# Promoting health sciences research in Brunei Darussalam

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## 1. The changing role of medical schools

The functions of a modern medical school include not only providing the traditional undergraduate and postgraduate training in medicine, and conducting research (involving basic, strategic and applied research or medical technologies), but also supporting the national health services, the wider community, the business sector and government with appropriate expert knowledge. The latter wider functions are particularly important if government or public funding is used in supporting the medical school. In organizing its Annual Academic Sessions, the Institute of Medicine of the Universiti Brunei Darussalam aims to fulfill this expected wider societal role.

## 2. Trends in expenditure on health and medical research

The health sector consumes a major part of the budget in most countries, being approximately 9% of the Gross Domestic Product (GDP) in most Organisation for Economic Cooperation and Development (OECD) countries [Figure 1, Ref 1]. In 2003, the USA spent 15.3% of GDP on health which is slightly more than four times that spent on defence. These figures give an indication of the priority ascribed to health in many human societies. In Brunei, approximately 6-8% of the national budget is presently devoted to Health, according to available government statistics. Data available for the years 1999 to 2004 for the OECD countries are presented in Figure 1. Importantly, the OECD data show that the proportion of GDP spent on health is increasing in most countries, including those with rapidly growing economies like Korea and Mexico [1]. In the USA, which may be regarded as being in the forefront of developing new knowledge pertaining to health, medical research is estimated to constitute approximately 5-10% of the total expenditure on health.

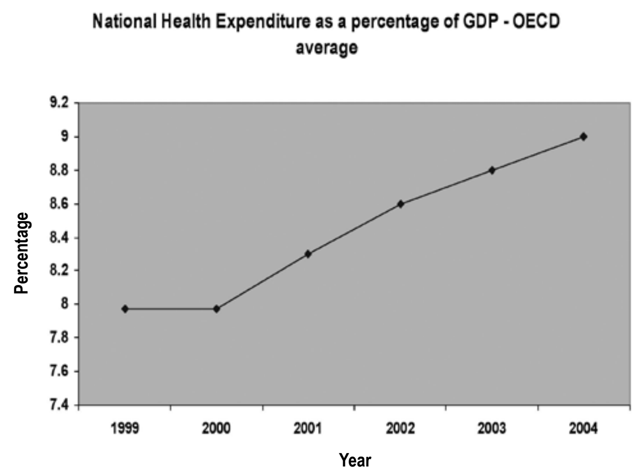


Figure1. Graph illustrating the trend in the average national health expenditure as a percentage of the gross domestic product in countries of the Organisation for Economic Cooperation and Development (OECD) for the period 1999 to 2004 [Data from Ref 1]

## 3. Promoting research in the health sector

Much of the increase in life expectancy in 1950-2000 is generally accepted as being due to advances in medical knowledge and medical technology, and not merely the better delivery and better use of existing knowledge and technology. It is therefore useful to analyze in detail some of the benefits of promoting health research.

1. Research provides appropriate training for improving skills of health-sector personnel in evidence-based medicine

2. Solutions for local health problems are often found through what is termed applied research

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3. Improving the delivery of health care involves what is termed health systems research

4. Research that seeks to advance human knowledge for its own sake, termed basic, fundamental or blue sky research, not only satisfies the innate curiosity of the brightest minds, but has been shown to yield unexpected applications in improving medical treatment and diagnosis. The discovery of monoclonal antibodies is a well-known example. Here, Kohler and Milstein stumbled upon the method of making monoclonal antibodies while investigating the basic molecular mechanisms involved in generating diversity in antibodies [2]

5. Most medical research however falls into the category of strategic or applied research, i.e. research that is ultimately designed to improve medical technology and knowledge, which in turn translates into better health care

6. Concomitant research activity often translates into better teaching by the faculty in medical schools. It helps to maintain interest in new developments and serves to attract and retain good faculty

7. Ultimate outcome in promoting research into health is of course the creation of a healthier society

**4. Key components to building capacity in health sciences research**

The essential components of building the capacity to perform health related research are:
1. Personnel
2. Institutions
3. Infrastructure
4. Regulatory framework
5. Investment

*4.1 Personnel*

There is a clear correlation between the state of economic and social development of different countries and the numbers of active researchers (scientists including medical scientists and engineers). The results from the annual United Nations Development Programme (UNDP) human development reports show the relationship between numbers of researchers and OECD countries, countries with a high human development index (regional examples are Brunei and Malaysia) and countries with a medium level of human development of which China, India, Russia and Thailand are examples [Figure 2, Ref 3]. OECD data also suggest that higher education and overall technological sophistication have a major impact on the capacity to innovate (measured in terms of patents obtained) in different countries [1].

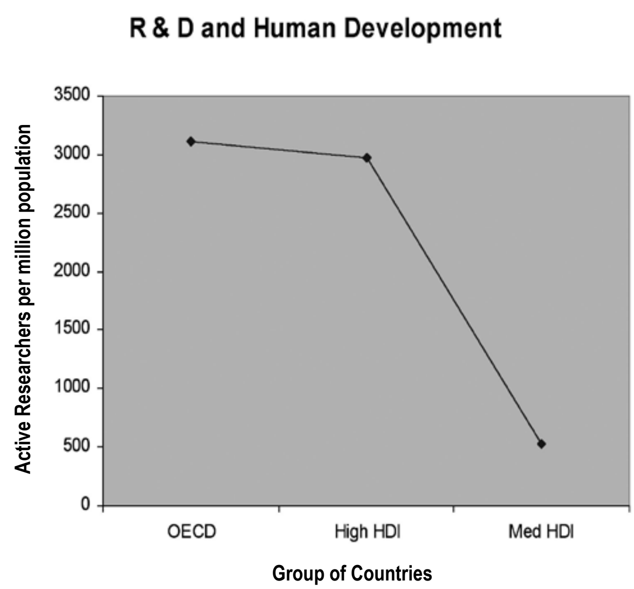


Figure 2. Graph illustrating the trend in the average numbers of researchers in the countries of the Organisation for Economic Cooperation and Development (OECD), countries with a high human development index (HDI) and medium human development index as defined by the United Nations Development Program

*4.2 Institutions and Infrastructure*

Where research and development is carried out, and its composition, has an additional impact on innovative capacity in different countries. In many OECD countries R&D spending by business is more productive than that by government. However government tends to support basic research unlike business. Innovation productivity is higher for countries specialized in (broad) technology areas, e.g. Korea in electronics.

Universities play important multiple roles in translating funding into innovation performance, and therefore good universities with adequate financial and infrastructure support are essential for productive research. Infrastructure is not only the buildings and laboratories or workshops where research is done, but also involves less obvious factors such as reliable water and electricity supplies, transport, maintenance, rapid procurement mechanisms for laboratory supplies, good housing for staff and provision of trained supporting staff such as technicians, secretaries and managers. Therefore national infrastructure investments and policies have a significant impact on innovative output.

*4.3 Regulatory framework*

Regulations protecting intellectual property and promoting openness to international trade also influence innovative capacity, particularly for business. The tax incentives provided by the government to commercial establishments for performing in-house research is a significant driver for innovation in many OECD countries.

*4.5 Investment*

Like investment in higher education for training scientists and engineers [Figure 2] correlating with the state of development in a country, there is a parallel relationship between national investment in research and development and the developmental status [Figure 3]. It is generally accepted that a minimum of 2% of the GDP of nations needs to be set aside for research and development for them to remain globally competitive in the 21st century.

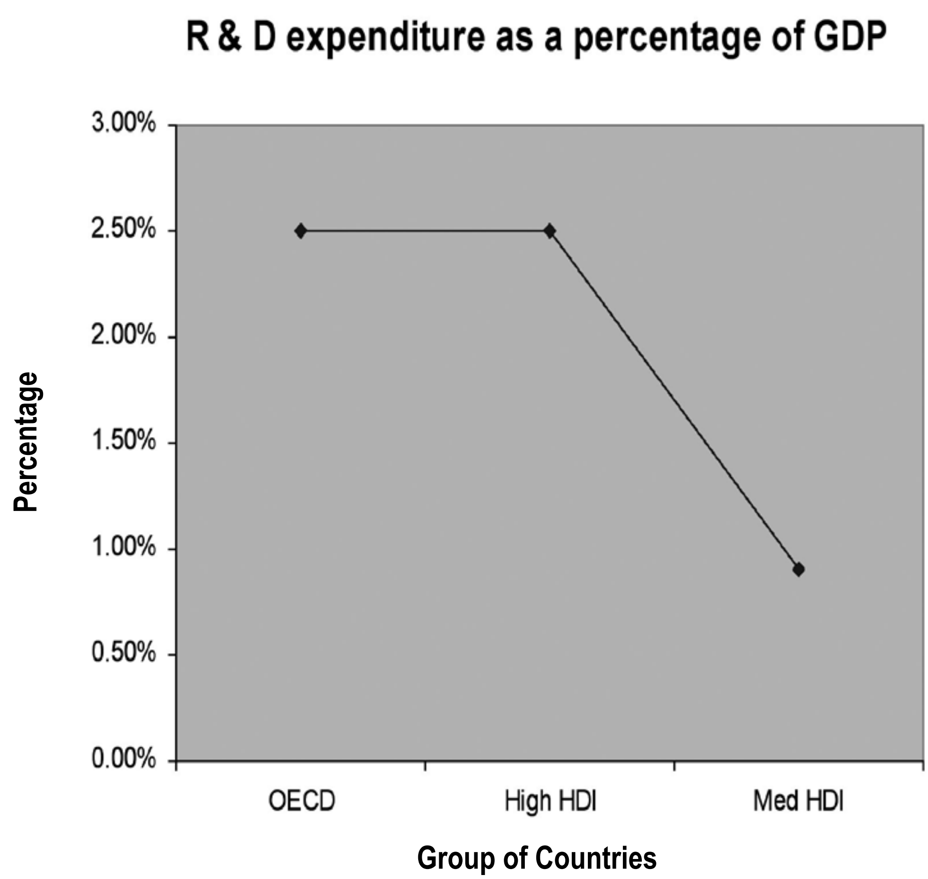


Figure 3. Graph illustrating the trend in the average proportion of the gross domestic product (GDP) devoted to research and development in the countries of the Organisation for Economic Cooperation and Development (OECD), countries with a high human development index (HDI) and medium human development index as defined by the United Nations Development Program

## 5. Requirements in Brunei Darussalam

Despite its high human development index as defined by the UNDP [1], Brunei clearly needs to develop more trained scientists for clinical and biomedical research to reach parity in research output with the OECD countries. Efforts can be made to attract medical graduates into research. However the requisite infrastructure in terms of research laboratories, major equipment, non-academic support staff, literature resources, needs to be developed in parallel to build human capacity for innovation and research.

There is also a need for specific funding for health sector research that should involve peer-review of proposals and block grants for developing infrastructure in specific fields. Additionally, collaboration with established centres of excellence in OECD countries is beneficial and desirable.

The regulatory framework should be improved further to facilitate research and innovation, e.g. purchasing speed, support on intellectual property issues, and greater freedom of interaction of staff between UBD and the Ministry of Health, and between UBD and foreign research centres

It is natural that the Institute of Medicine, UBD should play a key role in promoting health sector research in Brunei Darussalam. Well equipped laboratories and ongoing state of the art research at the Institute can attract collaboration from medical staff in hospitals and overseas scientists.

## 6. Some strategic advantages of Brunei in Health Sector research

Focusing on areas where countries have some advantages for innovative output in research is a common practice. These may be summarized in the context of the Bruneian health sector as follows:

1. Brunei has a small and easily accessible population. Good medical and personal records are maintained. This would facilitate studies on molecular epidemiology of human disease

2. The relative genetic homogeneity within distinct populations within the country is extremely useful for pharmacogenetic studies

3. The good hospital care and health sector infrastructure in the country easily permits clinical trials of new therapeutic procedures and drugs

4. The rain forests of Brunei and the surrounding seas are rich in biodiversity. There is also a local tradition of using plant extracts for medical treatment. Such traditional knowledge can provide useful leads for discovering new drugs

## 7. The way forward

The primary need in Brunei is to establish a specific fund for research in health sciences that would support relevant research at the Institute of Medicine and the Ministry of Health. This should not involve funding running costs of laboratories, but be a source of support for limited term research projects and also more generic programmes pertaining to strategic areas for development. The latter category of funding would need to be more substantial than the former. A joint committee of the Ministry of Health and the Institute of Medicine, UBD may be established to select research grant applications for funding and to develop procedures [e.g. regulatory] for an enabling research environment. Efforts should also be directed towards meeting the other requirements outlined in Section 5.

## 8. References

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# Adult crossed aphasia - case report and review of the literature

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**Abstract**

The Broca's doctrine in the last decades of 19th century assigned the left cerebral hemisphere dominance for language to dextrals (right handed) and right hemisphere language dominance for sinistrals (left handed), establishing a strict anatamo-functional connection. However in the same period, cases were reported with aphasia having right hemispherical lesions in right handed individuals. The term "crossed aphasia" to applies to any aphasic syndrome resulting from lesions ipsilateral to the dominant hand. Peter Marien and co-workers have carefully analysed all the published cases of Crossed Aphasia in Dextrals (CAD) and laid down the criteria to classify these patients into three different groups: unreliable, possible and reliable. However, no existing theory explains the anomalous organization of neurocognitive functions in this exceptional neurobiological condition. We report the case of a patient who developed CAD postoperatively where CAD was classified according to the criteria after cognitive testing and MRI examination.

## Introduction

The cerebral cortex of the human brain contains about 20 billion neurons spread over an area of 2.5 $m^2$ [1]. Brodmann numbered theses areas according to their cytoarchitecture and ascribed them functions. Large scale neural networks connect these areas to coordinate the cognitive and behavioral functions. The neural substrate for language is centered in the perisylvian region of the left hemisphere. The Wernicke's area is the posterior pole, situated in the posterior third of the superior temporal gyrus and is concerned with the comprehension part of the speech. The anterior pole of the network, known as Broca's area is situated in the posterior part of the inferior frontal gyrus and this area is concerned with the expression part of the speech. Wernicke's and Broca's areas are connected with each other and with other association areas by the perisylvian neural network. Any lesion in these areas or their interconnections can give rise to aphasia. Aphasia is a loss or impairment of the ability to use or comprehend spoken or written language.

The language network shows a left hemisphere dominance pattern in the vast majority of the individuals. In about 90% of right-handers and 70% of left-handers, aphasias occur only after lesions of the left hemisphere. In a small minority of right- handers, there is a right hemisphere dominance for language. A language disturbance occurring after a right hemisphere lesion in a right-hander is called crossed aphasia (Crossed aphasia in dextral).

Bramwell introduced the term 'crossed aphasia' in 1899 to denote, in a broad sense, to any syndrome resulting from a cerebral lesion 'ipsilateral' to the dominant hand [2]. Wada and Rasmussen demonstrated with sodium amytal test that in about 70% of left-handed people the left hemisphere was dominant for language [3]. Zangwill concluded after reviewing the crossed aphasia cases published in the literature that not more than 1 or 2% of right brain damaged population should suffer from CAD [4]. Brown and Wilson laid down criteria for CAD in 1973, as there were confusions in classifying the correct cases for crossed aphasia [5].

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Peter Marien and co-workers reported their criteria for crossed aphasia in dextrals after carefully analysing all the factors [6]. The following factors were considered mandatory to diagnose a genuine CAD; (1) clear-cut evidence of aphasia, (2) evidence of natural right-handedness not shifted, documented by a formal test, (3) evidence of lesion strictly confined to the right hemisphere, leaving the left hemisphere structurally intact, (4) absence of familial left-handedness or ambidexterity and (5) no history of early brain damage and or seizures in childhood. The following factors were considered for exclusion; (1) family history of left-handedness, (2) shifted right-handedness, (3) left hemisphere pathology, (4) previous neurological illness and (5) seizures in childhood

Marien and colleagues. analysed 152 cases which had been published till then and classified them as follows: 85 cases (55.9%), unreliable cases, 18 (11.8%) possible cases and 49 (32.2%)-reliable cases. We report a reliable crossed aphasia case, which fulfilled all the clinical and radiological criteria laid down by Marien and colleagues. This merits importance as there are only 49 reliable cases previously published in the world literature.

**Case Details**

A 40 years old Chinese male, a known hypertensive was admitted in an unconscious state with a GCS E1, V1, and M4 - 6/15 and left hemiplegia. His CAT scan revealed a right basal ganglionic haemorrhage. He underwent an emergency craniotomy, the clot was evacuated, and he was put on ventilatory support. After weaning off from the ventilator on the 7$^{th}$ post operative day he was found to be suffering from global aphasia and he had left hemiplegia.

After 8 weeks, he was walking with support and his language and other cognitive functions were assessed. He was a bilingual (Chinese and English) and studied up to Form 4. His handedness was tested with the Edinburgh Handedness Inventory and he was 100% right handed. All his seven siblings and parents were right handed. He had motor aphasia with left hemiplegia. His comprehension was good, he had acalculia and his reading, and writing were affected. His postoperative MRI brain scan did not show any lesion in the left hemisphere. He had no history of seizures or childhood neurological illness.

**Results**

This patient is a right-handed individual with no family history of left-handedness. He had a right hemispheric lesion with aphasia and left hemiplegia. There was no lesion in the left hemisphere as evidenced by the imaging studies. He did not suffer any previous neurological illness or seizures. Thus he fulfilled all the criteria for a reliable crossed aphasia in dextral.

**Discussion**

Crossed aphasia in dextral is an interesting neurobiological phenomenon and still there is no existing theory that explains the anomalous organization of neurocognitive functions in CAD. There has been a higher incidence in the Han ethnic group in China [7]. Bakar and co-workers studied three cases of CAD with functional imaging studies including Single Photon Emission Tomography (SPET) & Positron Emission Tomography (PET) [8]. They found extensive hypo-metabolism or hypo-perfusion in the right hemisphere with an initial reduction in left hemisphere as well. Abnormal dominance for at least some language functions in the right hemisphere underlies the syndrome of crossed aphasia. Diaschisis, or functional depression of the anatomically normal left hemisphere, was seen in all 3 patients during the acute phase, but not in patient 1 after recovery had begun. All the proven cases are undergoing neurolingustic and neuropsychological evaluation.

CAD is an interesting rare neurobiological phenomenon. Clinicians should be able to anticipate this rare problem while managing patients who are right handed having right hemispherical lesions. Neurosurgeons should establish the language dominance before operating patients who are right handed with right hemispherical lesions. Our contribution of this case material will help the neurocognitive scientists to do further research in this area as the numbers of reliable CAD cases are small.

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