigenetic phenomena**

That interactions between genetics and environment might play a role in disease development is not an entirely new concept and can be traced back to the 1960s as has been mentioned above in citing the thrifty gene hypothesis proposed by Neel (2). That the maternal environment already poses a risk in adulthood via the yet unborn child has been hypothesized by
Barker and nowadays can be considered as another epigenetic phenomenon (9). The essentials of the hypothesis state that undernutrition of the mother effects fetal growth and might result in chronic diseases such as coronary heart disease in adulthood of the offspring. In the original publication Barker presented a table summarising the supposed effects of ‘disproportional fetal growth’ (reproduced below in Table 1). The hypothesis is based on the results of longitudinal observations in England, Sweden and the United States.

The results of the investigations into the development of children into adults whose mothers were exposed to severe starvation during the ‘Dutch Hunger Winter’ are another well known example along with Barker’s hypothesis. In September 1944 the Second World War was in its final phase. The allied forces had landed at Normandy in France and had also already liberated part of Western Netherlands from the occupying German forces. At the end of the Second World War the exiled Dutch government suggested a railway strike within the still occupied parts of the Netherlands in order to make it difficult for the German army to transport much needed war equipment to the front. The strike was initiated, and the Germans retaliated with a blockade of the still occupied parts of the Netherlands, cutting off food supply to the more urbanized areas still under German rule. The blockade was given up in November 1944, but at that time it already was too late to bring food into the urban west from the rural east of the country due to the onset of a very harsh winter, frozen waterways (which in fact had been allowed to be used again by the German army) and a largely destroyed infrastructure (10). Before early 1945 about 18,000 people had died mainly because of starvation, and this only ended with the liberation of the Netherlands in May 1945.

Research in the aftereffects of the Dutch Hunger Winter

A great deal of research has been done to investigate the effects on the children of women who were pregnant during the Dutch Hunger Winter. One study involved a cohort of about 2400 singletons aged 50 years old and born around the time of the starvation in 1944 to 1945. The results from those born during the exact time of the famine were compared with those from individuals born before and after the famine. The unexposed had been born from 1 November, 1943, up to 6 January, 1945, and from 9 December, 1945, up to 28 February, 1947. The exposed were therefore born between 7th April, 1944, and 8 December, 1945. Compared with those not exposed, the exposed people were found to have more coronary heart disease, raised lipids.

Table 1 Summary of Barker’s hypothesis (9)
pattern, altered clotting, more obesity, and decreased glucose tolerance (11). More detailed investigations showed that in the exposed individuals methylation of a certain gene (IGF2) decreased and methylation at other genes increased (IL10, LEP, ABCA1, GNASAS, MEG3) (12). The authors of the paper stated that ‘these data are the first to contribute empirical support for the hypothesis that early-life environmental conditions can cause epigenetic changes in humans that persist throughout life’

Significance of epigenetic for public health

Barker’s hypothesis and the findings in connection with the Dutch Hunger Winter highlight the significance of epigenetic for public health. While for the clinical sector the promising fields of epigenetic research lie in the identification of diagnostic markers and the potential for gene therapy, for public health epigenetic effects are of particular interest in connection with obesity and metabolic diseases and, for instance, in the selection of relevant parameters for the screening of groups of individuals for diseases. Of special significance might be the epigenetic features in connection with embryogenesis and postnatal developments together with gestational diabetes and efforts for prevention within the framework of mother and child health services. Figure 9 illustrates how obesity, diabetes, hypertension and cardio-vascular diseases might be prevented through appropriate screening measures and clinical management within mother and child health care institutions and hospital wards. While encouraging people to make life-style changes is important, this would provide an additional opportunity for preventing diseases related to the metabolic syndrome. In reflecting on Barker’s hypothesis a decade after its publication, it has been pointed out that, despite the benefit of the fetal origins hypothesis, of additional major importance is the fact that to be thin at birth and during early childhood and then to engage in overnutrition and become obese in later life bears a high risk for the development of non-communicable conditions such as cardio-vascular diseases as adults (13). The interplay of epigenetic mechanisms and the environment is further complicated by the influence of non-epigenetic but genetic interference resulting in either low or high birth weight. This has been discussed in connection with the development of T2DM in later life and is illustrated in Figure 10 (3).
The most important organ in connection with pregnancy outcome and fetal programming is the placenta. Epigenetic mechanisms as well as the influence of maternal genes are channeled through the placenta to the fetus. In addition, environmental factors such as nutritional status as well as diseases during pregnancy will affect the fetus mainly through the placenta (15). However, epigenetic mechanisms might even be at work during the time of conception. During the process of completing meiosis there might be methylation imprints in the oocyte. As far as spermatozoon is concerned, a displacement of histones by protamines might have occurred (1).

It certainly cannot be a major task of public health to step into molecular- and genetic research. However, only to look into environmental factors in researching disease causation and primary and secondary disease prevention will be not sufficient in future. It will be necessary to follow up research results related to the interaction between the environment and genetics and start testing how discoveries in this field might be used to solve problems of public health on population basis. One might start by intensifying public health research into the defining, in special population groups, family aggregation of T2DM for screening and secondary preventive measures and by intensifying research into gestational diabetes within the framework of mother and child health care.

![Diagram: Genetic interference to develop T2DM in case of low and high birth weight](image)

Fig.: 10 Genetic interference to develop T2DM in case of low and high birth weight (3)

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Student affairs
Publish or vanish – the dilemma of doctoral students

Doctoral students need skills which they not have for publishing the results or part of the results of their theses in the international literature. Without publishing, a student cannot graduate. Publishing is, however, an unfair business and needs a high capacity for tolerating frustration. In order to be successful, the students must be closely supervised and need a great deal of help from the advisors.

Academics dependent on research grants and the support of their institutions in terms of staff and materials are under continuous and considerable pressure to publish their research results in reputable journals with a high impact factor. If they are unable to join the ‘rush-to-publish’ of their peers, they will soon lose the support of their superiors and finally their jobs. Hence – they will vanish. It is now a common practice in many universities for doctoral students to be required as a precondition for their final graduation to publish at least part of the results of their thesis in an ‘international journal’. The expectation of the universities is that this will assure the good quality of their institutions and directly or indirectly helps to push themselves up in the numerous regional and national rankings and finally in the list of universities all over the world.

Doctoral students in different countries get different support while publishing

For the doctoral student, this means that, if they cannot have one (some universities even require more) publications in the ‘international’ scientific literature, they will ‘vanish’ and that they will not even be able to obtain a good academic position since they will never graduate. Doctoral students in some of the higher income countries of Europe or America may have fewer problems with publishing because their thesis work is often integrated into a large-scale research project of their supervisors. The professors are highly motivated in terms of their own interests to have the results published, and so their students receive a great deal of help in publishing.

The situation is different in situations where a high number of doctoral students are accepted by various faculties and where three to five students (or even more) are supervised at the same time by one advisor, who did not initiate the thesis topic, but more or less followed the student’s initial idea of an interesting research issue, which turned out to be quite a difficult area to conduct a research project. The difficulties for the students to have a paper, based on their research, published in a peer reviewed ‘international’ journal are complex. There is not only the extremely high language barrier to be overcome (this can probably be managed either by paying a specialized company for ‘ghost’ writing or by the respective faculties having their own expatriate ‘consultants’ to assist the candidates), but the main problem is that the students have no idea what a scientific paper should be all about. The format and content of their thesis does not match with the requirements of a manuscript submitted to the editors of ‘international’ journals which have their own high standards.
**Publishing a research paper needs extensive literature research**

Most students don’t realise that a scientific paper is written to communicate results to a more or less exclusive group of experts. The key point here is to focus the paper to a new aspect of a particular research topic. To do this, it is necessary that the context of the paper is embedded into an ongoing development in a particular field of research. An extensive literature research should precede the research project and should not be done after the research study has been initiated. In fact, it is highly advisable to plan a thesis topic with the question in mind as to how it will be possible to publish at least the major results of the study. Usually, doctoral students may have few problems in defending their proposals and their final thesis in front of an examination panel, but they can then fail to publish the results of their study because the topic is nothing new, and the research results are already well known and for decades have been extensively reported and discussed in the international literature. Very often the students seem to start with the impression they are the only ones dealing with the topic, such as diabetes mellitus or a particular parasitic disease, while an internet search with a particular key word will quickly reveal a hundred thousand hits. To come up with an interesting research question the student needs to know the given research topic in most of its facets, and this only can be achieved by a detailed and extensive study of the international literature. This cannot easily be achieved in a week and can take months.

A practical way of proceeding with this is to look within the most popular search engines such as PubMed or Scopus for more recent review papers and try to find some controversial results or hints about missing information which might be taken up as a thesis topic. Once a working hypothesis has been established, it will be necessary to go into a more detailed review of the former research results in a particular field. It is worthwhile to keep in mind that, in the end, it is much easier to publish a paper based on quantitative results than one based on ‘qualitative’ investigations. Students tend to be afraid of being drawn into performing statistical analyses. However, it is not necessary to study mathematics to handle statistical software, and it is usually enough to understand the basis of a statistical test and its interpretation. There might even be statistical advisors on hand who are willing to talk to the ‘earthlings’ of non-statisticians and provide some hints as to how to handle the available raw data. It is much easier to follow the structure of a ‘quantitative’ study than that of a ‘qualitative’ one.

**Publishing in the international literature does not follow fair play**

Willingly or not, one has to accept that the universal language is English. Publication in the ‘international literature’ therefore means to write an English text. On top of this, one has to know how to write a scientific paper in the field of live science, including medicine and public health.

Doctoral students need to have a wide, in depth experience in publishing in order to have a slim chance to launch a paper in a journal listed in PubMed or other institutions. ‘Great experiences’ in publishing, however, isn’t exactly what the students can claim to have
Listening to lecturers and attending seminars how to publish hardly helps to fill the gap in experience, and this is also true for attending seminars held by scientists from countries whose mother tongue is English. The first thing one has to learn is to establish a high threshold of frustration each time the manuscript is returned after being rejected. Even after a working lifetime of experience a professor with numerous publications in the ‘international literature’ still cannot develop a defence against the deep frustration occurring when her or his papers are returned after being rejected. The system is very unfair, and this is especially true for everyone who is not a VIP in her or his field and is not a citizen of England or the United States of America. The rest of the world is facing ignorant, overworked referees who start to judge a paper after leaving home in a bad mood, probably after having quarrelled with their spouses. It is less time consuming for referees to simply reject a paper because they then never have to defend their decisions. Accepting a paper involves the need to point out shortcomings and mistakes and add suggestions to improve the manuscript. The referee might spend hours or even a whole day for the meaningful review of a manuscript.

Not so serious suggestions about what to do when the paper is rejected

So, what can one do after submitting the manuscript of a paper and while waiting for the response of the editor? Depending on your religious background, you might go to the temple and make donations or pray several times a day and have a sufficient stock of diazepam on hand for when the answer comes. In the meantime you can try to be positive, but expect the worse. If you are actually lucky and get a response which indicates that your manuscript might have a chance of being accepted provided you can improve it, then strictly follow the suggestions of the reviewer. If your paper receives an outright rejection, then submit it to another journal.

It might console you to know that even papers which finally won a Nobel Prize for the author had been previously been rejected. This was the case, for example, for two scientists, Novoselov and Geim, who were awarded a Nobel Prize in physics in 2010 for developing ultra-thin carbon. They had tried to publish their results in ‘Nature’, basically a British publishing house, only to find their manuscript was rejected. They were finally successful in publishing their papers in 2005 and 2006 in ‘Science’, a USA publication.

More serious suggestions

What would be the advice to doctoral students when it comes to publishing part of their thesis? Practical hints will be discussed in the next issue of this newsletter cum magazine. At this time, the following suggestions can be given: (1) only those who already have some experience might benefit from lectures or similar attempts to improve their writing skills; (2) inexperienced candidates must be closely guided and advised throughout the whole process of writing and publishing; and (3) to gain experience is a mentally painful and extremely frustrating process, and it never ends stop publishing, enter retirement, or die.
Why should anyone suffer at all? Doctoral students must go through the process otherwise they cannot graduate. However, as academics working in an academic institution, the suffering will go on and on because 75% of the standing of these institutions depends on the quality and quantity of papers published in international journals. Institutions providing research grants (national, international foundations) judge the standing of an application on the already published papers of the applicant (regardless of any other attempts to rank universities). Furthermore, climbing up the ladder of academic grades depends on the papers being published by the academic seeking promotion.

An additional important factor is the time needed to consider and think about what to write in a paper and then to actually do it. It is not possible to think about and compose a meaningful text within one or two hours once in a while squeezed in between meetings, giving lectures, or even at weekends.

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Journal club
Using fasting blood sugar for detecting diabetes mellitus in a screening exercise leaves over 50% of diseased individuals undetected

Type 2 diabetes mellitus (T2DM) is one of the pressing public health problems in Asia, including Thailand. In order to cope with the problem, the Ministry of Public Health has launched a screening trial for the detection of T2DM, especially in the rural areas of the country. Blood pressure and body mass index (BMI) are assessed in addition to capillary blood glucose (CBG). All adults 35 years and older are invited to participate in the programme which is conducted by the health officials at district and sub-district levels and supported by village health volunteers. Individuals with a CBG of $\geq 126 \text{ mg/dl}$ are referred to a community hospital where the results are confirmed by measuring venous plasma glucose (VPG), and further action is taken to treat the patient and control her or his blood glucose level.

The screening programme and its validation
On the initiative of the Research Group for Prevention and Control of Diabetes Mellitus, a team from the Faculty of Public Health at Khon Kaen University in Northeastern Thailand joined the officials in the field with the aim of validating the screening results. The outcome of this undertaking had been published in the BMC Public Health online journal (1).

Altogether, 669 villagers living in the Na Klang District of Nong Bua Lamphu Province which is a neighboring province of the Khon Kaen Province, were assessed. CBG and VPG were measured together with glycated haemoglobin (HbA1c) in all villagers. CBG and VPG values of 126 mg/dl and above were considered to be pathological, and the cutoff point for HbA1c of 7% was selected because at the time this was the guideline set by the MoPH.

It was found that 7.3% of the villagers had positive results as far as CBG was concerned and 6.4% when the measurements were done by VPG. However, the proportion of suspected T2DM increased to 10.4% according to the HbA1c analyses.

To validate the screening procedure, the sensitivity, specificity and positive predictive value were determined.

Sensitivity indicates how good the test is in detecting a diseased person, and specificity indicates how good the test is in identifying healthy individuals. Positive predictive value gives the proportion of positive screened persons who are truly diseased and is important for the hospital receiving the positive screened individuals, since the indicator provides an estimate of the workload for hospital staff. To calculate these indicators of the validity of a screening exercise a clinical reference or a ‘gold standard’ has to be selected, and a four-fold table is completed showing how many of those screened as ‘positive’ or ‘negative’ were similarly categorised against the clinical reference.
Use of capillary blood glucose (CBG) and venous plasma glucose (VPG) results in similar proportions of T2DM positive individuals, but the proportion exceeds CBG and VPG values to some extent when measuring HbA1c.

Using CBG as the screening test and VPG as the clinical reference, a sensitivity of 81.4% and a positive predictive value of 71.4% seem to be acceptable (Table: 1). Over 80% of those screened as positive for T2DM according to their CBG are in fact very likely to have T2DM when VPG is used as the criterion the presence of the disease, and over 70% of those sent to the hospital with a pathological CBG value will turn out to have T2DM according to their VPG determinations. Screening with CBG correctly detects about 88% those who are healthy.

Table 1: CBG as screening tool with VPG as clinical reference

<table>
<thead>
<tr>
<th>CBG</th>
<th>VPG Positive</th>
<th>VPG Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>35</td>
<td>14</td>
</tr>
<tr>
<td>Negative</td>
<td>8</td>
<td>612</td>
</tr>
<tr>
<td></td>
<td>43</td>
<td>692</td>
</tr>
</tbody>
</table>

Sensitivity = 35/43 = 81.4%  Specificity = 612/692 = 88.4%
Positive predictive value = 35/49 = 71.4%

The results are less acceptable when CBG and VPG are used as screening tools and HbA1c is the clinical reference. Sensitivity for CBG is only 45.6% (Table 2), and for VPG it is even lower at 39.7% (Table 3).

Table 2: CBG as screening tool with HbA1c as clinical reference

<table>
<thead>
<tr>
<th>CBG</th>
<th>HbA1c Positive</th>
<th>HbA1c Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>31</td>
<td>22</td>
</tr>
<tr>
<td>Negative</td>
<td>37</td>
<td>566</td>
</tr>
<tr>
<td></td>
<td>68</td>
<td>588</td>
</tr>
</tbody>
</table>

Sensitivity = 31/68 = 45.6%  Specificity = 566/588 = 96.2%
Positive predictive value = 31/53 = 58.5%
Neither of the CBG and VPG screening tools detect more than 50% of those individuals suspected to have T2DM, and CBG actually performs slightly better than VPG with a sensitivity of 45.6% compared with 39.7% for VPG. Both tests have positive predictive values less than 60%, and, while this might be acceptable for the hospital staff, it still means that over 40% of those diagnosed with T2DM according to the screening test will not have the disease, and this presents an unnecessary burden on hospital workloads. Since CBG turns out to have a slightly higher sensitivity than VPG, the latter need not be measured at the hospital, and instead HbA1c should be used directly for the diagnosis of T2DM.

Table 3: VPG as screening tool with HbA1c as clinical reference

<table>
<thead>
<tr>
<th>VPG</th>
<th>HbA1c</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>Positive</td>
<td>25</td>
<td>19</td>
</tr>
<tr>
<td>Negative</td>
<td>38</td>
<td>563</td>
</tr>
<tr>
<td></td>
<td>63</td>
<td>582</td>
</tr>
</tbody>
</table>

Sensitivity = 25/63 = 39.7%  Specificity = 563/582 = 96.7%
Positive predictive value = 25/44 = 56.8%

Reasons for the low sensitivity when HbA1c is taken as clinical reference remains unclear

The use of HbA1c has been controversially discussed for many years, and only recently the World Health Organization very reluctantly included this method in its recommendations for the diagnosis of T2DM with a cutoff point of 6.5%. The method has, however, been widely used in clinical settings for a long time. The discussion about whether or not to use HbA1c has been covered at length in the paper of Muktabhant et al. (1). One particular issue for mention here is that HbA1c values might be influenced by abnormal haemoglobins. Given that haemoglobin E (Hb E) is a very common source of haemoglobinopathy in Northeast Thailand, HbA1c values might be affected by this. However, it has been found that median values of HbA1c levels in Hb E groups were only slightly below those of normal controls (2) so that, even if Hb E plays a role in this part of the world, false negative results due to HbA1c being used as clinical reference should not be influenced by Hb E.

For a long time WHO favoured the use of the oral glucose tolerance test (OGTT) instead of HbA1c. However the low sensitivity associated with the current use of HbA1c does not look so bad in the light of this previous choice of OGTT as the ‘gold standard’ and a finding obtained some years ago in some rural districts of Khon Kaen Province (3). At that time, fasting blood glucose was used as screening test with a cutoff point of 140 mg/dl and OGTT was the recommended clinical reference with a cutoff of 200
mg/dl. The sensitivity of FBG screening test was equally low at 43.7%, and the positive predictive value was only 37.8%.

The reason why screening with CBG and VPG results in less than satisfactory sensitivities remains unclear. It could well be that villagers don't like to receive a positive test result. They are quite well informed about the features of T2DM and are aware of the fact that, by reducing the intake of food with a high calorie content and by avoiding sweet fruits and snacks, they can lower their blood glucose. What they don't know is that HbA1c reflects glucose levels for up to about 3 months before testing and that they cannot control it by fasting for a short period of time. Proof or rejection this hypothesis needs further investigation.

**How to improve the screening attempt**

The results of screening could be improved by increasing the prevalence of T2DM in the population being screened, and there are various suggestions about how this might be achieved:

Firstly, if possible, screening should be carried out without making villagers aware in advance. Secondly, random CBG measurements with a higher cut-off of 220 mg/dl might be used. Thirdly, the group being screened should include a higher proportion of those at risk of having T2DM. This could be done by increasing the age of eligible persons to 45 years and older, including only people with a BMI of 25 or above or only those with a close direct relative known to have a current or previous diabetes diagnosis. In addition, females who gave birth to a child with a birth weight over 4000 g also should be included in the screening group.

Reference List


The Faculty of Public Health, Khon Kaen University, launched a regional project of co-operation in 2012. Partners in this university network are, besides the Thai Faculty, the University of Potsdam, Germany, the University of Health Sciences in Laos PDR, and the Thai Nguyen University of Medicine and Pharmacy in Vietnam. The project is supported by the Deutsche Akademische Austauschdienst (DAAD) (German Academic Exchange Service) under the PAGEL initiative. PAGEL stands for the German words ‘Partnerschaft für den Gesundheitssektor in Entwicklungsländern’ meaning partnership for the health delivery sector in developing countries. The project is channeled through the Institute of Nutritional Science, Department of Physiology and Pathophysiology of Nutrition at the University of Potsdam, Germany, which is the principal stakeholder of the project. The aim of the university partnership is to improve and optimise university education, post-graduate qualifications and the establishment of professional networks within and between all stakeholders of the health sector related to existing and emerging problems of nutrition. Measures taken so far are to develop a curriculum consisting of different modules on nutrition-related diseases for a Master of Nutrition and Health Science, which will be adopted in part or in full by all four partners and will strengthen postgraduate training in nutrition related to public health in an international context, strengthen the professional capacity related to the double burden of malnutrition and facilitate an exchange of lecturers and students between all participating universities so that experience and expertise gained can be shared.

Within the framework of this project, a ‘summer school’ took place at the Faculty of Public Health, Khon Kaen University from the 27 October to the 2 November, 2013, with the title, ‘Nutrition in Transition – Nutrition and Emerging Non-Communicable Diseases’. Participants from Germany, Thailand, Lao PDR and Vietnam attended the workshop and also contributed to the lectures and discussions. Participants from the respective countries reported about public health relevant nutritional problems within South East Asia. The major topics of lectures and discussions centred on micronutrient deficiencies and the role of nutrition in the occurrence NCDs, especially in countries in the SEA region. Micronutrient
deficiencies of relevance discussed were Vitamin A, D, iron zinc and iodine. NCDs were covered by lectures about the metabolic syndrome, cardiovascular diseases and diabetes mellitus. Workshops conducted by the participants centred on the prevention of micronutrient deficiencies by fortification of food items and on public health measures to fight against over nutrition and obesity.

In the next issue of the Khon Kaen Public Health Forum it is intended to include some of the most significant lectures and results of discussions. So far, it can be concluded that the summer school covered an important spectrum of nutritional issues related to pressing public health problems, especially in SEA countries. The topics dealing with micronutrients provided a particularly interesting inside view of the newest developments within this field in relation to the relevance of micronutrients towards public health and prevention.

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