1. IBP high-altitude research: development and strategies

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The peoples of the high-altitude regions of the world have long fascinated both scientists and laymen from the lowlands. Early explorers from Europe discovered in the high-altitude regions of South America, north-eastern Africa and Central Asia highly complex cultures with substantial populations and often great wealth. The explorers also discovered that while these high areas caused them discomfort and often sickness the native populations seemed healthy and by the standards of their own physical capabilities considerably stronger and more fit. They continued over the centuries to carry back to the lowlands romantic stories of the health and wealth of these peoples. It is surely no accident that even today many laymen dream of a utopian Shangri-la hidden in the vastness of the Himalayas and even serious scientists still suggest that somewhere in the Andes and the mountains of the USSR there are human beings who live with a high degree of physical fitness to ages far exceeding those found for lowlanders.

With the beginnings of such organized sports as mountain climbing and balloon ascents a more serious scientific interest in the effects of altitude emerged. By the 1800s some of the more dramatic physical effects of high altitude on lowland man had been documented (Ward, 1975) and by the early 1900s physiological research on the causes of these effects were seriously underway. Interest in how the hypoxia of high altitude affected lowland man accelerated during the first half of the century so that by 1965 a review of the literature produced a bibliography of more than 5,000 published articles and books on the topic (Wulff, Braden, Shillito & Tomashefski, 1968).

Despite this great interest, knowledge about the biology of populations native to the world's high-altitude areas remained fragmentary. Beginning in the 1920s some research on the high-altitude peoples of the Peruvian Andes began. Under the strong leadership of Carlos Monge M., Peruvians, along with European and North American scientists, inaugurated studies on physiological responses to hypoxia of the Peruvian highland Quechua. Some early studies on the growth of natives were followed in the late 1950s and early 1960s by efforts to broaden the knowledge base concerning reproduction and specific altitude-related disease.

Information about the biology of Ethiopia's high-altitude people was essentially non-existent in the early 1960s while information on the biology

of the Asiatic high-altitude peoples was limited to a few observations made by members of English and New Zealand mountain climbing expeditions (Pugh, 1966).

The International Biological Programme project

When the International Biological Programme (IBP) was formulated in the early 1960s it was realized that such a broad-based biological program whose theoretical foundations lay in ecology would have to include a section devoted to the study of the effect of environment on biological man (Worthington, 1975). The project entitled Human Adaptability was convened by Professor Joseph Weiner who first developed and later co-ordinated the project for the life of the IBP. As part of the early development process Weiner was able, with the help of the Wenner–Gren Foundation for Anthropological Research, to hold a conference on our state of knowledge in human adaptability. I am sure that the mere twenty of us who contributed to the state-of-knowledge book which developed from this conference (Baker & Weiner, 1966) were inadequate to the task, but the information and research directions suggested in the book offer a base on which the information in this book may be judged.

As Weiner (1966, 1969) noted it was hoped that a significant segment of the Human Adaptability project efforts could be devoted to a few 'intensive multidisciplinary regional studies'. These were to be based on life in very stressful environments and on habitat and population contrasts. It was believed that such studies could progress beyond traditional descriptive information and provide insights into how our species had adapted biologically to such a broad diversity of environments, many of which were totally alien to the tropical lowlands in which we evolved.

Harrison, Pugh and myself (Baker & Weiner, 1966) writing on different aspects of man at high altitude all emphasized what we saw as the unique opportunities for understanding fundamental processes by the study of man at high altitude. Among the various environmental stresses to which man is exposed the hypoxia of high altitude is the one probably least subject to behavioral or technological amelioration. Thus, Harrison (1966) suggested that high altitude might offer a situation to which classic experimental design might be applied. Basically he suggested that a natural experiment situation should be found where four populations lived under the same conditions with the exception of the altitude of residence. Two should live at high altitude and two at low altitude. Of the two at high altitude, one should consist of migrants from the native low-altitude population. One of the low-altitude populations should be migrants who are high-altitude natives. The structure of this design and what could be deduced from studying these populations is outlined as follows:

(1) HAN: a group living at high altitude and native to altitude, in the sense of having a long generational history of high-altitude residence.

(2) HAN↓: a subdivision of group (1) who live under identical conditions but who have migrated down to sea level.

(3) LAN: a group living at low altitude with other conditions similar to those of group (1).

(4) LAN↑: a subdivision of group (3) which migrated up to the same altitude and conditions of group (1).

With these populations, intergroup comparisons would provide the following information.

HAN–LAN = total differences caused by altitude

HAN–LAN↑ = genetic features of altitude adaptation

LAN–LAN↑ = ontogenetic and physiological adaptations to altitude (acclimatization) plus detrimental effects of altitude

HAN–HAN↓ = ontogenetic and physiological adaptation (acclimatization) to downward migration plus detrimental effects of downward migration

LAN–HAN↓ = differences in response to sea-level pressure produced by genetic differences

Unfortunately, but perhaps not surprisingly, populations fulfilling these exacting design requirements were not found, but the IBP program in Ethiopia (Harrison *et al.*, 1969; Clegg, Pawson, Ashton & Flinn, 1972) and to some extent the studies in Peru (Baker, 1976*b*) were able to follow modified forms of this design.

The World Health Organization became interested in the development of the high-altitude project and co-operatively with the Pan American Health Organization and the United States IBP committee sponsored a major conference in 1967 to assess our state of knowledge and research needs in relation to man at high altitude. The final research recommendations of this conference were divided into three topical areas. They were: (1) physiological adaptation and acclimatization to altitude, (2) the study of human biology at high altitudes, and (3) the health aspects of altitude. The recommendations for research under these three topics were indeed comprehensive but in many instances it developed that IBP was not the appropriate vehicle for supporting the needed research.

While research on physiological acclimatization to high altitude and the health problems of high altitude continued after this conference they were generally not incorporated in the IBP-supported research of any country with the exception of the USSR. It is my further impression that research on these topics declined in the time after this conference as compared to the five preceding years. The reasons for a diminished interest in these significant scientific and practical problems is not clear to me.

While the promising start of IBP research on high altitude thus suffered a significant setback, the interest generated in the human biology aspects developed and formed the major segment of research specifically undertaken with IBP designation. Even this development was not without difficulties and some history of these problems may be useful for placing the studies reviewed in this book in perspective.

A significant problem for IBP high-altitude project was the inability of the scientists in most high-altitude countries to form IBP committees in their own countries. Although individual scientists in many Andean countries worked on IBP projects they received very limited support from within. In the Asian mountains the USSR was the only country to carry out a substantial research program on high-altitude peoples under the label of IBP. Since it was deemed appropriate to limit this book to the primary topic of high-altitude peoples, not all of the USSR research has been reviewed and Dr Mirrakhimov's chapter has been limited to the physiological aspects.

India did have an IBP committee but was unable to devote significant funds to high-altitude research so that the work completed on high-altitude natives in India was supported from sources other than IBP. The Tibetan area, as part of China, was not part of IBP and the studies in the Himalayan countries of Nepal and Bhutan were limited in part by the lack of native scientific participants.

Of the individual projects completed all suffered to some extent from funding limitations; nevertheless, the sum total of these projects were great enough so that a quite new and more synthetic picture of the biology of high-altitude peoples may now be developed. Principle among these long-term and multidisciplinary efforts were the following:

(1) WHO and Chilean sponsored studies of the Aymara in northeastern Chile.

(2) French and Bolivian studies on the Aymara and Quechua in the region of La Paz in Bolivia.

(3) US and Peruvian studies on the Quechua of southern Peru.

(4) British and Norwegian studies of the Amhara in northwestern Ethiopia.

(5) British, French, and US studies of the Sherpa, Tibetan migrants and other high-altitude natives of Nepal.

(6) Specialized Italian supported studies on the Quechua of Peru and Sherpa of Nepal.

(7) USSR studies on the native peoples in the Tien Shan and Pamir mountains.

(8) Selected studies of US populations in the high-altitude areas of Colorado.

In this book the authors have attempted to integrate the information gained from these projects with the previous information available and indicate some of the research needs growing from these results.

Research designs and methods

The conferees at the WHO/PAHO/IBP meeting in recommending the nature of the research needed on the biology of high-altitude peoples suggested a somewhat dualistic approach. On the one hand it was suggested that descriptive information was needed. The categories of information needed were structured in a manner which would provide a comprehensive description of the biological fitness of each population studied.

The recommendations of the human biology group as printed in the report (PAHO, 1967) were as follows:

It was agreed to recommend that, with the use of compositive methods of approach and standardized procedures, information should be obtained in the following categories:

(1) *Fertility and the components of fertility*

(*a*) by demographic needs,

(*b*) using methods in the reproductive physiology of man and of animals which could be applied to human population studies.

(2) *Growth, development and aging*

(*a*) age changes and variability in characteristics thought to be of adaptive value at high altitude,

(*b*) age changes and variability in characteristics in relation to the somatic fitness of individuals,

(*c*) such studies should not be divorced from the psychological and intellectual changes which occur during development.

(3) *Nutrition*

In all cases the nutritional assessment of the populations studied should be made in as detailed a manner as possible, commensurate with the resources available. Such assessments should include:

(*a*) the nutritional status of individuals,

(*b*) detailed nutritional surveys where possible,

(*c*) biochemical studies related to nutrition.

(4) *Special problems relating to work capacity*

Both physiological and psychological methods should be used.

(5) *Epidemiology*

(*a*) In all cases the pattern of disease distribution in populations should be studied. Where additional demographic information is available it is

highly important that more vigorous epidemiological studies should be made.

(*b*) It is of great importance that demographic methods should be developed which would enable the relationships between age, disease and morbidity to be ascertained.

(6) *Genetics*

Further information is required on:

(*a*) the distribution of polymorphic systems in high-altitude populations,

(*b*) the hereditability of quantitatively varying traits, particularly those presumed to be adaptive in nature,

(*c*) congenital defects, especially those presumed to have a genetic component.

(7) *General*

In all these studies the following are essential:

(*a*) There is as precise an analysis as possible of all aspects of the environment.

(*b*) Adequate precautions must be taken to insure statistical representation and control situations. This will often mean the study of lowland populations.

(*c*) The demographic background of the populations under study must be ascertained in as great a detail as possible.

While the descriptive data were considered essential there was a strong concern that the data should be collected whenever possible within a research design which would permit the development of conclusions on how the high-altitude populations had adapted to their environment. At that time short-term acclimatization, developmental biological responses and genetic adaptations were all considered possible mechanisms of adaptation and adjustment to high-altitude environments. In addition, it was clear that many biological responses in these populations had significance in relation to multiple environmental stresses such as reduced oxygen pressure, cold and aridity. It was, therefore, suggested that studies of a broad and multidisciplinary nature should be undertaken in an intensive manner on appropriate population samples.

These ideas appeared to be highly compatible with the desires of most investigators since almost all of the subsequent studies were in fact developed using a variety of population comparison strategies. Because of the financial and other problems cited earlier only a few of the studies were able to develop the disciplinary breadth and sampling procedures which were recommended.

A review of the research strategies utilized in the various projects is enlightening as it allows the reader of the subsequent chapters to evaluate

the relative informational and theoretical advances which each design produced.

Descriptive studies

The number of purely descriptive studies were quite limited but were of considerable value when they provided information on previously unknown populations or on fitness indicators which were unknown in partially described populations. Examples of this type of work include the study of Donoso, Apud, Sanudo & Santalaya (1971) on the work capacity of the high-altitude Aymara in Chile, Andersen's (1973*a*, *b*, *c*) similar studies of Ethiopia's Amhara, and Lang & Lang's (1971) general description of the Sherpa.

Population modeling

Another type of descriptive research which was only rarely attempted in the high-altitude projects was process or flow modeling. Recent research has suggested the great potential of this approach (Baker, 1976*c*) but the only attempts in relation to the high-altitude project were small studies of gene flow (Dutt, 1976*a*) and a community study of energy flow in the Peruvian Andes (Thomas, 1973, 1976).

Intra-group comparisons

Comparison within given population and community units was a research strategy used quite often to solve specific problems in high-altitude regions. Weitz (1973) compared the aerobic capacity of active porters in highland Nepal with less active males in the community. By contrasting these results with a similar study on Tibetans at low altitudes he was able to demonstrate that age and activity effects on aerobic capacity were identical for the two groups. Mazess (1969) used a similar strategy when studying students in a physical education school in southern Peru. By comparing these students with the rather inactive students in a nearby university he assessed the effects of short-term training on the aerobic capacity of the Quechua. Bouloux (1968) compared well-cared-for children in an orphanage to lower class children of the same genetic background to demonstrate that improved child care increased growth rates in high-altitude Bolivian children. In still a different type of intra-population comparison Baker (1969) divided individuals in a high-altitude Peruvian community into two groups in order to demonstrate that the more acculturated individual showed more age increase in systemic blood pressure than the traditional native.

Altitude contrasts

The most popular research design was probably the traditional one of contrasting native populations at different altitudes. In several of these studies populations at various altitudes were used to detect the relative effect while in others only very high-altitude populations were compared to near sea level ones of similar genetic history.

The altitude gradient approach was used to study altitude effects on a number of fitness indicators. Scientists in the USSR used this approach to study both oxygen transport (see Chapter 10) and the growth of children (Miklashevskaya, Solovyeva & Godina, 1972, 1974). Cruz-Coke, Cristoffanini, Aspillaga & Biancani (1966) used the altitude gradient in northern Chile to examine the effects of altitude on both genetic structure and demography. Dutt (1976*b*) also utilized data on populations at three altitude levels to examine the possible relationship between altitude and fertility.

In Peru a number of gradient designed studies were undertaken. Hoff *et al.* (1972) by studying the growth of Quechua children and adults at several altitudes were able to reconfirm that the large chests of the Quechua were basically genetic in origin and little affected by altitude. Garruto (1976) by the study of Quechua at several altitudes found that their hematology was apparently much less affected by altitude than that of lowlanders. One of the smallest significant altitude gradients was demonstrated by Frisancho & Baker (1970) who showed that the difference between residence at 4,000 and 4,500 m appeared to affect general body growth rates.

While several attempts to demonstrate altitude effects were made with comparisons of high- and low-altitude natives (Boyce, Haight, Rimmer & Harrison, 1974; Ruffie, Larrouy & Vergnes, n.d.) the most elaborate design was the one used by Haas (1976). He developed a design containing multiple intra-population comparisons of social class, urban versus rural residence, and ethnic background, all contrasted by altitude to demonstrate that in southern Peru altitude is the major factor affecting infant growth. His ideal design for sampling is presented in Fig. 1.1. In fact he was able to fill only eight of the twelve sample cells projected but these proved adequate for the demonstration.

Lowland migrants to high altitude

The use of migrant–native comparisons proved as popular as Harrison projected, although the entire design he recommended was never completely fulfilled. Of the migrant design models the most common one was a comparison of individuals brought to altitude for short times with

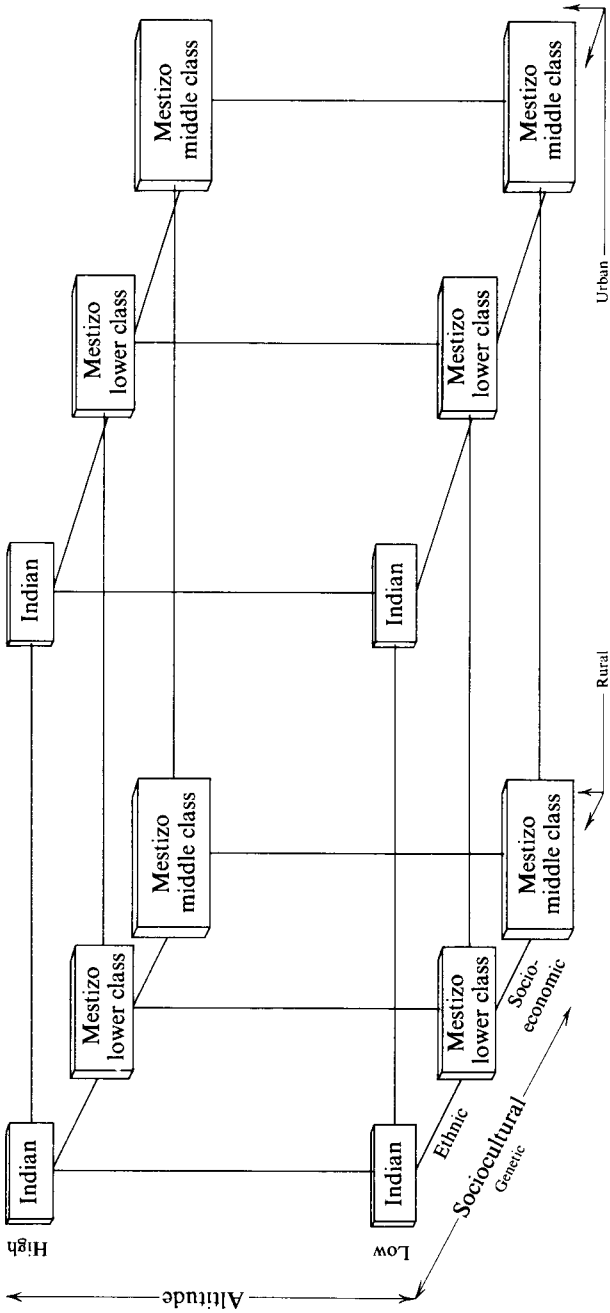

Fig. 1.1. Sampling design structure for analyzing the effects of altitude and other variables on infant growth and development in southern Peru.

high-altitude natives. In India this model was used to demonstrate that altitude had a greater impact on the hematology of upward migrants than it did on natives (Bharadwaj, Singh & Malhotra, 1972). In the Andes several investigators used this technique to demonstrate the superior oxygen transport of the natives at altitude compared to lowlanders who moved to altitude (Baker, 1969, 1976*a*; Buskirk, 1976; Kollias *et al.*, 1974). Comparable strategies were used by Morpurgo *et al.* (1970) to show the differing Bohr effect in high-altitude Quechua and by US investigators to show the unique aspects of Quechua temperature regulation (see Chapter 9).

The study of long-term migrants to high altitude was only rarely employed but proved highly useful. By the study of individuals who moved semi-permanently to altitude from lower altitudes both Le Francois, Gautier & Pasquis (1965) and Frisancho, Velásquez & Sanchez (1973) concluded that, with a sufficiently long exposure, aerobic capacity in migrants can reach native high-altitude values. It is not clear to me whether this requires growth at altitude as suggested by Frisancho *et al.* or only a sufficiently long exposure as suggested by Le Francois *et al.* Neither is it yet clear whether or not an Andean heritage is required (see Chapter 5).

On a different aspect of fitness, Galvez (1966) suggested from the study of long-term lowland migrants in the Central Andes that life at high altitude may lead to reduced systemic blood pressure.

Highland migrants to low altitude

As with several of the other research strategies discussed, the study of migrants from the high-altitude areas to the lowlands was used to examine the characteristics of the highland native (Velásquez, 1966). Several IBP-sponsored studies employed this approach. Lahiri, Edelman, Cherniak & Fishman (1969) explored the irreversibility of the reduced hypoxic drive in the migrants from highland Nepal. Pawson (1976*b*, *c*) studied the growth of lowland-born children of Tibetan migrants in Kathmandu. By contrasting their growth with the Sherpa at high altitude he was able to show that the very slow growth and late puberty of these children was probably more genetic in origin than a direct effect of altitude. In still a different fitness parameter, McClung (1969) measured the placentas and newborn from Peruvian mothers who migrated from high altitude. When she compared the results with those she obtained on the products of mothers in the high-altitude city of origin she was able to indicate precisely the amount of change produced by 3,300 m of altitude.