IN BRIEF

- Research collaboration with less developed countries should be of mutual benefit
- Global research necessitates practical and ethical considerations
- Untreated populations may offer advantage for study over those in the developed world
- Institutional alliances with less developed countries create a fruitful partnership
- Cultural understanding promotes success

Extending scientific horizons in the developing world — the Central American experience

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The juxtaposition of 'oral disease' and 'developing countries' invariably evokes thoughts of how one might assist these nations in attaining 'a healthy mouth for all' according to Western standards. In this discussion, the emphasis is shifted to consider collaborations between the industrial nations and those less developed countries, in the conduct and development of research. This potentially fruitful partnership can produce scientific, educational and cultural rewards for mutual benefit.

It is indisputable that the vast majority of clinical research findings published in the medical literature are the product of studies that have been conducted in industrial nations rather than the developing world. This is no doubt a natural consequence of the greater availability of both funding and education, and the resultant concentration of researchers in these industrial nations. But perhaps it is time to think more tangentially, to cross borders and to conceptualise how we may work with developing nations in the name of scientific advancement, and for mutual benefit.

THE DEVELOPING WORLD

In the classification of countries on a global scale, typologies to date have invariably been based on the level of economic advancement, as measured by per capita income. Whilst far from ideal, a current approach is to divide countries into 'least-developed', 'developing' and 'developed'. Since there is a general understanding that even the most developed countries are still undergoing development, these countries are often referred to as 'industrial', or we can reclassify nations in an even less specific manner as either 'less developed' or 'more developed' These typologies are by no means exhaustive but are adequate for current discussion. The industrial nations include The USA, Japan and those of Western Europe and these are by far the wealthiest countries, in monetary terms. Least-developed countries, comprising much of sub-Saharan Africa, and developing countries, including much of Latin America and Asia, currently constitute 80% of the world's population.

A third of the population in these less developed regions is under the age of 15 and thus approaching their high reproductive period (cf more developed regions: 18%), so that world population growth is and will be heavily weighted towards these countries. With the significant contribution in terms of sheer numbers and the increasing recognition of the need for international co-operation, the onus is on us to involve these less developed regions in the international community, so ensuring their active participation in all areas, including scientific research and technological development.[1] We will return to this theme throughout the ensuing discussion, which will also highlight the shared rewards of collaboration with these countries.

But to firstly take the perspective of opportunism, what can we, as researchers in the developed world, gain from packing our probes and trekking off to the far corners of the earth? If you are an avid traveller, an explorer of the unknown, then the journey for journey's sake is reason enough. But this is digressing from scientific purpose and will not impress funding bodies.

RESEARCH OFF THE BEATEN TRACK — THE PROS AND CONS

Under what circumstances does data from the developing world offer advantage over that from the more developed world? Since each country is defined by a unique blend of geographical and climatic characteristics, cultural traditions, religious beliefs and political persuasions, any succinct answer to this question is clearly an over-generalization. Nevertheless, common themes do exist throughout the developing world and this forms the central premise of the current discussion on the merits and limitations of performing studies in developing countries, with particular reference to rural communities. There are two main

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elements when considering the conduct of a study and its outcome, firstly the nature of the information gleaned, and secondly logistical considerations in planning and successful execution of the study.

In recent years, our own clinical investigations have been conducted largely in rural indigenous communities (Mayan Indian descent) of Guatemala, Central America[2–6] and, consequently, our views naturally emanate from our experiences here. It should be stressed that all our studies have been conducted following protocol approval by the Institutional Review Boards (Research Ethics Committees) of the University of Texas Health Science Center at San Antonio, USA and Universidad Mariano Galvez, Guatemala. A brief digression is warranted at this point to emphasize the importance of ethical considerations globally.

Observing the highest standards of ethical practice in less developed countries is no less important than at home, and approval for study conduct should be obtained from both the primary investigator institution and an appropriate organization in the host country. It is distressing to learn of inappropriate conduct by reputable pharmaceutical companies and apparently respectable clinical researchers who circumvent or ignore local or international ethical as well as legal guidelines for the conduct of research. The morality of companies and organizations that commercially exploit communities in these developing countries for ultimate gain in the developed world has to be questioned.

The importance of ethical considerations in international clinical research is being increasingly addressed as issues continue to arise. Mechanisms are being instituted to tackle these concerns, and this has been succinctly summarised by Lansang.[8] More specific to oral health studies in developing countries, the International Association for Dental Research recently hosted a workshop entitled '*Case studies in International Collaborative Oral Health Research: Ethical Dilemmas*' at their 2002 annual meeting. This is also scheduled for inclusion in the annual meeting in 2003.

The study population

Populations in less developed regions share common characteristics: they are relatively young and exhibit a traditional age pyramid, sibships are generally large (in Guatemala, average number of children borne per female in life is 4.8, cf UK 1.7), families live in close proximity and, in rural communities, population influx is extremely low.

To focus more on these rural and isolated communities, whilst a hierarchical structure invariably exists, there is considerably more socio-economic and thus environmental homogeneity than one would find in industrial countries, consequent upon the lack of choice imposed by very limited resources. This environmental homogeneity is enhanced by villagers traditionally being of the same ethnic background (Fig. 1) and thus culturally similar, unlike those amalgamated societies such as exist in The USA and Europe. In studying disease, this uniformity minimizes the potential impact of confounding factors on data interpretation. In this respect, both cigarette smoking and access to carbonated drinks are perhaps the two examples most relevant to oral health studies.

To continue with this theme, the variability of access to dental care, whether preventive or treatment orientated, in the industrial nations can confound data interpretation. In less developed countries access to dental care in rural communities, when available, is invariably limited to extractions for tooth pain, so that treatment experience is universally restricted. In epidemiological research, a beneficial consequence is that tooth retention tends to be high so that valuable information is conserved. However, given the population age structure (percentage of population over the age of 65 years in Guatemala is 3%, cf UK 16%), one inevitable limitation imposed upon us is the dearth of older subjects available for study recruitment within the community.

Research can, of course, extend beyond epidemiological investigations. Intervention studies, including clinical trials, are all feasible, but pragmatism must be balanced by ethical considerations. As an example, it would be perfectly feasible to conduct a clinical study in an isolated community evaluating a new dental implant, provided the surgical facilities could be established. However, following conclusion of the study, absence of long-term support would surely raise ethical concerns in a community where regular dental care is absent.

Operations in the field

If the subject participant provides the very foundation of any clinical study, then it is logistical matters that form the framework for successful study execution. As has already been alluded to, why then set up camp in a less accessible region of the world where we expect to be logistically-challenged? Certainly, hauling clinical supplies and personnel to a remote leech-infested jungle or perilous mountain face for the benefit of scientific advancement could be somewhat of a challenge. Such extremes, however, are rarely necessary in order to accomplish the scientific goal, with isolated rural communities often being accessible within half a day's drive from an urban centre. In some respects, there is considerable advantage of working in these communities over those in those in the more developed world. In industrial nations, subject recruitment for clinical studies can be both expensive and time-consuming. Moreover, there is often a degree of ascertainment bias through self-selected participation so that there is less assurance of obtaining a random sample. In the developing world, these concerns can be alleviated to some extent by the immense enthusiasm of villagers to participate as well as their concentration within a relatively small area.

To highlight only the logistical advantage of working in these communities would, however, be misleading. Indeed, as discussed below, cultural, language or geographical barriers are encountered, but these are rarely insurmountable.

In Guatemala, as in many other less developed countries, traditional culture continues to play a central role in the lives of the indigenous people and such traditions need to be respected if misunderstandings and resultant loss of trust of these people is to be avoided. Consequently, the successful execution of a field study in rural Guatemala requires considerable groundwork to gain the confidence and

Fig. 1 Cakchiquel people (Mayan descent) of a village in rural Guatemala

Figs 2a,b The village of San Juan La Laguna, situated on the north-facing shore of beautiful Lake Atitlán

respect of the local community. As an example, in one Guatemalan village, it was proposed to take venous blood samples from a subset of study participants. Initially, this seemed an unpopular decision with the villagers since their perception was that their life source was being drawn from them. This concern was addressed by a concurrent injection of Vitamin B12, to replace the losses resulting from venipuncture. However, mistrust was still not totally avoided in this community since, as the study progressed, it became apparent that some people were unhappy with having their blood pressure taken with an electronic sphygmomanometer, which they interpreted as their transformation into numerical terms. It is not always possible to predict such difficulties but, naturally, the more one can respect and understand local culture, the more likely success is ensured.

Language barriers may also impose communication difficulties, particularly where indigenous languages are spoken. In Guatemala for instance, indigenous people comprise more than 60% of the population and speak one of 21 native Indian languages. In our principal field study site, San Juan La Laguna (Fig. 2), communication has been possible through a common language, Spanish. However, the elderly subjects often speak only the local Indian language (Tzutujil), which is translated by a village member to Spanish and the information then recorded in English.

By definition, isolated communities present a potential challenge in terms of access and availability of utilities. With continual expansion in these developing nations, access is rarely an insurmountable problem, and whilst we may have to allow additional time for travel, its significance is minimized where investigations are longer. For oral examination, adequate and standardized lighting is important and, if sample storage is needed, refrigerated or frozen storage facilities may be required. In remote communities, electricity is unlikely to be available 'at the flick of a switch' and this is a potential concern, although one readily resolved through the use of a portable generator. Transportation of samples may also be challenging, particularly with heightened security in the aftermath of the 2001 terrorist acts. In our experience, with appropriate approval, samples can be shipped in 2–4 days between various locations in Guatemala and The USA. This can obviously be a problem where immediate processing is necessary, as for example where cultivation of oral bacteria from dental plaque samples is required. With careful planning, we can circumvent this issue by collecting plaque samples on the last day of a study and transporting them by hand to reach the laboratory in The USA within 36 hours.

One might expect that a field study conducted in a relatively isolated area of the world would be considerably more expensive than a comparable study performed in Europe or The USA. Certainly, extra costs are incurred with respect to studies in these less developed countries, both in communication for study planning and while on-site (particularly travel, hotel, subsistence). However, since costs incurred in running the clinical site and subject reimbursement are directly linked to the per capita income, it transpires that the costs of conducting a study in rural Guatemala and within Europe or The USA are comparable.

MAKING CONTACTS AND CULTURAL ADJUSTMENT

To attempt clinical investigation in a foreign country without the assistance of local facilitators is to be seen as little more than an interloper, with the result that one is unlikely to break through cultural barriers and be successful. Making such local contacts requires appropriate introductions and some skills in networking, but sustaining these contacts and nurturing the professional relationship requires so much more. The 'contact' is more than just an acquaintance, and to use them as such does not make for long lasting success as collaborators. Mutual respect is essential and, for this, cultural understanding from both sides is paramount. While local researchers may have had enough exposure to Western influences so that they are able to adapt to some extent to our *modus operandi,* what is of undoubted benefit is our ability to adapt to their way of thinking. In Latin America, dominated by Hispanic culture, business plans mingle naturally with social intercourse and one must be prepared to conform. To fail to recognize this prerequisite for adaptation can be a recipe for failure.

By the same token, the cultural environment of the educated and relatively wealthy local investigators may be very different to that in the proposed rural study site. However, their aptitude in enlisting the assistance of villagers for both subject recruitment and study execution underpins the success of the investigations and the smooth running of the study.

In the village of San Juan La Laguna in the Central Highlands of Guatemala, where the vast majority of our studies have been conducted, village members have constituted a significant proportion of the onsite operational staff, following their training in basic study protocol. This is standard practice in ethnographic and archeological studies, for example, and naturally reduces suspicion amongst the locals, particularly the elderly, personalizes the study and demonstrates our level of respect. However, there is potential for inadvertently sparking dissent within the community through envy induced by selective employment, and disharmony within the family where the wife is employed and the husband perceives he is losing financial control in a male dominated society. On the other hand, enhanced and unexpected benefits may accrue. In the remote village of Chioya, in The Northern Highlands of Guatemala, following request for recruitment by the local priest, all villagers without exception, appeared for oral screening examination. Unsolicited, village officials subsequently produced a hand-drawn map of their village together with the names and dates of births, if known, of all inhabitants of each dwelling. Clearly, this could be of great benefit in planning future studies.

FOR MUTUAL BENEFIT

While we have thus far focused on the benefits of this collaboration to us, as

researchers in our established setting, can we help to create a more symbiotic affiliation? Hopefully, yes, and at several levels.

In the first and most obvious way, subject compensation provides material benefit to the villagers with whom we work. Whilst we have never provided direct financial recompense for participating in a study, compensation has been provided as food or cooking utensils and, on occasion, a donation, such as a basketball hoop, is made to the village for the benefit of the community. For those enlisted locally to conduct the study, there is short-term and sporadic employment. Occasionally, it is possible to extend this to the acquisition of particular skills. In one instance, in order to enhance subject co-operation and allay potential fears, we trained one of our helpers to perform phlebotomy. Beyond these immediate benefits, one would like to think that the longer term outcome of the studies conducted in the communities might return the dividend of health benefits, whether directly or indirectly. In this respect, it is important to emphasise here that we are not onsite to provide village healthcare, but rather to conduct investigational research. Clarification of this issue with the community is usually necessary since their contact with visiting medical professionals from the developed world is usually in the form of church-associated medical teams that provide short-term healthcare. Of course, we are occasionally confronted by a child or adult with an acute medical problem, in which case we naturally intervene. Overall, in explaining the rationale for the study to participants, honesty is the best policy, and it is essential to clarify that any potential healthcare benefits to the community or individual are almost certain to be years away.

Beyond providing continuing education in basic and applied science, our collaborative efforts should also sow the seeds for the establishment of their own research activities

From a professional perspective, an indirect and positive consequence of our lasting collaboration with university colleagues in less developed nations is being able to foster the discipline of scientific enquiry. For obvious reasons, professional activity in these developing countries has been restricted to the provision of health care for those who can afford it, rather than the conduct of scientific research. Consequently, medical and dental students have little or no exposure to research and the scientific method. From our privileged perspective, we have the opportunity to articulate the raison d'être for research to the medical and dental community and recruit their enthusiasm. This is not always easy, where historic precedent prevails. In El Salvador, we encountered the incredulity of Deans and senior Professors when trying to articulate the need for their institution to fund individuals in their research activities. In such countries recuperating from civil war, however, we need to understand that simply rebuilding damaged physical plant is naturally the priority.

Developing local research

Beyond providing continuing education in basic and applied science, our collaborative efforts should also sow the seeds for the establishment of their own research activities. This would go hand-in-hand with the development of postgraduate training, which is currently limited in the majority of these less developed countries. In Guatemala, for example, whilst there are three dental schools in the capital, only one postgraduate programme exists. This course in orthodontics provides comprehensive clinical training but has only a limited research component.

This situation exists throughout much of the less developed world and naturally hinges upon not only the academic and cultural precedence, but also on the availability of funding. It is here that we can also play a positive role as, increasingly, funding agencies are providing collaborative grants to encourage partnership between developing and industrial nations. These financial resources should not be limited to supporting the efflux of promising academics to recognized institutions of higher education in the more developed world. While this benefits the individual and should, theoretically, sow the seeds for academic development on their return home, the reality is that many of these highly competent individuals, having seen the opportunities afforded in the wider community, remain ex-patriated. Logically, the longer term objectives will be better served by deploying financial resources, both private and public, within the country for the establishment of a scientific infrastructure more suited to their own needs.

Pockets of scientific competence have emerged, for example in India, Brazil and Mexico. At the Universidad Autónoma de Nuevo León, Monterrey, Mexico, the highly regarded postgraduate programme in Periodontics celebrated its 25th anniversary in 2001. The research activity has followed closely on the development of the clinical programme, such that student projects are published in peer-reviewed journals.[8]

SHIFTING PARADIGMS

According to our own culture and tradition, advancement in scientific understanding occurs as a progression of thought and thus relies heavily upon the conclusions drawn from previous findings. The risk is that this can result in a rather insular approach to the study of disease and its treatment, with little room for unorthodox innovation. This was stated succinctly by Claude Bernard some 150 years ago: 'It is what we know already that often prevents us from learning'. In the context of oral disease, the opportunity afforded in less developed countries for study of untreated disease allows us to think more laterally *a propos* disease management of both dental caries and periodontal disease.[9,10] Limiting our Western preconceptions in the study of the natural history of disease could result in a refreshing perspective on prevention and treatment, and this could lead to a more appropriate use of their limited resources and funds.

THE CHANGING ENVIRONMENT

By definition, developing countries are those seeking to instigate considerable change in terms of industrialisation and improvement in the quality of life for society as a whole. Whilst transformations do not occur overnight, stable and progressive government is likely to catalyse rapid change in many of these countries. In the Central Highlands of Guatemala, where we have been conducting studies since 1995, this is clearly evident. In the heart of the region lies Lake Atitlán and, at the time of commencement of the studies, unpaved road only existed between discrete communities on the 50 or more miles of lake shoreline. By 1999, the unpaved road had been extended to permit circumferential access. In parts, the road has already been paved, as is evident in San Juan La Laguna, where an asphalt road now connects the village to the nearby larger village of San Pedro. Moreover, a small inn has recently been completed in San Juan La Laguna, primarily built with commercial interest in mind. Indeed, the time scale of transformation of this traditional Mayan community has been remarkable. As the popularity of adventure travel increases, no doubt tourism will create further rapid change in Guatemala, and beautiful Lake Atitlán is unlikely to be spared this foreign invasion

and its effects on the lifestyle and cultural identity of the indigenous people.

With regards to clinical studies in the field, whilst this change corrupts the pristine nature of these communities, it could be perceived as scientifically beneficial in the conduct of longitudinal investigations to observe changing patterns of disease concomitant with environmental change.

CONCLUDING PERSPECTIVES

Historical colonialism has undoubtedly influenced the conduct of clinical field research in the less developed nations, with the limited epidemiological data pertaining to oral disease in these countries collected principally by Northern European investigators. Latin America has been somewhat neglected in this respect and, while The USA has shown interest in the region, this has been predominantly from a political rather than scientific perspective. As clinical researchers we, however, have been fortunate in being able to pursue our scientific objectives in the fruitful environment of Central America. In the process, it is hoped that an increased understanding of the ethos of diverse societies and cultural idiosyncrasies will lead to mutual respect, lasting collaborations and shared gain. The significant dividend is to gain a fresh perspective on disease, and life, and to remove the blinkers of Western preconceptions.

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