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Endemic Goitre in the Gilgit Agency, West Pakistan

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ENDEMIC GOITRE IN THE GILGIT AGENCY, WEST PAKISTAN†

WITH AN APPENDIX ON DERMATOGLYPHICS AND TASTE-TESTING

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A study has been made of an iodine-deficient population living in an extended village in the Karakoram Himalayas. There is evidence that the incidence of goitre increases towards the lowest part of the village, in accordance with the findings of McCarrison, who worked in the same region in the early years of the twentieth century. McCarrison ascribed the variation of goitre incidence to increasing pollution of drinking water as it travelled downstream, and postulated a bacteriological goitrogenic factor. However, the observations reported here show no correlation between goitre incidence and the bacterial concentration of drinking water, nor are there iodine-metabolizing micro-organisms present in the water. It may be that a differential iodine deficiency throughout the village can account for the variation in goitre incidence, since the soil can adsorb appreciable amounts of radio-iodine. The indices of thyroid function show that all the inhabitants are exceptionally iodine-deficient, although most of them are clinically euthyroid. As well as having a greatly enhanced mean thyroid iodide clearance the population has a mean renal iodide clearance which is lower than normal. Intra-muscular injections of iodized oil were acceptable to the villagers, and 477 injections were administered. Fingerprints and palm prints were collected from a sample of the population, yielding a pattern distribution comparable with other populations in the Indian subcontinent. The ratio of PTC tasters to non-tasters among the inhabitants is not significantly different from the ratio found in Europe.

1. Introduction

Goitre in the north-west frontier district of West Pakistan

It has long been recognized that the mountainous country forming the northern border of the Indian subcontinent is one of the most goitrous regions in the world. Gilgit, which is the principal town of the northernmost frontier districts of West Pakistan, lies within the goitre belt. Here, at the turn of the century, Sir Robert McCarrison began the researches into the aetiology of goitre which were to be a major part of his life's work. He examined the incidence of goitre in many villages in the Gilgit Agency and neighbouring Chitral, often finding that about half the population had visible goitres.

The situation is not improved today. A recent survey carried out by the World Health Organization showed that 72 % of the schoolchildren in Chitral had enlarged thyroids (Matovinovic 1960). It is not unusual to find exceptional goitres so large that the physical pressure exerted by the gland threatens to suffocate the patient. Figure 11 (plate 43) shows a woman who presented for treatment at Gilgit hospital during our visit.

Bacteriological factors in goitre

When McCarrison first visited Gilgit, the township consisted of a string of nine hamlets sharing a common water supply. He observed (McCarrison 1906) that the incidence of goitre among the inhabitants of the hamlets increased on travelling downstream along the increasingly polluted water supply. He concluded that a bacteriological factor was causing the goitre: goitres produced experimentally in men and animals through drinking the polluted water added weight to this hypothesis. (McCarrison's results are discussed in more detail in the historical note at the end of this paper.) More recently, Vought & London (1967) have also reported a correlation between water pollution and goitre incidence, following a study in Virginia, a region where goitre is not endemic. It therefore seemed worthwhile to return to the scene of McCarrison's work to re-investigate the bacteriological hypothesis in the light of present knowledge of iodine metabolism and using modern techniques. This was the primary purpose of the present survey.

Gilgit is now a continuous town with a large bazaar and a population which includes many officials and traders who are not settled there. It is no longer possible to repeat McCarrison's observations in Gilgit itself. But five miles away, on the other side of the Gilgit River, the village of Dainyor remains a nearly self-sufficient rural community. Only in the last few years has a suspension bridge carried a jeep road to Dainyor, which has remained isolated and probably quite similar to the Gilgit of fifty years ago. A preliminary inspection indicated that the incidence of goitre in Dainyor was substantial, but not so high that no variations would be detectable in different parts of the village. Houses are scattered along the whole length of the extended water supply through the village, and the water becomes increasingly heavily polluted as it flows downstream. Dainyor thus provided an ideal location for the survey.

Prophylactic treatment for goitre

The villages most well known to local people for a high incidence of goitre and cretinism are situated in remote places, in upper Chitral and along the Shigar valley in Baltistan. The inhabitants are primitive, living outside a money economy, and goitre prophylaxis by the use of iodized salt is not appropriate. Salt is a luxury, traditionally distributed as rock salt, and to persuade people to abandon old-established customs and to buy iodized salt in its place can only be a long-term aim.

An alternative method of supplementing an iodine-deficient diet is by the injection of iodized oil into muscle. Iodized oil is cheap, and studies in New Guinea have shown that a single injection can provide the body with adequate iodine for several years (Buttfield *et al.* 1966). The organization of an injection programme is more straightforward than the distribution of iodized salt. Doctors and dispensers based on the hospitals at Gilgit, Chitral and Skardu already tour the villages in their district, and iodized oil injections could become a routine duty during these tours. In a stay of a few days in a small village a doctor assisted by a dispenser could give a high proportion of the children and women of child-bearing age an injection of oil.

A subsidiary objective of the present expedition was to initiate a pilot scheme of goitre prophylaxis by injection of iodized oil. Our experience shows that the inhabitants of Dainyor, although reluctant to give blood samples, were almost all prepared to accept injections.

2. Clinical observations

The aim of the clinical study was to examine a substantial proportion of the population of Dainyor for the presence of thyroid disease. It was also hoped to take blood samples from a high proportion of the subjects for iodine and antibody studies and to carry out radio-iodine investigations on a sample of the population.

Organization

A data sheet was prepared for each household included in the survey. The occupants of a house were members of an extended family, sometimes comprising more than twenty members. This family group received a code number, and within the group each individual was allocated a further number for personal identification. For all subjects the name, age, sex, relationship to the head of the household, goitre class, age of onset of goitre, type of goitre, thyroid state and abnormalities were recorded, together with other relevant comments. Although not everyone in a family might attend, a full list of its members was obtained from the head of the household. The data sheet also recorded the location of the dwelling within the village, specified with reference to the system of water distribution. The villagers designated the water channels through the village by numbers, and ordered the houses according to their distance along each channel. Thus an address might be 'The third house on channel six'. The correctness of the locations was later checked on the ground.

Clinical examination was carried out by one or other of the four medical members of the survey (G.T., K.M., S.M., M.A.S.). Female subjects (except children) were examined by the lady medical officer of the Gilgit Agency Hospital (K.M.). Particular attention was directed to examination of the thyroid and to a clinical assessment of thyroid function. Goitres were graded O (absent), I, II or III according to WHO recommendations (Perez, Scrimshaw & Munoz 1958); many of the class III goitres were very large. Thyroid function was graded as euthyroid, hypothyroid, myxoedema and cretinism; no hyperthyroid individuals were seen. Notes of other diseases present were made. Clinical photographs were taken of a high proportion of subjects. The villagers were asked to provide blood samples, but despite some initial success, few were willing to undergo venepuncture. Of 589 persons who were clinically examined, only 75 donated blood. The blood was taken with disposable plastic syringes and transferred into chemically clean sterile glass containers. It was allowed to clot at ambient temperature and then placed overnight in a paraffin-operated refrigerator at 4 to 6 °C. The following day the expressed serum was removed with a sterile Pasteur pipette into sterile plastic tubes. No centrifugation proved necessary. The separated sera were stored in the freezing compartment of the refrigerator.

After clinical examination and, where possible, venepuncture, subjects were either further investigated by radio-iodine techniques or were offered a dose of iodized oil by intramuscular injection. Most of those offered injection accepted the treatment and 477 doses of iodized oil were administered. Investigations of taste-testing and fingerprinting were also carried out on some subjects.

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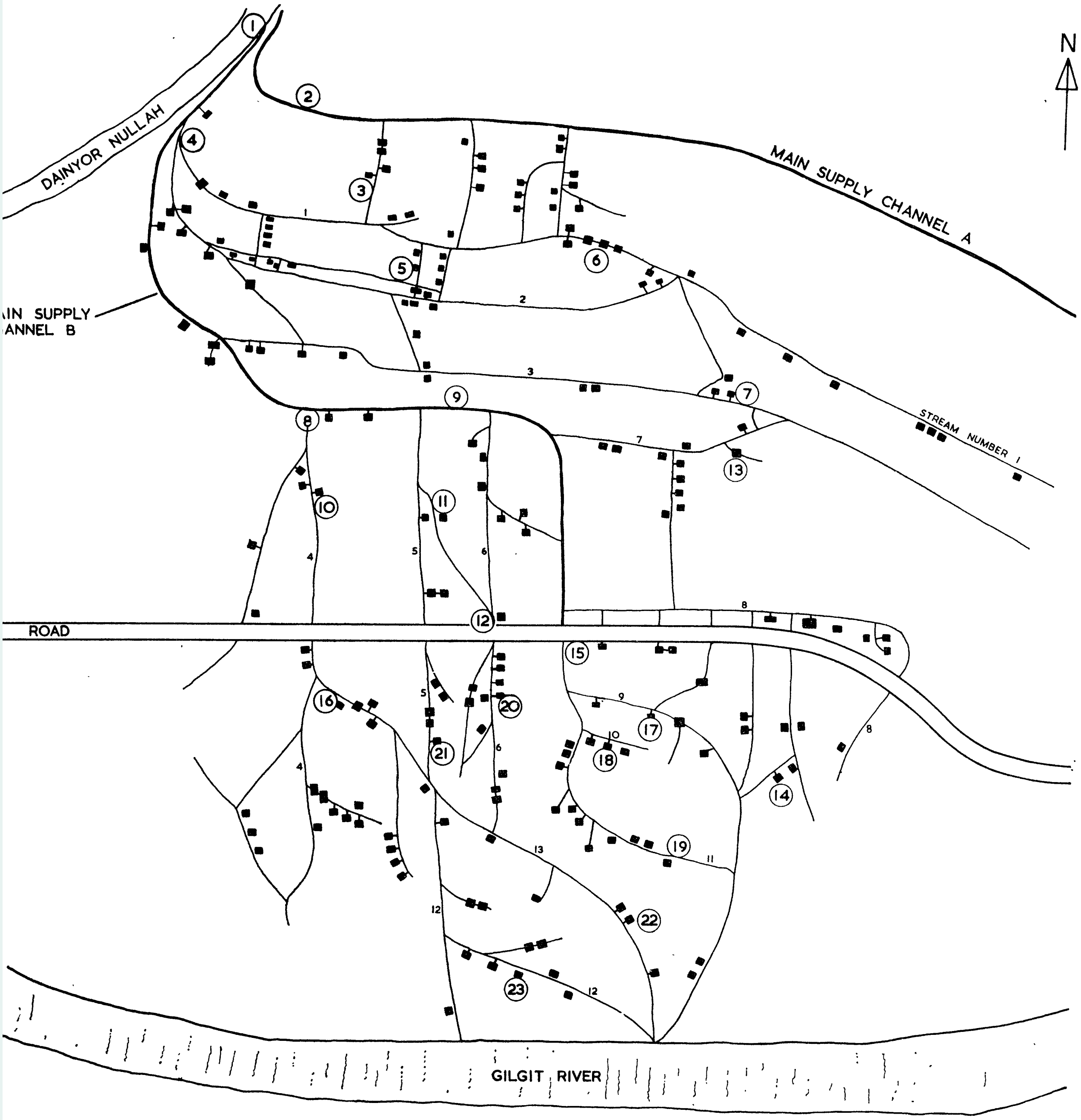

FIGURE 1. A sketch map of Dainyor, showing the network of water distribution channels. The circled numbers indicate the sites where water samples were collected for bacteriological analysis.

Goitre incidence and thyroid function

The survey was limited to the eastern part of Dainyor, which has a self-contained system of water channels supplying 189 households and an estimated population of rather more than a thousand. A map of this part of the village is reproduced in figure 1; the name of the head of every household shown on the map was known. Subjects from 140 of the 189 family groups were examined, amounting to a total of 589 individuals of whom 335 were male and 254 female.

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The predominance of male volunteers is almost certainly due to the unwillingness of some females to be examined, even by a female doctor. The age distribution is shown in table 1. There is a greater proportion of males in the older age groups. It is unlikely that this represents a true age/sex distribution within the total population and is almost certainly a reflexion of the shyness of older females.

Table 1. Age and sex distribution of population sample

	number of persons of age (years)					
	0–10	11–20	21–30	31–40	41+	total
males	144 (43%)	57 (17%)	33 (10%)	35 (10%)	66 (20%)	335
females	122 (48%)	50 (20%)	41 (16%)	20 (8%)	21 (8%)	254

Table 2. Distribution of goitre in age groups

age (years)	number of males with goitres of grade O	I	II	III	total	number of females with goitres of grade O	I	II	III	total	total (both sexes)
0–10	54	71	19	0	144	40	58	24	0	122	266
11–20	10	22	24	1	57	7	23	15	5	50	107
21–30	10	14	5	4	33	3	13	20	5	41	74
31–40	13	6	14	2	35	1	8	5	6	20	55
41+	17	22	19	8	66	0	4	11	6	21	87
total	104	135	91	15	335	51	106	75	22	254	589

The over-all incidence of goitres classes I to III was 74%. The age and sex incidence of classes O, I, II and III are shown in table 2. It will be seen that in the age groups 0 to 10 years and 11 to 20 years there is no real difference in the goitre incidence and grading in males and females. Beyond this age there is a greater tendency for females to be goitrous than males. Thus, for adults aged 21 years and over, 40 of the 134 males were in group O (30%), whereas only 4 of 82 females were non-goitrous (5%). This difference is unlikely to be due to sampling error, and is probably caused by the iodine demands of pregnancy and lactation.

The majority of the goitres were of the diffuse type; nodularity was present in only 17.5% of all goitres. There was no significant difference in the incidence of nodularity in males as compared with females. The incidence of nodular goitre is analysed in table 3.

Estimations by activation analysis of total serum iodine are available in 57 subjects (excluding cretins). Table 4 shows the mean TI levels compared with goitre grading.

Clinical signs of cretinism were found in 10 of the population sampled. Eight of the 10 cretins were male, giving an apparent incidence of 2.4%. There is unlikely to be a genuine difference in incidence of cretinism in the two sexes and it may be that female cretins did not appear for examination. Two male cretins were stated to be 60 years old, but the reliability of this is suspect. Other cretins were aged 30, 37, 15, 14, 13, and 12 (males) and 4 and 21 (females). The cretins appeared to be well cared for by their family group and tended to associate with children of their own mental age. A clinical photograph is shown in figure 12 (plate 43). Serum samples were obtained from only four cretins. The mean total serum iodine (TI) level of these samples was 1.4 μg/100 ml.

Deaf-mutism without clinical evidence of thyroid deficiency was found in six individuals. In contrast with the cretin group they had relatively normal TI levels (mean of three samples, 3.2 μg/100 ml).

Table 3. Age and sex incidence of nodular goitre

	number of cases of goitre/number of persons examined				
age group ...	0–10	11–20	21–30	31–40	41 +
male	4/144	8/57	4/33	6/35	17/66
female	2/122	8/50	12/41	9/20	6/21

Table 4. Mean TI levels compared with goitre grading

goitre grade	no. in group	mean TI (μg/100 ml)
O	5	3.5
I	21	3.0
II	22	1.9
III	9	2.3
all non-cretins	57	2.7

Hypothyroidism (excluding cretins) was clinically diagnosed in 24 subjects in the sample of population examined (4 %). This is appreciably lower than that observed in the Khumbu region by Sir Edmund Hillary's expedition (Ibbertson, Pearl & Tait 1969). No great difference was observed in incidence between the sexes (males 15, 4.5 %; females 9, 3.5 %). Only four samples of serum were obtained from the hypothyroid group. The mean total iodine level was 1.0 μg/100 ml. This compares with a mean TI in non-hypothyroid subjects of 2.7 μg/100 ml. (57 subjects). The low incidence of hypothyroidism is odd in view of the high proportion of subjects with very low TI levels. Twenty-two of 56 sera (39 %) from individuals considered clinically not to be hypothyroid had TI levels of less than 2.0 μg/ml. By standards applying in this country these individuals would all be expected to show obvious signs of hypothyroidism. There is no doubt that the population as a whole is very iodine deficient, but that by some means the majority appear to have adapted very well to this deficiency.

Other morbidity in the population

Many individuals attended the clinic to seek advice and treatment for various conditions. In addition, abnormalities were detected at clinical examination in some individuals. Although no accurate statistics on the incidences of non-thyroidal disease are possible, it is of interest to record the types of illness observed.

The two commonest conditions for which we were consulted were pyrexias of unknown origin and nematode infestation of the gut. In the former group a proportion were malaria, and both *Plasmodium vivax* and *falciparum* trophozoites were detected in blood smears. Tuberculosis appears to be common. Deformities were seen resulting from Pott's disease of the spine and from inadequate treatment of fractures. Several cases of leprosy were observed. A condition known locally as Dainyor sore was claimed to be common and was said to occur in children, usually with fatal outcome. One case was seen which fitted the local description. Clinically this appeared to be cutaneous anthrax. No attempts were made to isolate the organism as it was

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considered to be too hazardous under the primitive laboratory conditions available. The child responded well to benzyl penicillin.

The pattern of goitre in Dainyor village

It has already been noted that Gilgit in the early 1900s consisted of a number of separate villages and that McCarrison, in comparing the incidence of goitre in these villages, found the highest incidence in the village farthest downstream, with the most polluted water supply. Our observations in Dainyor cover a continuously settled area, but for the purpose of studying the pattern of goitre incidence, as it is related to the water supply, the village can be divided into three parts in a natural way. The three parts are:

(1) Shikas Das, the topmost section of the village, running right up to the steep slopes of the mountains.

(2) The part between Shikas Das and the jeep road which contours across the village.

(3) The part below the road.

The map in figure 1 shows that there are two principal supply channels, called channel A and channel B, which run directly from the Dainyor river. Channel A supplies Shikas Das. The lower network of streams branching from channel B is fed chiefly by this channel, but also receives the polluted outflow from Shikas Das. From the results of bacteriological survey discussed in the next section we know that the water becomes more and more polluted towards the bottom of the village, and the inhabitants of parts 1, 2 and 3 are drinking progressively poorer water.

The incidence of goitre in the three parts of the village is given in table 5. In the third column is the percentage of subjects with visible goitres (i.e. the percentage allocated to goitre classes II and III); this is presumably a measure of the incidence of the disease comparable to McCarrison's 'percentage of population goitrous'. This percentage increases towards the bottom of the village. Thus the pattern of goitre incidence in Dainyor at the present time does indeed resemble that observed by McCarrison in Gilgit many years ago.

Table 5. The distribution of goitre in different parts of Dainyor

	goitre distribution			serum iodine	
part of village	no. of subjects	percentage in goitre classes II and III	$\bar{g}$	no. of subjects tested	mean TI
1. Shikas Das	46	22 %	0.76 ± 0.11	2	(2.7; 3.7)
2. above road	297	29 %	1.07 ± 0.06	27	2.65 ± 0.35
3. below road	238	38 %	1.19 ± 0.06	32	2.29 ± 0.25

An attempt was made to assess the statistical significance of these observations. In the clinical examination, each individual was assigned a goitre class $g_i = 0, 1, 2$ or 3 (i.e. O, I, II or III on the WHO classification). As an index of the whole goitre distribution, the mean goitre class

$$\bar{g} = \frac{1}{N}\sum_i g_i$$

and the standard deviation of $\bar{g}$ are also given in the table for the populations of each section of the village. Although $\bar{g}$ increases uniformly, one cannot be certain that this is not the result of a chance fluctuation. If the goitres are distributed randomly, then the change in $\bar{g}$ is significant

FIGURE 11. A woman with an exceptionally large goitre.

FIGURE 12. A female cretin. This subject, although about 20 years old, is only 2 ft 6 in high.

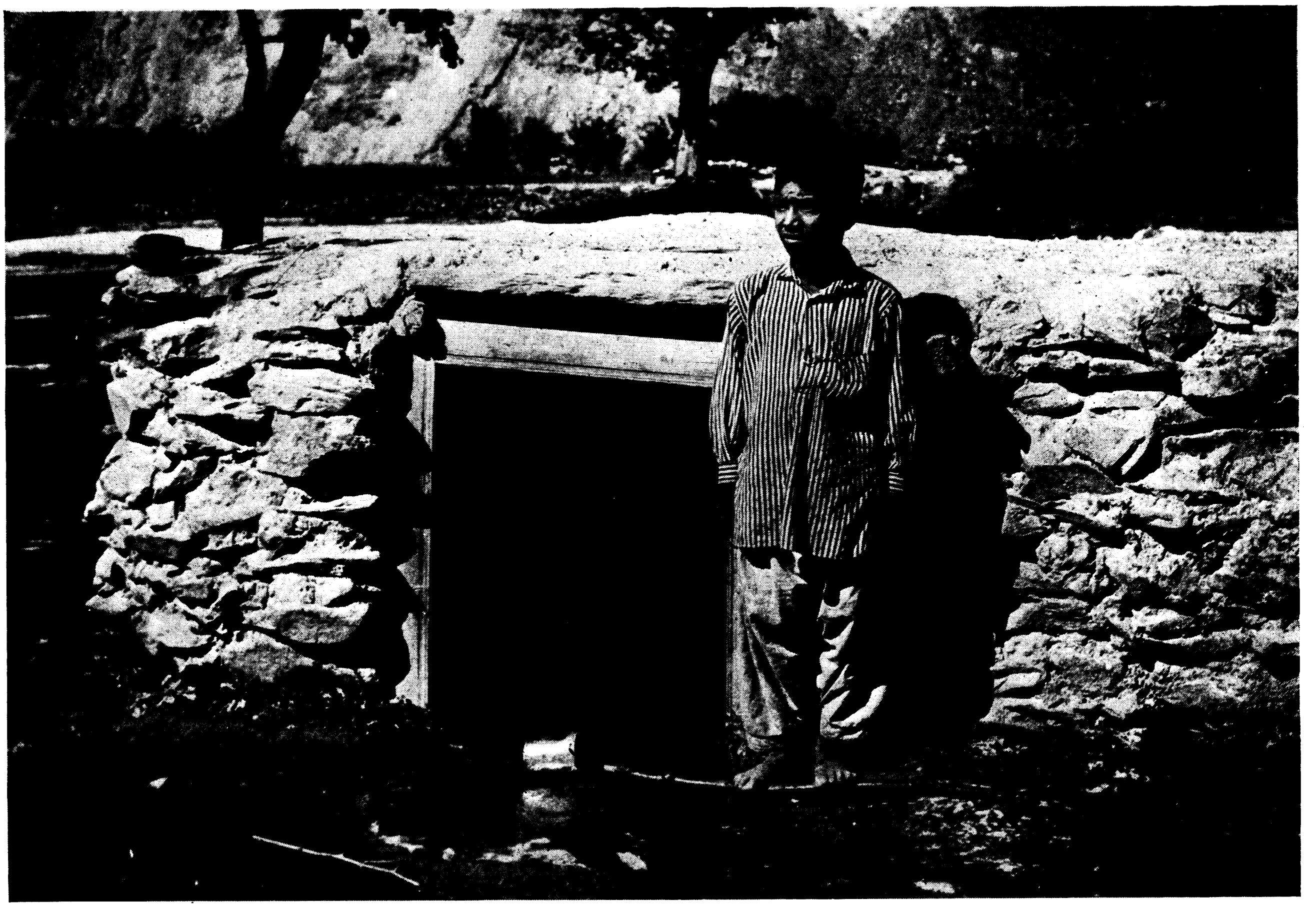

FIGURE 14. A covered water-storage tank.

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FIGURE 15. Measurement of iodine uptake.

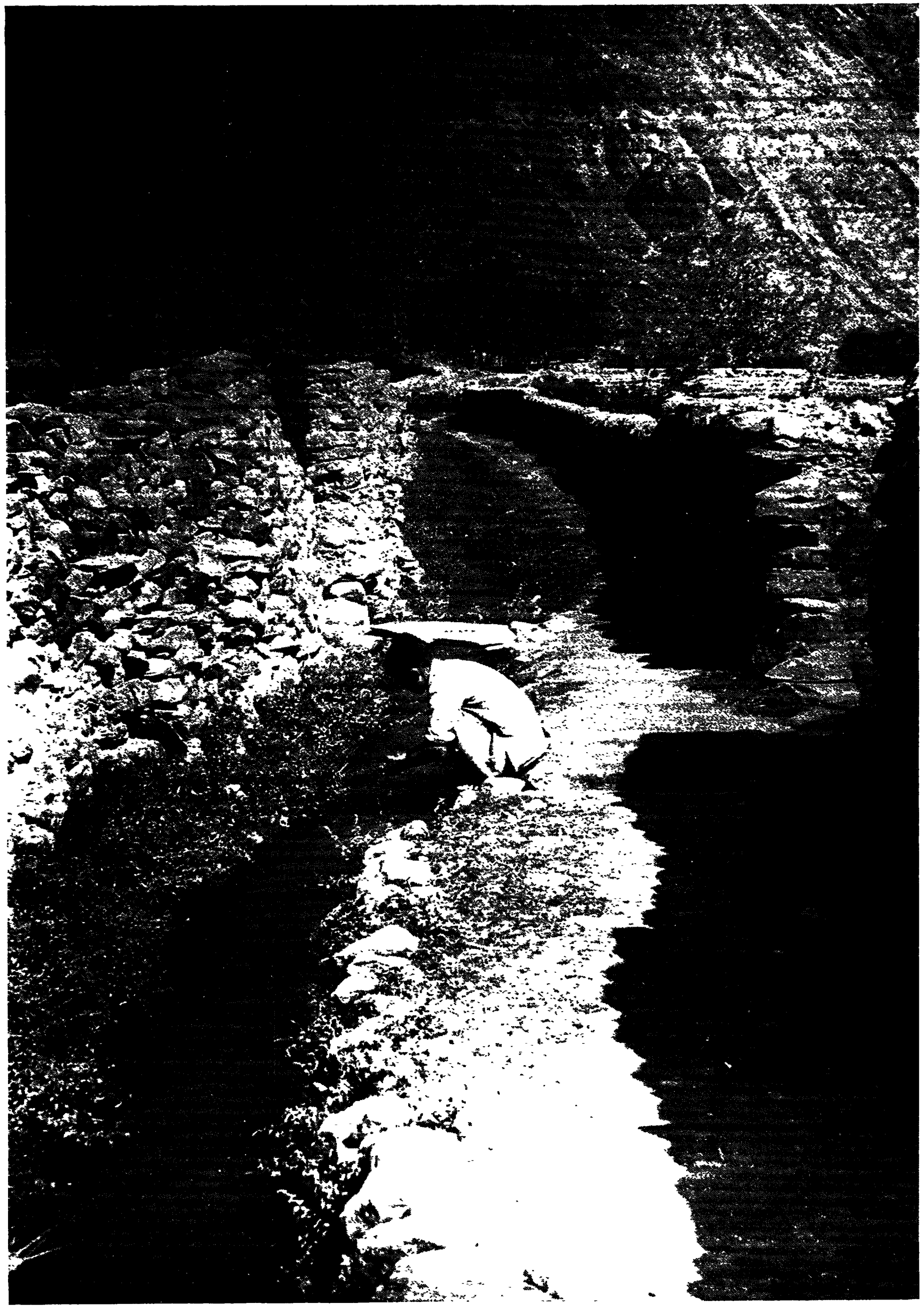

Figure 13. One of the principal channels in Dainyor, supplying water for drinking and irrigation.

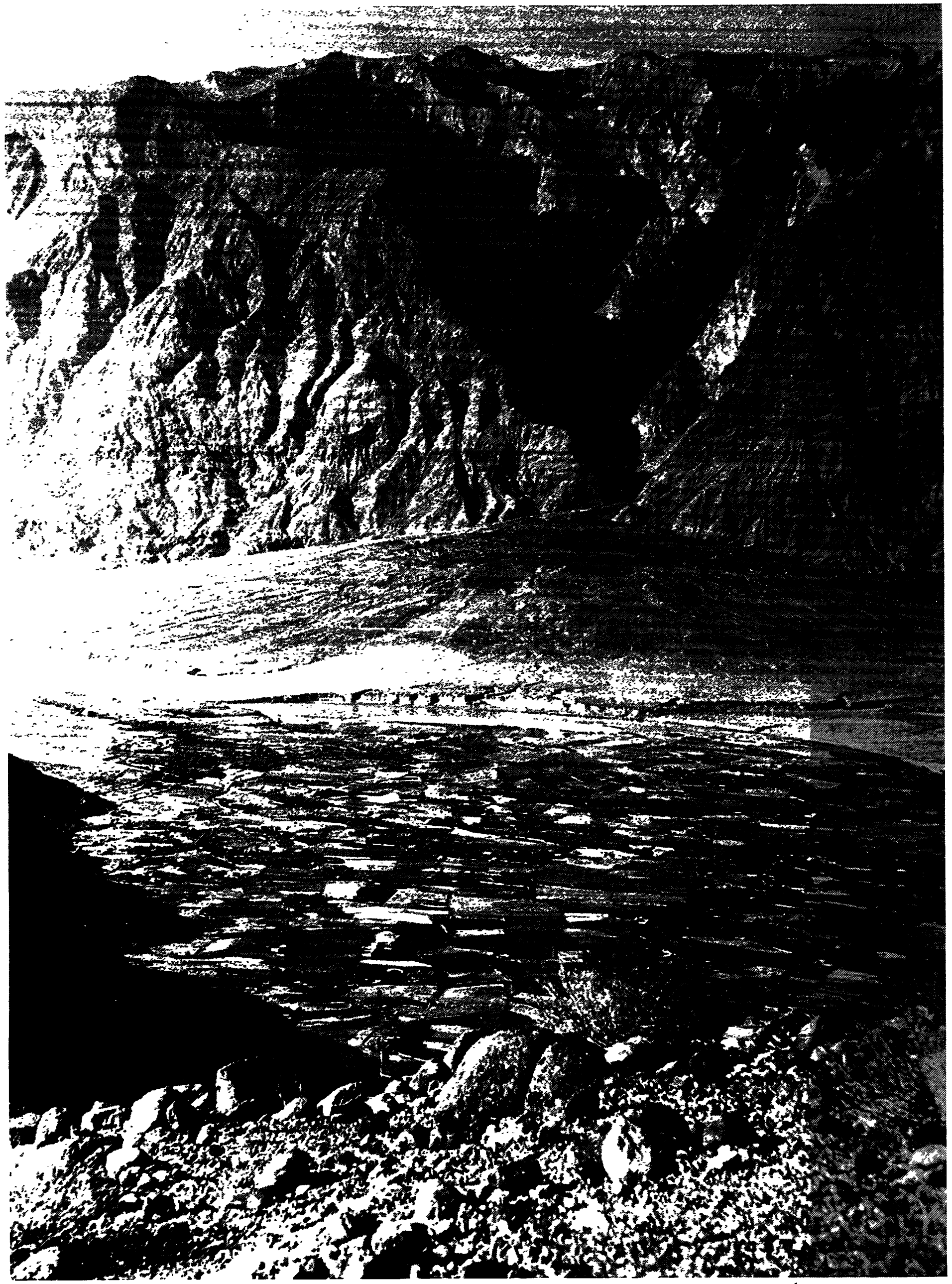

Figure 16. Alluvial fans on either side of the Gilgit River. The nearside cultivated fan is the village of Dainyor. The barren unirrigated fan on the far side is typical of the formations which occur wherever a tributary joins the wide river valley.

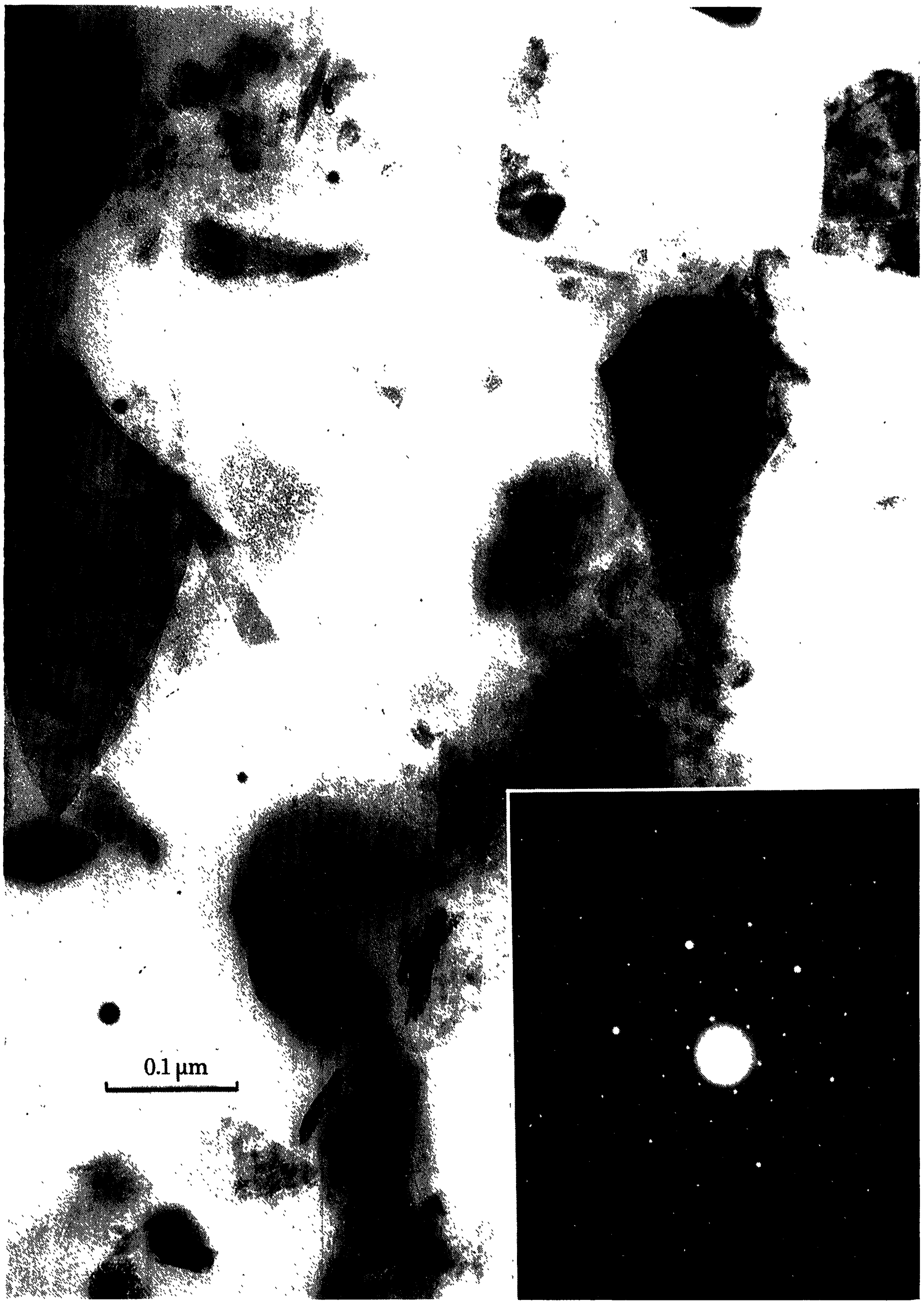

FIGURE 17. An electron micrograph of particles in suspension in Dainyor water. The particles were dried down onto collodion-filmed grids and examined at an electron-optical magnification of × 30 000. The final magnification after photographic enlargement is indicated by the calibrating mark. The smallest particles detectable were about 10 nm in thickness. A selected-area diffraction pattern from a single larger particle is shown inset; the pattern is typical of clay minerals.

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at the 0.1 % level. The assumption that goitres are randomly distributed is questionable, if only because of the relationships between people in different households (of which we have no record). Nevertheless, in a community like Dainyor the people are probably genetically fairly well mixed. In similar villages in nearby Swat, 40 % of marriages take place between men and women from different villages (Barth 1956).

Another hint that the variation in goitre incidence is real comes from the measurements of total serum iodine, also listed in table 5. Because of the small size of the population sampled, the standard deviations of the mean serum iodine is rather large, and the difference between the values in the regions of the village above and below the road is not by itself significant. Nevertheless, the difference is in the expected direction, with a lower serum iodine in the more goitrous part of the village.

3. Bacteriological and immunological studies

The eastern part of Dainyor, where the clinical observations were made, has its own water supply, independent of the rest of the village. Water samples taken from this part of the village showed a systematic variation in bacterial concentration, the pollution increasing rapidly as the water flowed downstream. This confirmed our view that the village was well suited to a search for a correlation between goitre incidence and the degree of pollution of drinking water. As we shall now show, we were unable to detect any such correlation.

The water supply to Dainyor is derived from the river flowing down the nullah (ravine) behind the village. The river is fed by glacier melt from the southern slopes of Rakoposhi, one of the highest mountains in the Karakoram Himalayas. During the summer months the water carries a heavy load of silt, and has the appearance of diluted milk. The water is channelled by means of streams, some of which are always flowing and some controllable by means of simple wooden dams. A typical stream is shown in figure 13 (plate 45). The water is used partly for domestic requirements and partly for irrigation, and water available to a particular household appears to be used indiscriminately for both purposes. Individual families have one of three types of water supply. They may collect water directly from a nearby stream which is not within the family compound (these tend to be relatively large streams with a high flow rate), they may have a minor, slowly flowing stream passing through the compound, or they may have a 'tank'. Tanks are large holes in the ground often surrounded by a low wall and covered by a roof (see figure 14, plate 44). Water is periodically run into the tank and some settlement of the large silt particles occurs. Tanks are stagnant and often have considerable vegetation around the edges and sometimes growing in the water.

Water samples were taken from various sites along the extended water system, from streams and from tanks. The map (figure 1) illustrates the water supply system and the points sampled. Sterile water sampling bottles were used and bacteriological examination was carried out within an hour of collection. Measured volumes of sampled water or dilutions in sterile water were filtered under pressure through membrane filters with a pore size of 0.45 μm. Two or three samples of the water from each collecting point were filtered. After filtration the membranes were removed aseptically. One was pressed onto the surface of a nutrient agar plate, one onto a MacConkey agar plate, and when three filtrations had been carried out, one onto a blue-green algae medium. The MacConkey plates were incubated at 37 °C and the nutrient agar and blue-green algal medium at ambient temperature (20 to 30 °C). After 48 h incubation colonies were counted; on the MacConkey medium non-lactose fermenting colonies were ignored. From these counts the total bacterial count and the lactose fermenting count could be determined. Lactose-fermenting colonies from the MacConkey plates were subcultured for purity and then further subcultured on nutrient agar slopes for return to Manchester where Eijkman testing was carried out, and the faecal coli count determined. The results of the bacteriological investigation are given in table 6.

TABLE 6. BACTERIOLOGICAL RESULTS OF WATER SAMPLING

water sample no.	type of supply	total count	L-F count	faecal coli count
1	M	280	2	0
2	M	6400	30	0
3	T	69000	10000	2500
4	M	340	4	1
5	T	8600	1200	600
6	T	61000	3000	2400
7	T	23000	2000	700
8	M	1800	8	2
9	M	5800	20	0
10	T	34000	1000	200
11	M	5700	500	0
12	M	83000	3800	1900
13	T	92000	3600	1200
14	T	62000	2600	1300
15	M	35000	200	50
16	T	62000	600	100
17	T	130000	2600	1800
18	T	30000	200	50
19	M	183000	6000	3000
20	T	79000	9000	1300
21	T	45000	1400	450
22	T	120000	7000	3500
23	T	51000	400	200

M = main stream; T = tank. All counts expressed per 100 ml. No blue-green algae were isolated from any specimen of water. L-F = count of lactose-fermenting bacilli.

As expected, the water supply entering Dainyor is of reasonable bacteriological quality. The flow rate here is very high and there is no settled habitation upstream, although some pastures are used for summer grazing of animals. The map in figure 1 shows the two principal supply channels which flow through the village, and the network of main streams branching off from them. Water in the irrigation network becomes progressively more polluted as it passes through the village. This is reflected in progressive increases in total bacterial count, in lactose-fermenter count, and to a less extent in faecal coli count. Thus water specimens 1, 2, 4, 8, 9 and 15 are taken from the principal supply channels at increasing distances from the source. Total counts in these samples (viz. 280, 340, 1800, 5800 and 35000) increase regularly. The last figure is very high and this sample (15) also contained a high faecal coli density. It was taken from the channel just after it has passed under the road near the mosque at the centre of the village. Sample 12, taken from a stream just outside the mosque, also had a very high faecal coli count. Inhabitants of the village tend to congregate in the area around the mosque and children play in and out of the water. It is suggested that this accounts for the sudden increase in count samples 12 and 15. Thus the water even in the flowing streams can be very polluted. No attempt is made to avoid contamination, and indeed alongside the streams there are always paths, on which children play and animals are driven. The highest total count of all was found in sample 19 taken from a stream at the very bottom of the village.

The families obtaining their water from running streams are using the supply of the best available bacteriological quality, poor though it is. All the samples of tank water are extremely unsatisfactory, having high values for all three types of count. Presumably the water from the slowly flowing subsidiary streams passing through the compounds of some households is of intermediate quality. The mean goitre class $\bar{g}$ was calculated for the three groups of families taking their water from main streams, from subsidiary streams and from tanks. The mean class $\bar{g}$ for each group of families is shown in table 7. There is clearly no correlation between the type of water supply and the incidence of goitre.

Table 7. Mean goitre class of families with different types of water supply

type of water supply	no. of individuals	$\bar{g}$	percentage in goitre classes II and III
main stream	204	1.11 ± 0.07	35
subsidiary stream in compound	82	1.09 ± 0.11	26
tank supply	225	1.11 ± 0.07	32

All the households upstream of a particular family are a potential source of contamination of their water supply, and the number of such households should be a rough index of pollution. We have calculated $\bar{g}$ for families grouped according to the number of intervening households between each family and the relatively pure principal supply channel. The results, given in figure 2, do not indicate any variation of $\bar{g}$.

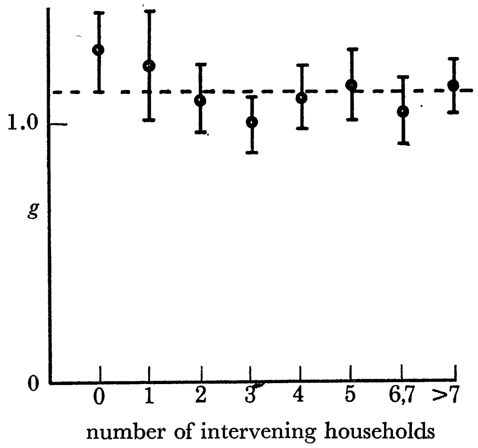

Figure 2. The mean goitre class $\bar{g}$ plotted against the number of intervening households below the principal supply channel.

The lack of correlation between $\bar{g}$ and the type of water supply (stream or tank), or between $\bar{g}$ and the number of intervening households, suggests that there is no direct relationship between the bacteriological purity of the water supply and the incidence of goitre. Further evidence supporting this conclusion comes from 36 individuals who were examined clinically, and who lived in households whose water supplies had been sampled. For these households the correlation coefficient between goitre class and the total bacterial count was +0.15, whilst the coefficient with respect to faecal coli count was −0.07. To judge from the 'Student' *t* test, neither correlation coefficient is significantly different from zero.

Thus the evidence shows that although we were able to repeat McCarrison's observation of increasing incidence of iodine-deficient goitre with respect to increasing distance down the village his suggestion that this was directly due to bacterial pollution is not substantiated.

Thyroid auto-antibodies in Dainyor

On return to Manchester all samples of serum were tested for the presence of both anti-thyroglobulin and anti-microsomal antibodies. Of the 75 samples of serum tested for anti-thyroglobulin antibodies by the tanned red cell technique and for anti-microsomal antibodies by complement fixation, 13 (17 %) were positive in one or both tests. The results are shown in table 8. It will be noted that all subjects with thyroid auto-antibodies were goitrous, and that most were in classes II and III. The incidence of positive results is very much higher than is found in unselected sera in this country. This is particularly so of the incidence of anti-microsomal antibodies. In serum samples examined from the survey in Khumbu (Ibbertson *et al.* 1968), less than 10 % had anti-thyroglobulin antibodies, and anti-microsomal antibodies were said to be rare. In Bhutan thyroid antibody studies were essentially negative (F. S. Jackson, personal communication). The incidence of anti-thyroglobulin antibodies in our series is in agreement with that in Khumbu, but, with an incidence of 13 %, positive anti-microsomal antibodies can hardly be described as rare in Dainyor. Other differences between the Khumbu and Dainyor populations are the higher incidences of both goitre and hypothyroidism in Khumbu. This implies either greater iodine deficiency or less efficient adaptation to this deficiency in Khumbu. It is therefore possible that in Dainyor there is a greater tendency for more frequent minor change in thyroid state, that is improvement followed by deterioration, leading to periods of thyroid hyperplasia and involution. Under such circumstances minor degrees of thyroiditis often develop. This would probably be reflected in the presence of circulating thyroid auto-antibodies.

Table 8. Thyroid auto-antibodies

subject	TCA anti-thyroglobulin titre	CFT anti-microsomal titre	age (years)	sex	goitre class	goitre type
8/0	—	5	35	M	I	diffuse
8/6	—	5	32	F	III	nodular
14/0	—	20	17	M	I	diffuse
19/0	40	40	15	M	III	nodular
19/2	—	40	13	F	II	nodular
20/0	—	30	80	M	III	diffuse
75/0	20	—	40	M	II	diffuse
80/0	320	40	50	M	II	nodular
80/10	—	5	10	M	I	diffuse
82/1	40	—	10	M	II	diffuse
97/3	20	10	20	F	III	diffuse
103/2†	40	—	15	M	I	diffuse
131/1	20	10	30	F	II	diffuse

† cretin.

4. Iodine metabolism

In addition to the measurements of total serum iodine concentrations mentioned above, urine iodine concentrations were measured and some simple tests of iodine metabolism made in the field using the radioactive isotope ^{131}I. The field tests were necessarily haphazard, since they had to be made whenever willing villagers were available. Radio-iodine uptakes, for example, were not as usual measured at 4 or 24 h after the dose, but at random times. Nevertheless, the data provided most of the required information. All the results are consistent with extreme iodine deficiency. The indices of thyroid function of the inhabitants of Dainyor are closely similar to those of the Sherpas of Khumbu, the only Himalayan population with a comparably iodine deficient metabolism which has previously been studied.

Stable iodine in serum and urine

After irradiation in a flux of 10^{12} neutrons $cm^{-2}\ s^{-1}$, the samples were added to a ^{127}I carrier solution and heated with concentrated sulphuric acid to break down organically bound iodine into iodide. Analysis of standard thyroxine solutions checked that the breakdown was complete. The iodide was distilled off and separated from active contaminants, notably ^{38}Cl, by repeated solvent extraction. The efficiency of separation, measured for each sample by precipitating and weighing the ^{127}I carrier, varied from 50 to 80%. Repetition of the analysis of a sample of pooled serum indicated an accuracy of about 10% for an individual measurement on a 0.5 ml ample of serum.

The correlation between the total iodine concentration in serum and clinical symptoms has already been discussed. The mean concentration from all our samples is 2.3 μg/100 ml, a very low value indeed, somewhat lower even than the concentration of 2.8 μg/100 ml observed among the Sherpas of Khumbu. In view of the excellent adaptation of the Dainyor population to iodine deficiency, it would be interesting to know the distribution of serum iodine among the different circulating thyroid hormones. We have made no attempt to measure the concentration of separated hormones.

Some urine ^{127}I concentrations were measured in order to estimate daily iodine turnover. Healthy individuals are not usually in iodine balance, and it has been reported (Vought, Maisterrana, Tova & London 1965) that on a time scale of a few days there is no correlation between iodine intake and excretion. Nevertheless, it should be pointed out that there was a large quantity of iodized oil in our camp site, and that some subjects must surely have ingested iodine derived from the oil. Urine samples may also have been directly contaminated with oil.

It was difficult to persuade the Dainyor villagers to make 24 h collections, but those who did so produced volumes of urine suggesting that the collections were complete. The shorter collections were taken primarily for renal clearance measurements, and since there was no record of when the subjects had previously evacuated their bladders, these samples give a high estimate of the iodine excretion rate. The urine results are given in table 9, which shows that the average iodine excretion rate is less than 50 μg/day. Some individuals were undoubtedly excreting only a few micrograms of iodine daily.

^{131}I uptake

^{131}I was given orally in capsules supplied by the Radiochemical Centre, Amersham. The capsules were flown to Gilgit in a single consignment, with a range of activities wide enough to ensure that a dose of rather less than 10 μCi was available during the whole of the survey. Thyroid activity was measured with a 2 in (5 cm) NaI(TI) counter which was calibrated daily in a water-filled phantom neck made of Perspex.

TABLE 9. ^{127}I EXCRETED IN URINE

sample no.	volume of sample	collection period	^{127}I excreted per day
1	810 ml	24 h	0.5 μg
2	770	24 h	154
3	715	24 h	63
4	1600	24 h	2.9
5	1170	24 h	2.0
6	675	24 h	420
7	190	1 h 45 min	4.1
8	270	1 h 40 min	0.6
9	35	1 h 35 min	3.6
10	63	1 h 35 min	4.3
11	195	1 h 35 min	2.3
12	133	1 h 25 min	10

Sample 6 was collected from the village schoolteacher, who was not a native of Dainyor. The collection time for samples 7 to 12 are lower limits, since only a single urine specimen was passed at the end of the period when the subjects were under our control. The estimates of their daily iodine excretion are therefore likely to be too high.

Figure 15 (plate 44) shows a villager having his iodine uptake measured. The counter was simply tied to a post, and the subject, with his chin resting on a stiff wire, was manoeuvred until his neck was 40 cm from the front face of the counter. All the villagers submitted docilely to this treatment, and it was quite easy to keep them still for the duration of two 2-min counts.

For reasons of weight the collimator did not conform to the I.A.E.A. standard. It had a flat central response, and the count rate of the ^{131}I photopeak fell to 90 % of the maximum at $7\frac{1}{2}$ cm on either side of the centre in the horizontal direction and at 6 cm in the vertical direction. Beyond these distances the count rate fell rapidly. Some goitres were so large that part of the thyroid activity may have lain outside the flat part of the counter response curve. In large goitres both the distance of the source from the counter and the attenuation of the radiation are uncertain in any case, and no correction has been made for goitre size. Nor has any correction been made to allow for a contribution to the observed activity from ^{131}I not trapped in the thyroid.

In order to compare the uptakes measured at different times after ingestion of the ^{131}I dose, the results have been expressed as the uptake U_∞ after an infinite time. When two or more uptakes are known for one subject, it is assumed that iodine absorption from the gut is rapid, and that thyroid radio-iodine increases towards U_∞ with a single exponential time constant. The average value of this time constant for 25 individuals is only $1\frac{1}{4}$ h, indicating an avidity for iodine even greater than is found in thyrotoxicosis. For patients who appeared only once for iodine uptake measurement, at a time less than 3 h after the dose, the total uptake U_∞ was calculated assuming a $1/e$ decay time of $1\frac{1}{4}$ h for plasma radio-iodine.

The uptake measurements are correlated with clinical classification in figure 3. The two individuals Shahji and Haider Jan are not typical. Shahji was the owner of our campsite and Haider Jan our bearer: both had undoubtedly been in contact with iodized oil. The other subjects of goitre class zero have very high uptakes, on average about the same as goitre class II subjects, and higher than those of class I. In class II, both cretins and clinically hypothyroid subjects have lower uptakes than euthyroid individuals. Only half-a-dozen of the uptake measurements were made on females, too small a sample to detect any difference between the sexes.

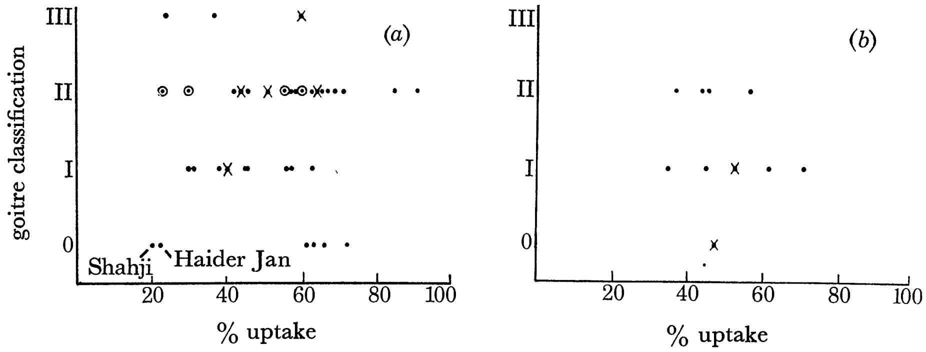

FIGURE 3. The correlation of ^{131}I uptake with clinical classification. (*a*) normal individuals, (*b*) cretins. ×, women; ⊙, clinically hypothyroid.

Thyroid and renal clearances of iodine

A better measure of the iodine avidity of the thyroid than iodine uptake is the thyroid clearance, which is defined as the rate of trapping of iodine by the thyroid divided by the plasma iodide concentration. Because of the difficulty of persuading the villagers to submit to venepuncture, the thyroid ^{131}I clearance was measured for only fourteen individuals. Eleven of the fourteen passed satisfactory urine samples, allowing their renal clearances to be calculated also. Plasma and urine activities were detected in the NaI(TI) well crystal biased, like the uptake counter, to count only the ^{131}I photopeak. Corrections were made to allow for the variation of counter efficiency with sample volume.

The technique recommended by Wayne, Koutras & Alexander (1964) for measuring clearances is to collect urine and measure uptake at $\frac{1}{2}$ h and $2\frac{1}{2}$ h after administration of the radio-iodine dose, and to take a blood sample at $1\frac{1}{2}$ h. This method is not appropriate to the conditions in Dainyor, because of the short life-time of the plasma iodide. It is not possible simply to telescope the technique to a shorter time-scale, because the urine samples would then become unrepresentative. We made only a single collection of urine and made a single uptake measurement, immediately after taking a blood sample about $\frac{3}{4}$ to 1 h after administration of radio-iodine. When dealing with primitive people under field conditions this procedure has the advantage that the subjects have to be persuaded to return only once after taking the radio-iodine dose. Also, the single urine sample is likely to be a good measure of the total radio-iodine cleared by the kidney up to the time when the sample is passed.

As before, we take as the model for iodine kinetics a rapid absorption in the gut followed by removal of iodine from the plasma with a decay constant λ. If all the measurements are made at a time T after administration of the dose, then

$$\text{thyroid clearance} = \frac{\%\ \text{uptake}}{\%\ \text{dose/ml of serum}} \times \frac{\lambda e^{-\lambda T}}{1-e^{-\lambda T}}$$

$$\approx \frac{\%\ \text{uptake}}{\%\ \text{dose/ml of serum}} \times \frac{1}{T},$$

if (λT) is small. Similarly:

$$\text{renal clearance} \approx \frac{\%\ \text{dose in urine}}{\%\ \text{dose/ml of serum}} \times \frac{1}{T}.$$

The approximate expressions hold if the plasma iodide concentration varies linearly, but overestimate the clearances for an exponential decay. On the other hand, delayed absorption in the gut causes the approximate expression to underestimate the true clearance. A check on the consistency of the results can be made by calculating the iodide space. Using the mean lifetime of $1\frac{1}{4}$ h derived from all uptake measurements, and the mean thyroid and renal clearances of 228 and 14 ml/min, the iodide space is found to be 18 l. This is close to the value found in more controlled conditions (Myant, Corbett, Honour & Pochin 1950) and suggests that our results for clearances are accurate, at least to within 20 % or so.

As a check of our procedure the thyroid and renal clearances were measured for Husain Mahmud, the husband of Dr Khalida Mahmud. The values were 37.7 and 39.5 ml/min respectively, both well within the normal range. The renal clearance of 39.5 ml/min is much larger than was observed for any of the Dainyor villagers.

Table 10. Thyroid and renal clearances

subject	thyroid clearance (ml/min)	renal clearance (ml/min)	goitre class	clinical state
16/0	660	—	2	euthyroid
36/0	213	6.1	2	cretin
39/4	144	—	2	euthyroid
41/0	365	24.3	1	euthyroid
57/1	181	14.1	2	hypothyroid
67/0	77	6.9	3	cretin
80/10	137	17.3	1	euthyroid
103/0	65	—	2	euthyroid
103/2	140	—	1	cretin
124/0	360	20.5	2	euthyroid
130/0	168	10.9	0	euthyroid
	mean = 228	mean = 14.3		
32/0	36	—	0	euthyroid
120/0	51	12.4	0	euthyroid

The last two entries in the table refer to the owner of the camp-site and our bearer, both of whom helped at the clinic and had handled iodized oil.

The *ratio* of thyroid and renal clearances is not subject to any uncertainties arising from details of the iodine kinetics, because the thyroid uptake measurement and the urine collection were made at the same time. These ratios were clearly inconsistent with the assumption that only the thyroid and the kidney are competing for radio-iodine, because the clearance ratio is about 15, yet the average thyroid uptake is much less than 90 %. The missing iodine is presumably never absorbed from the gut: unfortunately it was not feasible to make measurements of faecal radio-iodine, and we have only the indirect evidence of a gap in the ^{131}I balance sheet to suggest that the inhabitants of Dainyor are unable to utilize all of the little iodine they ingest. For Husain Mahmud the balance-sheet was complete. His radio-iodine uptake approached $U_\infty = 46.5\,\%$, and since the ratio (renal clearance/thyroid clearance) was 1.05 in his case, the total proportion of radio-iodine eventually excreted in the urine was $46.5\,\% \times 1.05 \doteqdot 49\,\%$. Thyroid and urine together accounted for all but a few per cent of the initial dose.

Individual values of thyroid and renal clearance are presented in table 10. The thyroid clearances are enormous, the mean value of 228 ml/min being ten times the normal for a population not deficient in iodine. The clearance is much larger than the mean value of 44 ml/min measured in a region of extreme iodine deficiency in the Congo (de Visscher *et al.* 1961). The only comparable observations are in Khumbu, where the Sherpas have a mean thyroid clearance of 229 ml/min, fortuitously almost identical with our result (Ibbertson *et al.* 1969), and in New Guinea, where the mean of the thyroid clearances of four subjects was 370 ml/min (Choufoer, van Rhijn, Kassenaar & Querido 1963).

The renal clearances are definitely low, the average of 14 ml/min being less than half the average for a normal population. Again our results compare with those of Ibbertson *et al.* who found the mean renal clearance of a sample of 27 Sherpas to be 19.7 ml/min, a distinctly low value. Several independent surveys of renal clearance in normal populations are quoted by Wayne *et al.* (1964) and all have averages above 30 ml/min. We conclude that diminished excretion of plasma iodide is an important part of the mechanism of adaptation to iodine deficiency among Himalayan populations.

Perchlorate discharge

Four euthyroid individuals, one each of goitre classes O, I, II and III, were given oral doses of 500 mg of potassium perchlorate. Their thyroid uptakes thereafter remained constant and near the value measured at the time of ingestion of the perchlorate. Evidently the organic binding of trapped iodide is rapid in these cases, and the goitres are not caused by the presence of a goitrogen of the thiouracil type in the Dainyor villagers' diet.

Perchlorate was also given to three deaf-mute cretins. Two of the cretins, who were brothers, did show a small perchlorate discharge. Their uptakes diminished from 50.9 to 45.6 % and from 34.7 to 31.6 %, a 10 % decrease in each case. A congenital impairment of organic binding presumably contributes to the thyroid malfunction of these brothers. The third cretin (figure 12, plate 43) was a female about 20 years old, severely retarded mentally, and only 2 ft 6 in (76 cm) high. She did not exhibit perchlorate discharge.

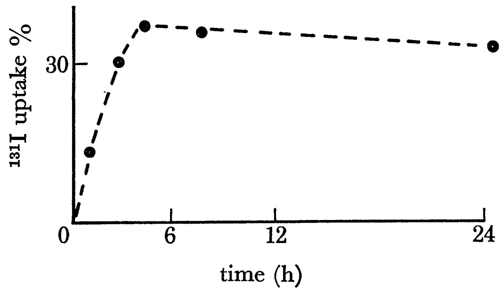

FIGURE 4. The iodine uptake curve for an elderly cretin.

Protein bound radio-iodine

Only one individual, an elderly cretin, was willing to donate two blood samples. The second sample, taken at 24 h, contained 0.74 % of the radio-iodine dose per litre of serum. All of this activity was bound, since the serum had the same activity after passing over a resin column to remove inorganic iodide. The ^{131}PBI value of 0.74 % per litre is high, indicating a rapid turnover of iodine. The uptake curve for this subject is shown in figure 4. Because of the rapid secretion of labelled hormone, the curve has already turned down after 24 h.

5. Iodine in water and soil

The observations of iodine metabolism in the inhabitants of Dainyor demonstrate that they are suffering from classical iodine-deficient goitre. Yet there does appear to be a variation in the incidence of the disease from the top to the bottom of the village. The soil in Dainyor is new and iodine-poor, and would be expected to take up appreciable amounts of iodine from water: it may be that removal of iodine from the water channels leads to a slight differential iodine deficiency across the village. With this possibility in mind we made some investigations of the interaction between iodine and the solid material carried in the channels. The most important interaction is found to be an adsorption of inorganic origin.

Field tests of the iodine binding capacity of water-borne particulate matter

The bacteriological survey showed no correlation between goitre incidence and bacterial concentration in drinking water. However, organic material in water could indirectly affect incidence of the disease. One possible explanation of the increased incidence in the lower part of the village is that iodine is progressively removed from the water by micro-organisms during its passage. Such micro-organisms might take up iodine and convert it to some non-utilizable form or sequester iodine in the stream bed. Preliminary experiments to investigate this possibility were carried out in Dainyor.

Table 11. Retention of ^{131}I by samples of Dainyor water

water sample	percentage ^{131}I retained on membrane
1. Membrane-filtered water passed through an Amberlite IRA 400 column in the Cl^- state	0.8
2. 'Good' water from the upper part of the principal supply channel	1.1
3. Membrane filtrate of 'good' water	3.0
4. 'Good' water after autoclaving	1.0
5. 'Poor' water from a tank supply	1.4
6. Membrane filtrate of 'poor' water	4.4
7. 'Poor' water after autoclaving	0.6
8. A living nutrient broth culture of 'poor' water	0.8
9. A membrane filtrate of 8 above	0.8
10. Nutrient broth culture as 8, after autoclaving	0.4
11. Sterile uninoculated nutrient broth	0.7

Volumes of 20 ml were prepared of eleven different samples of water; the treatment of each sample is given in table 11. To each sample was added 2 ml of a solution of carrier-free ^{131}I of known specific activity. The samples were mixed and left at ambient temperature for 18 h. The samples were then membrane filtered and the membranes washed with large volumes of membrane filtered de-ionized water. The radioactivity remaining on the washed membranes was determined and expressed as a fraction of the added dose. The percentages are listed in table 11.

Three points emerge from this somewhat superficial examination:

(i) There is no significant binding of iodine by the micro-organisms of water when grown to high concentration in nutrient broth.

(ii) Autoclaving of water or nutrient broth cultures appears to diminish slightly the iodine binding properties, although the values of binding obtained were in the unautoclaved state already low (1.1 to 1.0; 1.4 to 0.4; 0.8 to 0.4).

(iii) Membrane filtration of water, on the other hand, increases the iodine binding considerably – 1.1 to 3.0 % and 1.4 to 4.4 %.

Time and conditions in Dainyor prevented further experiments along these lines. The results with membrane filtered water suggest some physical change, perhaps in very small filterable particles, might be responsible for the increase in iodine binding. It was therefore decided to collect samples of water and silt for further investigation in Manchester.

Composition of the soil

Almost all the iodine in the village must have been carried there by the water in the Dainyor river. As noted previously, the river is fed by glacier melt from the southern slopes of Rakoposhi, and falls steeply towards Dainyor, flowing very fast and carrying a heavy burden of silt in the summer months. At the junction with the Hunza River, silt has gradually been deposited to build up the alluvial fan, shown in figure 16 (plate 45), on which the village now stands. Similar fans are found in this district wherever a tributary joins a main stream. Nothing grows on the fans without irrigation, but they are relatively easily watered by channels from the tributary streams, and they make up most of the cultivated land in the Gilgit Agency. The uncultivated land is desert, partly because of the low rainfall, which is on average only five inches a year in the Gilgit valley. Precipitation is not an important source of iodine.

The soil in Dainyor has supported vegetation only since the village was settled, and is even now being freshly deposited by irrigation water. A sample of silt† taken from the bed of one of the water channels contained 0.34 parts/10^6 of iodine, a typical value for the magmatic rocks of which the silt is chiefly composed. The principle minerals in the silt are given in table 12. X-ray fluorescence showed, in addition to the major constituents O, Si, Al, Ca, Mg, Na, K, Fe and Ti, traces of Mn, Sr, Rb, Zn, P and S. The silt contains a high proportion of very small particles and the milkiness of the Dainyor water does not completely disappear even when it is allowed to stand for several months. An electron micrograph of the residual suspended solid material (figure 17, plate 46), shows that it is composed mostly of thin platelets a few tens of nanometers across in their least dimension.

Table 12. Mineralogical analysis of a sample of silt from Dainyor

mineral	percentage	mineral	percentage
quartz	65	epidote	2
biotite mica	11	magnetite	1.5
calcite	10	muscovite mica	0.35
pyroxene-amphiboles	8	ilmenite	0.1
tourmaline	2	garnet	0.05

Concentration of iodine in water

About a litre of water was collected from the main supply channel B and from a subsidiary stream near the centre of the village. Iodine concentration was measured by removing 3 ml under clean conditions, and irradiating for activation analysis using the same technique as for serum and urine. Analyses were carried out: (*a*) after shaking and allowing only large particles to settle; (*b*) after filtration; (*c*) after prolonged standing to allow settlement of all but the very smallest particles. The results are given in table 13 showing separately the results of repeat

† We are using the word silt in the layman's sense to indicate all the solid material deposited in the bed of the channel, including clay particles as well as those of diameter greater than 2 μm.

measurements whenever they were made. The addition of a ^{127}I carrier and the chemical treatment after irradiation ensures that any iodine adsorbed on silt particles is included in the analysis. When dealing with iodine in such minute concentrations it is difficult to be sure that there is no contamination, but our procedure was very simple, and the repeated analyses agree within counting errors, with the exception of the two analyses (*a*) on water from the main channel. These two analyses were made on two separate samples which may have contained different amounts of solid material. Also included in table 13 are analyses of samples collected in September 1970, at a time when the water entering the village was clear.

The results in table 13 indicate that the concentration of dissolved iodide in the Dainyor water is a little less than 1 μg/l. By comparison with concentrations observed elsewhere in the world, this value is below average, but not exceptionally small. The high values measured on samples from the main channel after shaking and after filtration suggest that appreciable amounts of iodine may be absorbed on particles small enough to pass through the pores of the filter.

Table 13. Iodine concentration in water

	iodine concentration in				
	main channel		centre of village		
	sample 1	sample 2	sample 1	sample 2	sample 3
Collected in August 1968					
(*a*) after short settling period	2.3	5.9	—	—	—
(*b*) after filtration	5.2	—	1.0	0.9	—
(*c*) after prolonged settlement	0.6	0.7	1.0	—	—
Collected in September 1970					
clear samples	< 1.5	< 1.3	0.8	0.8	< 1.1

All concentrations are given in μg/l.

Adsorption of ^{131}I on silt particles

We demonstrated that the finely divided solid matter from the water channels can adsorb appreciable amounts of iodine by using carrier-free ^{131}I. Once adsorbed, the ^{131}I is not easily removed, and the silt remains active after repeated washings. Figure 5 shows that activity of a sample of silt from 50 ml of Dainyor water, which had been equilibrated overnight with ^{131}I and washed several times with 50 ml of de-ionized water.

The observations described above have already suggested that there is no organic fixing of iodine by Dainyor water. To confirm that the adsorption is inorganic, a silt sample was separated by successive decantings into fractions of different average particle size. ^{131}I adsorption was measured for each fraction with the results shown in table 14. The absorbing power per unit mass of solid material increases uniformly as the particle size diminishes, suggesting that the adsorption is simply determined by the surface area of the minerals making up the silt.

Measurements of silt adsorption are not very reproducible, no doubt because of non-uniformity of the samples themselves, but the adsorption certainly shows a marked dependence on pH. Figure 6 shows a set of values of adsorption in buffer solutions from pH 4 to 9, after ^{131}I had been equilibrated with about 0.25 g of silt overnight. Repeated observations indicated the same main features of the pH dependence, namely a peak at pH 7 to 8, a sharp decrease at pH 9, and an increase in the most acid buffer solution. The effect of equilibrating and washing in solutions of different pH is shown in figure 7.

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

There are few other studies of the soil chemistry of iodine. In two samples of Californian clay, Raja & Babcock (1961) found an iodine adsorption which they ascribed to non-living organic reactions. Hamid & Warkentin (1967) had results rather similar to our own in a Canadian clay subsoil, which adsorbed more strongly in acid than alkaline solution.

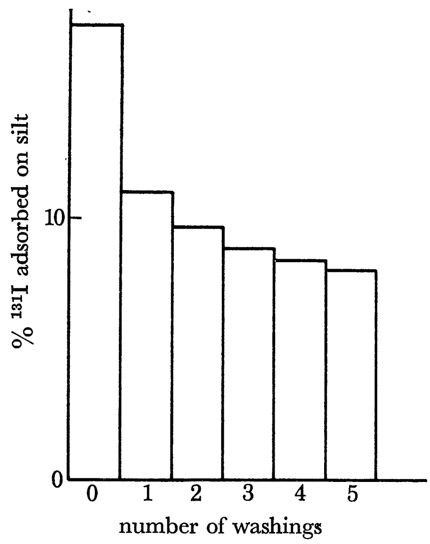

FIGURE 5. The percentage of ^{131}I remaining adsorbed after successive washings.

TABLE 14. ADSORPTION OF ^{131}I BY FRACTIONS OF SILT OF DIFFERENT AVERAGE PARTICLE SIZE

fraction	mean particle size / μm	weight of silt / g	percentage adsorption	percentage adsorption per mg
1	large particles	—	—	—
2	45	0.181	15.7	0.087
3	19	0.098	16.4	0.17
4	6.3	0.086	27.6	0.32
5	3.9	0.027	23.3	0.86
6	2.3	0.0090	18.6	2.1
7	1.4	0.0063	12.1	1.9
8	—	0.0009	6.8	7.5
9	—	0.0008	7.0	8.8
10	—	—	2.0	—

Although the ^{131}I adsorptions are only a few per cent, each sample contained only about 0.25 g of silt, and inorganic adsorption may very well have a significant effect on the availability of iodine to the Dainyor villagers. For example, the silt in unfiltered drinking water may effectively fix some of the iodine ingested in food. Such a fixing would account for the incomplete iodine balance we found in urine and thyroid uptakes. The adsorption will also influence the distribution of iodine throughout the village, concentrating it in plants and soil in the top of the village. This concentration would be reflected in the iodine intake of people in different parts of the village, since most of the farmers own their own land and to a large extent live off it. Another possibility is that there are pH variations, affecting the amount of iodine adsorption and also the availability of iodine to plants. It has been reported in work on pasture (Simpson 1930), oats (Katalymov & Churbanov 1960) and barley (Umaly 1967) that alkaline soils do not give up their iodine to the plant so readily as do acid soils.

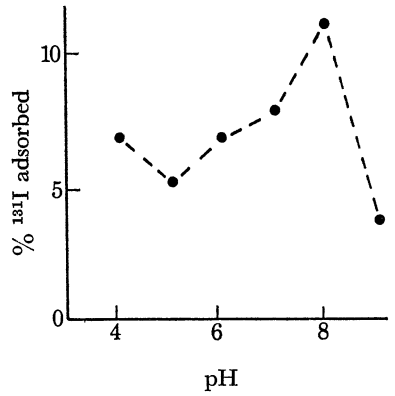

Figure 6

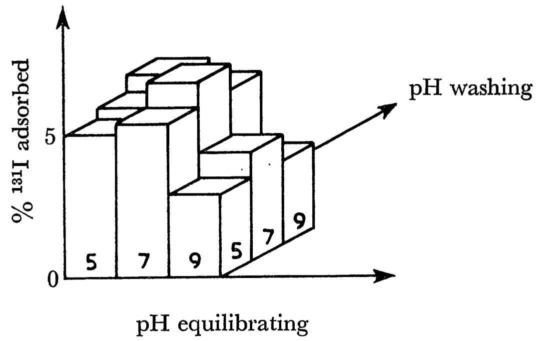

Figure 7

Figure 6. Adsorption of ^{131}I by silt in solutions of different pH.

Figure 7. Adsorption of ^{131}I after equilibrating and washing in solutions of various pH values.

6. Historical note: the work of Sir Robert McCarrison in the Gilgit Agency

Although our own survey has led us to conclude that bacteriological factors are not important in the aetiology of goitre in the Gilgit Agency, we ought not to ignore McCarrison's original observations. During his work in the Agency he obtained three pieces of evidence in support of his hypothesis of a bacteriological factor. These were:

(i) The increased incidence of goitre among the villages at the bottom of the Gilgit fan, where the water supply is most polluted (McCarrison 1906).

(ii) The experimental production of goitre in subjects drinking polluted water (McCarrison 1909, 1911).

(iii) Historical evidence from the town of Nagar, where the disease was reputedly introduced only after some goitrous families had settled there (McCarrison 1906).

We shall consider the three lines of evidence in turn.

(i) *Incidence of goitre in Gilgit*

McCarrison's data are reproduced in table 15. The village called Basin was the one nearest to the source of the water supply in the Kirgah nullah. The network of water channels passed through the other villages in the order they appear in the table. At Majinpharri a separate but smaller supply from the Barmis nullah joined the main channel. The last column of the table shows the percentage of the population in each village with visible goitres. The highest and lowest villages had incidences of goitre markedly different from those of the intermediate villages, in which the incidence is more or less constant. McCarrison attributed the arresting of the increased incidence to the presence of the pure water from the Barmis nullah.

It was interesting to discover that the water supply in Gilgit still follows the same general pattern,† and that some of the old village names are still known. Basin is still a separate village, about two miles away from the present town, immediately below the Kirgah nullah. Umphris, Damyal and Majinpharri are all close together at the centre of the modern Gilgit. No one knew the names Ky–K and Sonyar, but Kashrote is the part of the town near the airport, about a mile away from the centre in the opposite direction from Basin. Looking again at the table, it is immediately obvious that the two villages with an anomalous incidence of goitre, namely Basin and Kashrote, are both a long way from the central cluster of villages. The central villages all have nearly the same incidence of goitre, although to judge from our experience in Dainyor, the bacteriological pollution must certainly have increased progressively through these villages.

Gilgit is spread out over a considerable distance, and is not, like Dainyor, a single alluvial fan. Basin is on the fan below the Kirgah nullah, the central villages on the fan below the Barmis nullah, and Kashrote on the flat plain through which the Gilgit River cuts its course. It is not surprising that the three localities had different incidences of goitre.

Table 15. McCarrison's data on the incidence of goitre in the villages of the Gilgit fan

village	population	percentage of population goitrous
Basin	93	11.8
Umphris	385	20.0
Damyal	181	18.8
Majinpharri	718	20.0
Ky–K	229	26.9
Sonyar	458	24.5
Kashrote	128	45.6

(ii) *Experimental production of goitre in man*

In experiments between 1906 and 1910, McCarrison required a total of 36 individuals to swallow daily some of the silt carried in the Kashrote water channel. The experiments lasted over a period of between 30 and 55 days. Fifteen of the thirty-six subjects developed enlargements of the thyroid. In control experiments, 31 individuals were given the same silt after it had been boiled. None of these subjects developed an enlarged thyroid.

Swallowing large quantities (a quarter of a pound a day!) of iodine-adsorbing silt would be expected to affect the availability of ingested iodine. It is rather surprising that there is such a clear-cut difference between the main experiment and the control group. However, boiling might well alter the adsorptive properties of the silt, and these experiments cannot be given much weight as evidence of bacteriological goitrogenic factor.

McCarrison carried out similar experiments on animals, but they were much less conclusive.

(iii) *Introduction of goitre to Nagar*

According to the local people, goitre had been unknown in Nagar before 1893 when the little princely state was forcibly brought into contact with the outside world during the Hunza–

† The sketch map in McCarrison's book *The etiology of endemic goitre: The Milroy Lectures* (1913) is incorrect. It has been imposed the wrong way round on the outlines of a photograph in such a way that both the Gilgit River and the water channels are shown flowing in a direction opposite to their true flow. We were able to decipher this map only after locating the positions of the villages.

Nagar campaign. Just before 1900 four goitrous individuals came to settle in the town of Nagar, and they reputedly introduced the disease. McCarrison made two visits to Nagar, and found thirty-odd cases of goitre. He took this to indicate 'a slow and steady spread of goitre amongst susceptible individuals as a result apparently of the importation of the disease into a locality formerly free from it' (McCarrison 1913). The complete unreliability of hearsay evidence was amusingly illustrated on our first visit to Dainyor when we were told that there was no goitre in the village, and that if we wished to see the disease we must go to a village 10 miles away. Thirty-three per cent of the population of Dainyor have visible goitres! (McCarrison examined the people of Dainyor and found a goitre incidence of 65% (McCarrison *et al.* 1927)).

Two of us (J.A.C., I.S.G.) went to Hunza on the opposite side of the Hunza River from the town of Nagar, but we were not allowed to cross into Nagar. In Hunza we examined 25 subjects who had been to the court of His Highness the Mir of Hunza. Twelve had palpable goitres, and of these four were visible. The people of Hunza and Nagar are of a different stock from their Shina-speaking neighbours, but it does not seem very likely that their susceptibility to goitre is any less.

To sum up, McCarrison's observations in the Gilgit Agency can be explained without the presence of a bacteriological goitrogenic factor. In reaching this conclusion we are not belittling the importance of his contribution to the study of endemic goitre. His clinical examination of large populations and physiological experiments with carefully chosen control groups were models of good practice. His conclusion that bacteriological pollution causes goitre was incorrect, but it remains true that the introduction of simple sanitation is the most important public health measure which needs to be taken in the Himalayan villages.

7. Appendix on dermatoglyphics and taste-testing

(*a*) *Digital and palmar dermatoglyphics*

Little dermatoglyphic information is available for Himalayan–Karakoram peoples, and so far as we know this is the first time that such information has been obtained in the Gilgit region. A small number of palmar prints (23 pairs) were collected from Dainyor males, and fingerprints from a total of 151 people. Of these, 126 (114 male, 12 female) were obtained in Dainyor, and the remaining 25 in Karimabad in the Hunza valley, all from males attending the court of the Mir of Hunza. Hunza is as isolated and semi-autonomous state bordering on Sinkiang and lying to the north-east of Gilgit, with which it is connected by a 60-mile jeep road following the gorges of the Hunza River. Nothing is known about the origins of the Hunza people: they speak Burushashki, a language which is not Indo-European and is indeed unrelated to any other known language. A substantial fraction (perhaps about a quarter) of the Dainyor villagers are of Hunza stock, and it is problematic whether or not any significance can be attached to differences between the Hunza and Dainyor samples.

The sample population in Dainyor included a number of individuals known to be related to one another. These included sibs and father–son and father–daughter relationships and the digital dermatolgyphic sample included, as far as was known, 23 related pairs, 12 related groups of three and two related groups of four. Elimination of second and subsequent members of families will thus reduce the sample population from 126 to 72. No attempt was made to select a sample of unrelated individuals in this way and it is probable that unrecognized close relationships would still be present even when known relationships were eliminated. So far as could be determined, the sample population of 25 individuals in Hunza consisted of unrelated individuals.

The sample of 23 males supplying the palmar patterns included seven related pairs and one related group of three. About half the palmar prints were from children with ages less than 13 years.

Standard methods for obtaining rolled fingerprints, employing a metal plate inked by a roller, were used (Holt 1968). In the hot climate it was found that the most satisfactory prints were obtained when subjects washed and dried their hands thoroughly beforehand, with a final wipe on a cloth wetted with methanol. Ridge counts were made on all digital patterns with the exception of three Dainyor males and one Hunza male, whose fingers were scarred or mutilated. Palmar prints were recorded on paper rolled over an empty lemonade bottle. Ridge counts were measured on 10 pairs of prints.

Table 16. Digital patterns

	number of patterns of different types																
	right hand							left hand								both hands all digits	
	digits					all digits		digits					all digits			
	1	2	3	4	5	total	%	1	2	3	4	5	total	%	(1–10)	%
Dainyor males (114)																
arch	—	3	2	1	—	6	1.05	—	6	3	1	—	10	1.60	16	1.4
ulnar loop	41	32	73	38	78	262	45.96	64	31	69	49	88	301	52.81	563	49.38
radial loop	—	21	—	1	—	22	3.86	—	17	—	—	—	17	2.98	39	3.42
whorl	73	58	39	74	36	280	49.12	50	60	42	64	26	242	42.46	522	45.79
Dainyor females (12)																
arch	—	2	—	—	—	2	3.33	1	2	1	—	—	4	6.66	6	5.0
ulnar loop	5	6	11	4	8	34	56.66	3	6	9	8	8	34	56.66	68	56.66
radial loop	—	1	—	—	—	1	1.66	1	—	—	—	—	1	1.66	2	1.66
whorl	7	3	1	8	4	23	38.33	7	4	2	4	4	21	35.0	44	36.66
Hunza males (25)																
arch	—	—	1	—	—	1	0.80	—	—	2	—	—	2	1.60	3	1.2
ulnar loop	5	10	18	13	20	66	52.8	7	12	15	15	23	72	57.6	138	55.2
radial loop	—	8	—	—	1	9	7.20	—	4	—	—	—	4	3.2	13	5.2
whorl	20	7	6	12	4	49	39.2	18	9	8	10	2	47	37.6	96	38.4

Digit 1 is the thumb.

Results

The results of analysis of the dermatoglyphic data are given in tables 16 to 19.

Table 16 shows the number of qualitative patterns of different types (arches, ulnar and radial loops, and whorls) occurring on each digit for each sex in the Dainyor sample, and for the Hunza sample. Compared with the Dainyor males, the females show a slight elevation in total frequency of loops and diminution in whorls that is not unusual in direction or magnitude. The frequency of loops in the Hunza males is greater than that in the Dainyor males. As usually observed, the right hand shows slightly more whorls and radial loops than the left in all samples.

Monomorphism tended to be low with 13.2 % of Dainyor males and 25 % of females showing either all whorls or all ulnar loops on all ten digits (table 17).

Comparing patterns on the corresponding digits of both hands, out of the 630 Dainyor couplets there are 479 (76 %) homologues (i.e. digits in which the pattern is the same on both

TABLE 17. NON-HOMOLOGOUS DIGITS AND MONOMORPHISM

	number of persons showing this pattern among		
	Dainyor		Hunza
	males	females	males
number of non-homologous digits			
0 digit different	27	3	10
1 digit different	46	6	6
2 digits different	30	3	7
3 digits different	9	—	2
4 digits different	2	—	—
non-homologous patterns on particular digits			
digit 1	35	3	2
digit 2	44	3	11
digit 3	24	2	7
digit 4	17	2	2
digit 5	19	2	4
monomorphism			
with ulnar loops	6	2	2
with whorls	9	1	—

TABLE 18. RIDGE COUNT BY DIGITS

	mean ± S.D. of ridge counts among		
	Dainyor people		
counts on	males (111)	females (12)	Hunza people (24 males)
right digits			
1	18.2 ± 4.8	17.0 ± 4.9	20.9 ± 3.4
2	13.1 ± 6.2	9.3 ± 6.0	14.1 ± 7.1
3	13.0 ± 5.6	13.2 ± 6.6	12.3 ± 5.4
4	15.8 ± 5.7	16.6 ± 6.3	15.4 ± 4.2
5	13.6 ± 4.5	13.0 ± 5.3	12.8 ± 3.5
right hand	14.7	13.8	15.3
left digits			
1	17.5 ± 5.4	13.5 ± 6.1	20.6 ± 3.5
2	11.5 ± 6.3	10.2 ± 6.5	12.8 ± 7.5
3	14.0 ± 6.4	14.0 ± 6.9	12.4 ± 5.7
4	16.8 ± 5.9	16.3 ± 6.6	16.3 ± 4.0
5	14.5 ± 4.4	13.8 ± 6.4	13.6 ± 4.1
left hand	14.8	13.5	15.2
total ridge count	148 ± 45	137 ± 50	151 ± 34

hands), and 151 non-homologues. Of the latter 139 occur in the 114 males and 12 in the 12 females. This is shown in table 17, which also shows the number of Dainyor males and females according to the number of digits which possess different patterns on the two hands. The small sample of females means that little significance can be attached to the slight difference in the two distributions. The analysis by individual digits suggests that, in both sexes in Dainyor, digits 1 and 2 have the most bimanual differences; on no single digit do the females have any significantly depressed frequency of homologues, although here again the smallness of the female sample makes the results inconclusive. In the Hunza population digits 2 and 3 possess the most bimanual differences.

It was possible to make a quantitative analysis by ridge counting in 123 out of 126 sets of Dainyor prints and in 24 out of 25 Hunza prints. The mean total ridge count was 148 in 111 Dainyor males, 137 in the females and the standard deviations are respectively 45 and 50. The total ridge count for the 24 Hunza males was 151, with a standard deviation of 34. The counts by individual fingers are set out in table 18 and, for the males, these show the usual pattern of the highest counts on the first digit, the next highest on the 4th and the lowest on digits 2 and 3. The anomalous results for the females are not significant in view of the small sample size.

Table 19. Palmar patterns: Dainyor males only

(*a*) *atd angles*

atd angle	number (and percentage) of palms with this angle	
< 45 degrees	18 (41)	The mean total atd angle for both hands is 98 degrees for 22 pairs of palms
45–56 degrees	15 (34)	
> 56 degrees	11 (25)	

(*b*) *number of palms with a true pattern in the thenar, interdigital and hypothenar areas*

	number of palms with				
	thenar patterns	interdigital pattern in web			hypothenar pattern
	I	II	III	IV	
left	0	0	12	10	5
right	0	0	12	10	4
number of pairs of palms in sample	20	20	20	20	21

(*c*) *hypothenar patterns on left and right hands*

	number of palms	
	right hand	left hand
open field	18	16
radial loop	3	2
ulnar loop	0	1
ulnar loop/radial loop	0	2

(*d*) *total a–b ridge count*

78 ± 10 (10 pairs of palms)

(*e*) *average number of digital tri-radii per palm*

right hand	4.1	21 pairs of palms
left hand	4.1	

The results obtained from an analysis of the Dainyor palmar patterns are presented in table 19. The (atd) angle (Holt 1968) was measured in 22 out of the 23 patterns (all male) and the mean value of the total atd angle for both hands was 98°. Forty-one per cent of individual palms possessed an atd angle less than 45° and 25 % were above 56°. The percentage of palms with a true pattern in the thenar, interdigital and hypothenar areas is given, together with an analysis of hypothenar patterns. The total (*a–b*) ridge count (Holt 1968) was measured on 10 pairs of palms and provided a mean value of 78 with a standard deviation of 10. The average number of digital tri-radii per palm is also shown.

Of the 126 Dainyor subjects from whom fingerprints were taken, nine, at least, were cretins or deaf-mutes. Of the 23 pairs of palm prints, seven were from cretins or deaf-mutes. None of the parameters measured appeared to be abnormal in these individuals, although it was noted that, out of the nine cretins and deaf-mutes from whom fingerprints were taken, only two possessed more than two whorls.

Discussion

Detailed quantitative analysis of the data has not been attempted and the present discussion is largely concerned with a broad comparison of the qualitative data with those obtained by other surveys. Information on ridge counts in Asian populations is limited and provides little with which the present sample can be compared. The male Dainyor and Hunza mean total ridge counts of 148 and 151 respectively fall within the range found in six male samples from N. India (Singh 1961; Geipel 1961); for these six samples the mean total ridge count ranged from 143 to 161. The female mean relates to too few individuals for useful comparison.

The percentage frequencies of arches, loops and whorls for the two populations are:

	A	L	W
Dainyor (114 males + 12 females)	1.8	53.3	44.9
Dainyor (114 males only)	1.4	52.8	45.8
Hunza (25 males)	1.2	60.4	38.4

The samples show fewer arches and more whorls than are characteristic in Europe and Africa and the results fit generally into the spectra of frequencies found in Asia, particularly in the Indian sub-continent. Comparative data for a number of Asian samples are set out in table 20.

Also shown in table 20 is the Pattern Intensity Index (P.I.I.), representing the number of digital tri-radii per individual and estimated by assuming that each whorl has two tri-radii,

Table 20. Comparison of dermatoglyphic data on Asian populations

(Much of this information was obtained from Hughes (1967) and from Roberts, Coope, Jackson, Turner & Ward (1968))

sample	number (all male unless otherwise stated)	A	L	W	P.I.I.	reference
Dainyor	126 (incl. 12 ♀)	1.8	53.5	44.9	14.3	present study
Dainyor	114	1.4	52.8	45.8	14.4	present study
Hunza	25	1.2	60.4	38.4	13.7	present study
Nuristan (Afghanistan)	31	7.8	50.9	41.2	13.3	Hughes (1967)
Punjabis	220	2.5	56.0	41.3	13.9	Srivastava (1965)
Tharus (Himalayan Terai)	379	3.9	54.7	41.4	13.8	Srivastava (1965)
Lunana (Bhutan)	62	2.1	59.0	38.9	13.7	Roberts *et al.* (1968)
Indians 'general'	299	3.3	60.0	36.7	13.3	Renes (1948*a*)
Bengalis	40	2.3	55.2	42.5	14.0	Biswas (1936)
Rajputs	80	5.4	53.6	39.2	13.2	Singh (1961)
Sikhs	100	7.4	59.3	33.3	12.6	Singh (1955)
Tamils	1054	3.1	57.4	39.4	13.6	Olivier (1911)
Malids	450	1.2	53.1	45.8	14.5	Olivier (1961)
Kazan Tatars	209	5.0	55.3	39.6	13.4	Gladkova (1957)
Lebanese	106	2.5	52.2	45.4	13.3	Cummins & Shanklin (1937)
Arabs	181	2.8	61.3	36.0	13.3	Renes (1948*b*)
Kazak (Central Asia)	85	2.7	45.1	52.5	15.0	Heet, H. L., quoted by Roberts *et al.* (1968)
Kirghiz (Central Asia)	100	2.5	51.5	46.3	14.4	Heet, H. L., quoted by Roberts *et al.* (1968)
Uzbek (Central Asia)	100	3.1	47.5	49.4	14.6	Heet, H. L., quoted by Roberts *et al.* (1968)
Turkman (Central Asia)	100	4.2	49.2	46.6	14.2	Heet, H. L., quoted by Roberts *et al.* (1968)

each loop one tri-radius and each arch none (Cummins & Steggarda 1936; Cummins & Midlo 1943). Tented arches with one tri-radius and occasional whorls with three tri-radii were ignored. A single arbitrarily-defined index such as the P.I.I. may yield misleading comparisons and a more satisfactory method of comparing the percentage frequencies of arches, loops and

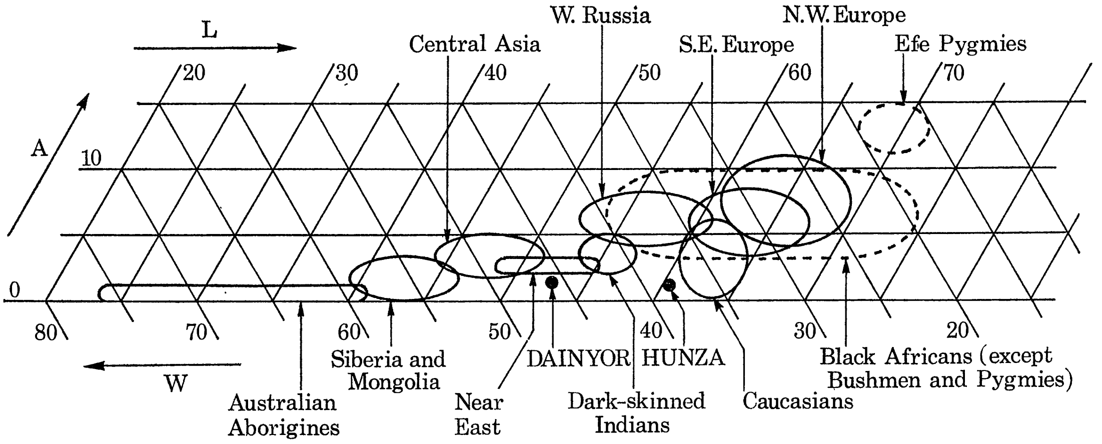

FIGURE 8. Triangular plot of digital pattern frequencies for various races. This plot, and that shown in the next figure, were constructed from data given by Chamla (1963), Hughes (1967) and Holt (1968), and from data appearing in Table 20.

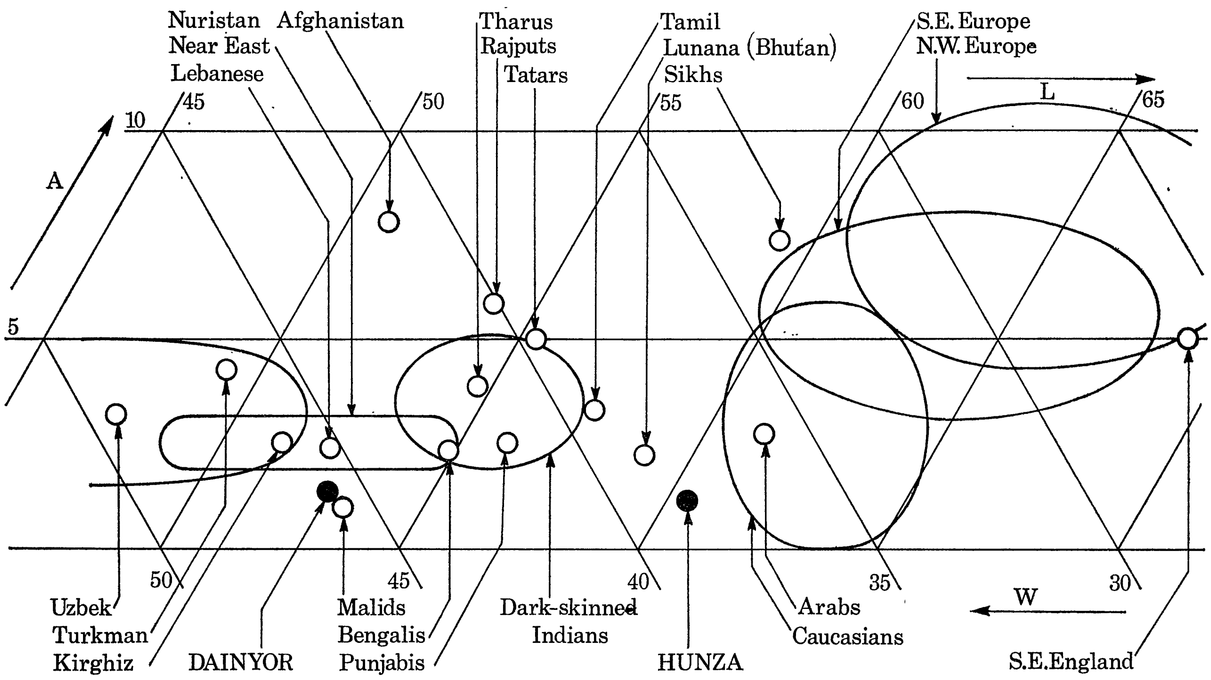

FIGURE 9. Enlargement of lower central region of figure 8.

whorls from different populations is to display the frequencies directly on a triangular plot with the A, L and W axes arranged cyclically around an equilateral triangle. Figure 8 shows on such a plot the distribution of frequencies from Indians and other races, using, for the most part, the figures quoted by Chamla (1963); only the lower part of the triangle is necessary as the frequency of arches is rarely greater than 15%. Figure 9 is an enlargement of the central region and compares the Dainyor and Hunza frequencies with those of the other peoples of table 20.

The smallness of the samples makes it difficult to evaluate the significance of the Dainyor and Hunza results other than their location in the broad spectrum of frequencies previously noted for the Indian sub-continent. It is interesting, however, that the mean value for the Hunza sample is not far removed from mean values typical of Caucasian peoples. It is evident that further genetic information about the inhabitants of the Hunza valley would be of great interest.

(*b*) *PTC taste-testing*

It has long been known that phenylthiourea (PTC) tastes bitter to some people and not to others (Fox 1932). In Europeans and white Americans the distribution of taste thresholds is bimodal with about 30 % of the individuals tested falling into the less sensitive (non-taster) class. These non-tasters are probably homozygous for a single recessive gene. (Blakeslee 1932; Snyder 1932). Some connexion may exist between the PTC taste response and thyroid disease (Harris, Kalmus & Trotter 1949; Kitchin *et al.* 1959). The incidence of non-tasters is claimed to be slightly greater than normal in individuals with adenomatous goitre and slightly less than normal in patients with toxic diffuse goitre.

The purpose of the present investigation was to determine the distribution of taste thresholds in a sample population in the village of Dainyor. Too few individuals were studied to allow any conclusion to be drawn about possible relationships with thyroid disease.

Methods

The method used was essentially that described by Harris & Kalmus (1950), Kalmus (1956), Kitchin *et al.* (1969) and Weiner & Lourie (1969). All water used was coarse-filtered to remove most of the heavy contamination of suspended silt and was boiled for at least 5 min. The concentrated solution was obtained by adding 1 l of the warm (65 °C) filtered water to 1.3 g of phenylthiourea ('pure' grade from Koch–Light Laboratories, Ltd, Colnbrook, England). This was stirred, left at air temperature overnight, and then refiltered. This concentrated solution is described as solution no. 1.

The serial dilution steps used were broader than those employed by Harris & Kalmus and by Kitchin *et al.* with a factor of 4 (instead of 2) between adjoining steps. Thus the first dilution was obtained by adding $\frac{3}{4}$ l of water to $\frac{1}{4}$ l of solution no. 1; to retain the notation used by others, this solution is described as solution no. 3. Solutions 5, 7, 9, 11 and 13 were prepared similarly by serial dilution.

After the approximate threshold had been established, each subject was given eight randomly arranged plastic beakers, four of which contained the PTC solution at the concentration under test, the other four containing water. He was then asked to separate the two groups. If this was done correctly he was asked to repeat the 8-beaker trial with the next weaker solution, if incorrectly with the next stronger. The threshold was taken as that solution which could just be tasted correctly. The selection was taken to be 'correct' if six out of eight beakers were accurate. Great care was taken to avoid mislabelling errors.

Results and conclusions

Altogether, 62 subjects in Dainyor were tested, all male. The findings are summarized in figure 10.

The bimodal distribution observed is very similar to that noted by others in normal populations of Europeans and white Americans (see, for example, Kitchin *et al.* 1959). It is customary to take the dividing line between tasters and non-tasters between serial dilutions 4 and 5 (i.e. at the anti-node); in our case this will be between 3 and 5, shown by the dotted vertical line in figure 10. Thus, out of 62 individuals 20 were non-tasters and 42 were tasters, giving an incidence of 32 % of non-tasters.

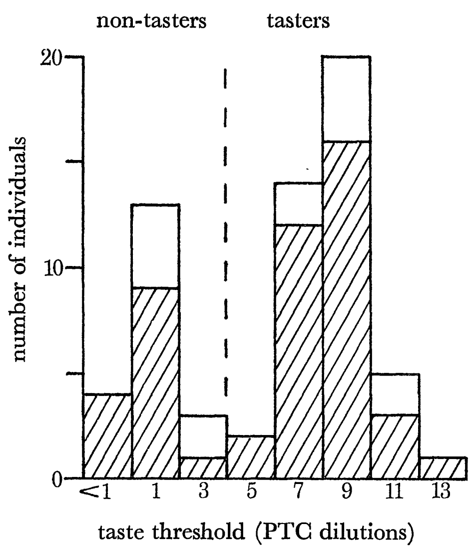

FIGURE 10. The distribution of PTC taste thresholds in a population of 62 males in Dainyor. The shaded regions refer to 48 unrelated individuals.

It was known that the sample included some groups of related individuals; with such a small sample, this could introduce bias due to the concentration of certain genes in families. The results were therefore replotted with only the first-tested members of known families included, reducing the sample population to 48 individuals. The results are indicated by the shaded region of the histogram of figure 10. Fourteen subjects were non-tasters giving an incicence of 29 % of non-tasters.

The main conclusion is that the population of the village of Dainyor in the Gilgit Agency of W. Pakistan shows a similar distribution of PTC taste thresholds to that observed in normal Europeans and white Americans. From the small sample studied no deductions can be made about any possible relationship between the ability to taste PTC and thyroid disease.

We wish to thank the Wellcome Trust for giving us, at very short notice, a grant to cover all the expenses of work in the field. The activation analysis was carried out under a research contract awarded by the International Atomic Energy Agency to the Manchester–Liverpool Universities Research Reactor: we wish to thank Dr Gilmore and his colleagues at the reactor for their collaboration.

The Pakistan Atomic Energy Commission not only seconded Dr M. A. Shahid to join the Goitre Survey in Gilgit and paid his expenses, but gave help by handling the scientific equipment on its arrival in Pakistan, and kindly performed a mineralogical analysis of a sample of soil from the Dainyor nullah. The Agency Surgeon at the Gilgit hospital allowed Dr Khalida Mahmud leave to become a member of the survey. Without her assistance we should have had no clinical data on adult women.

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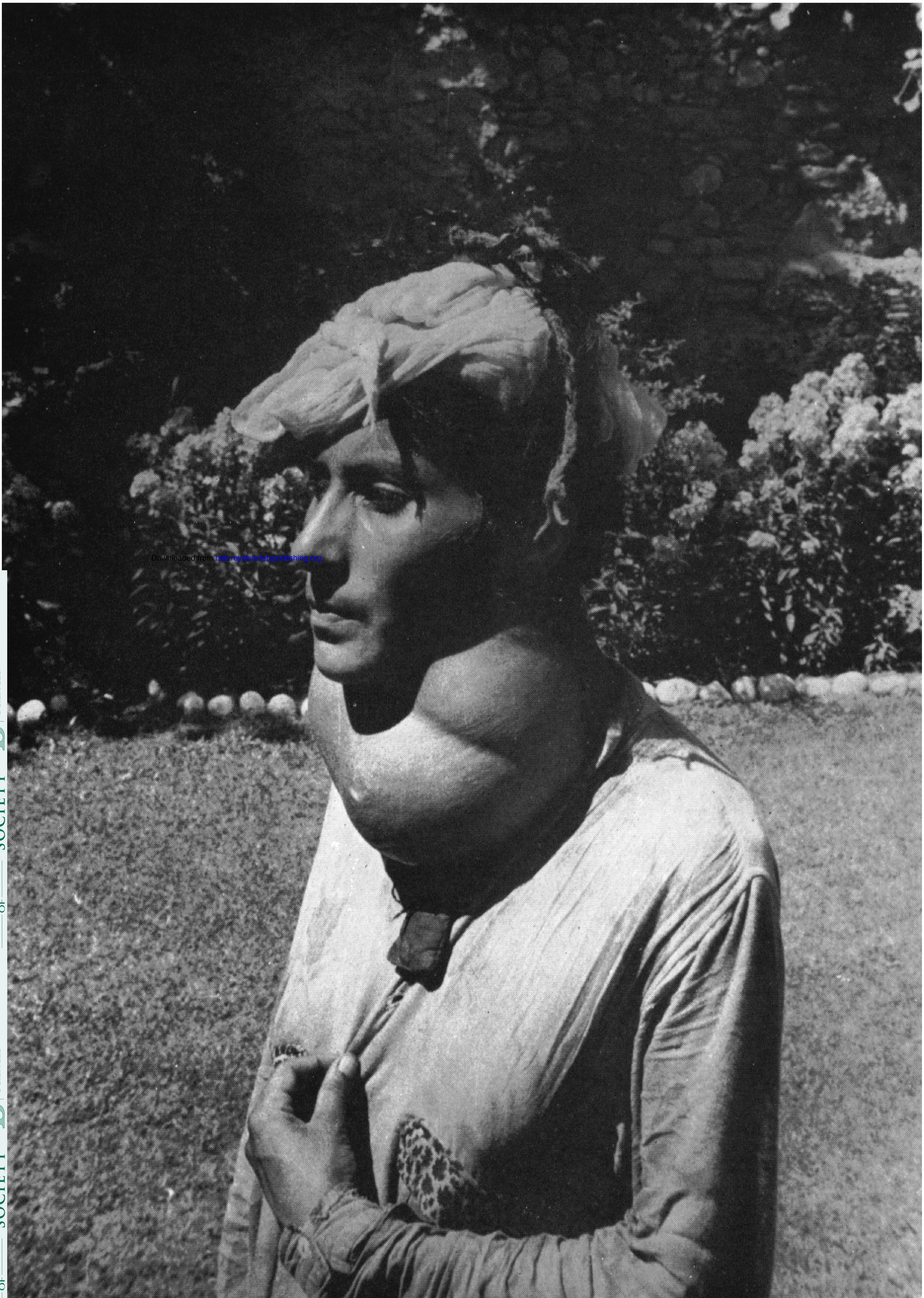

FIGURE 11. A woman with an exceptionally large goitre.

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FIGURE 12. A female cretin. This subject, although about 20 years old, is only 2 ft 6 in high.

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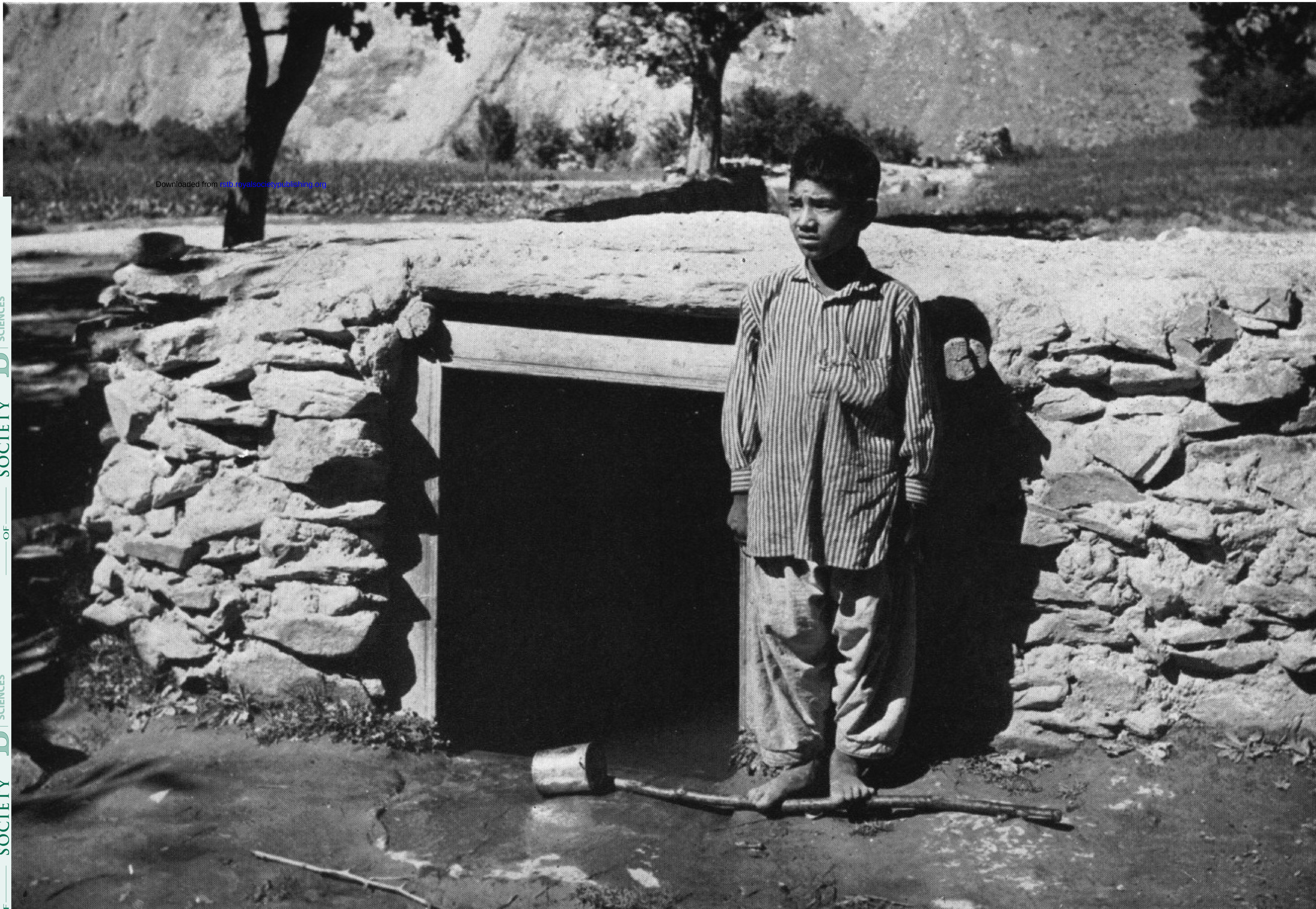

FIGURE 14. A covered water-storage tank.

FIGURE 15. Measurement of iodine uptake.

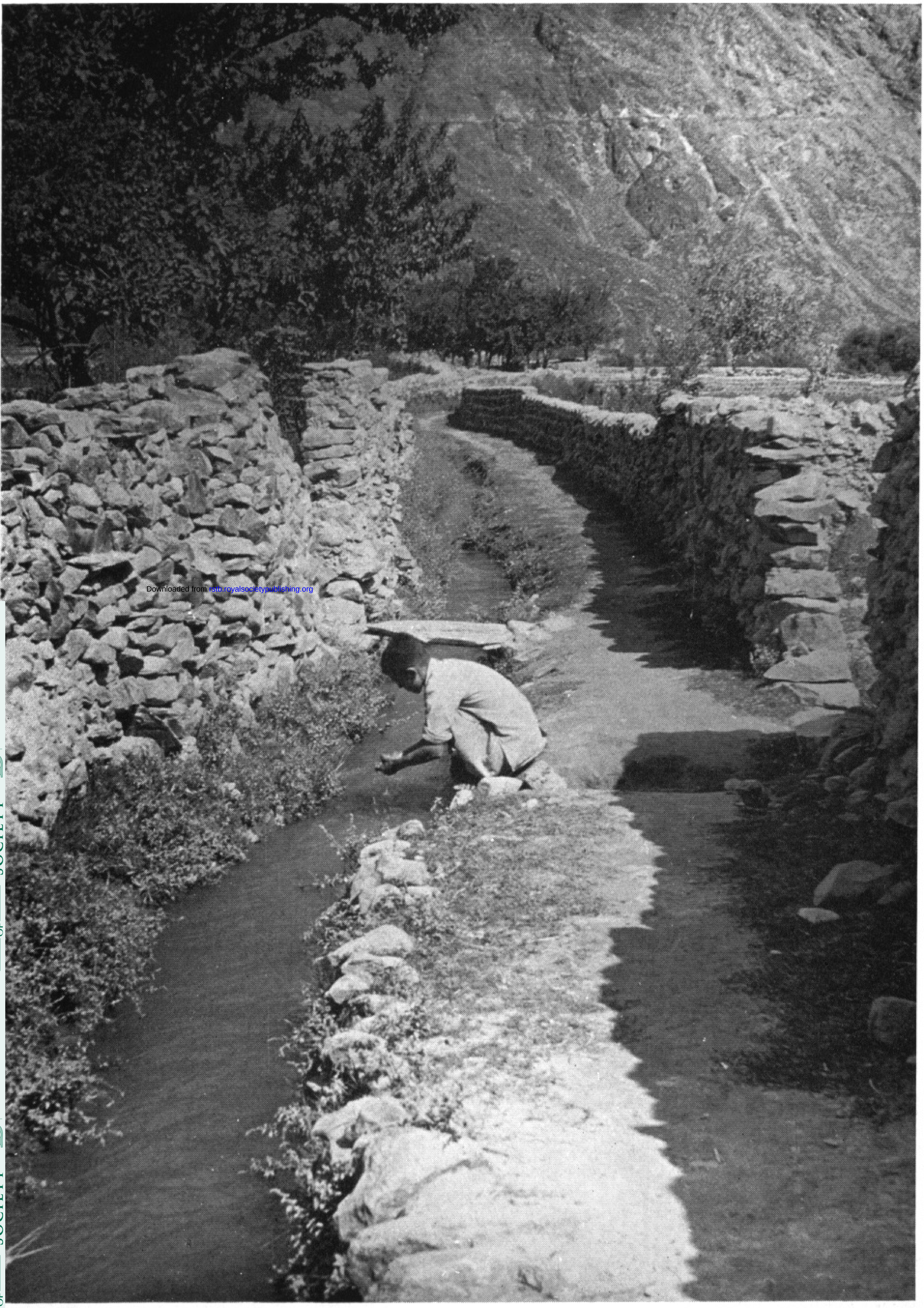

FIGURE 13. One of the principal channels in Dainyor, supplying water for drinking and irrigation.

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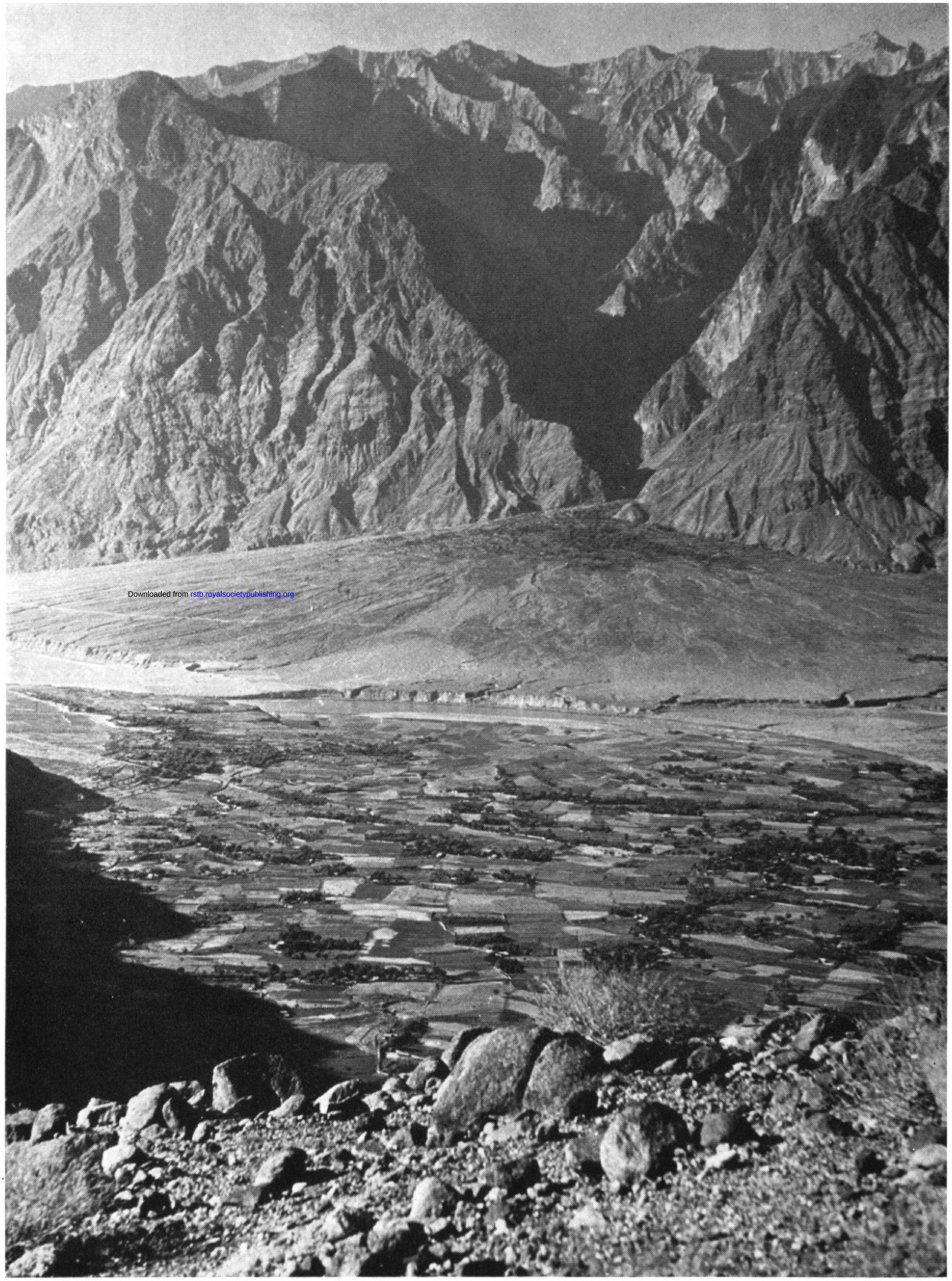

FIGURE 16. Alluvial fans on either side of the Gilgit River. The nearside cultivated fan is the village of Dainyor. The barren unirrigated fan on the far side is typical of the formations which occur wherever a tributary joins the wide river valley.

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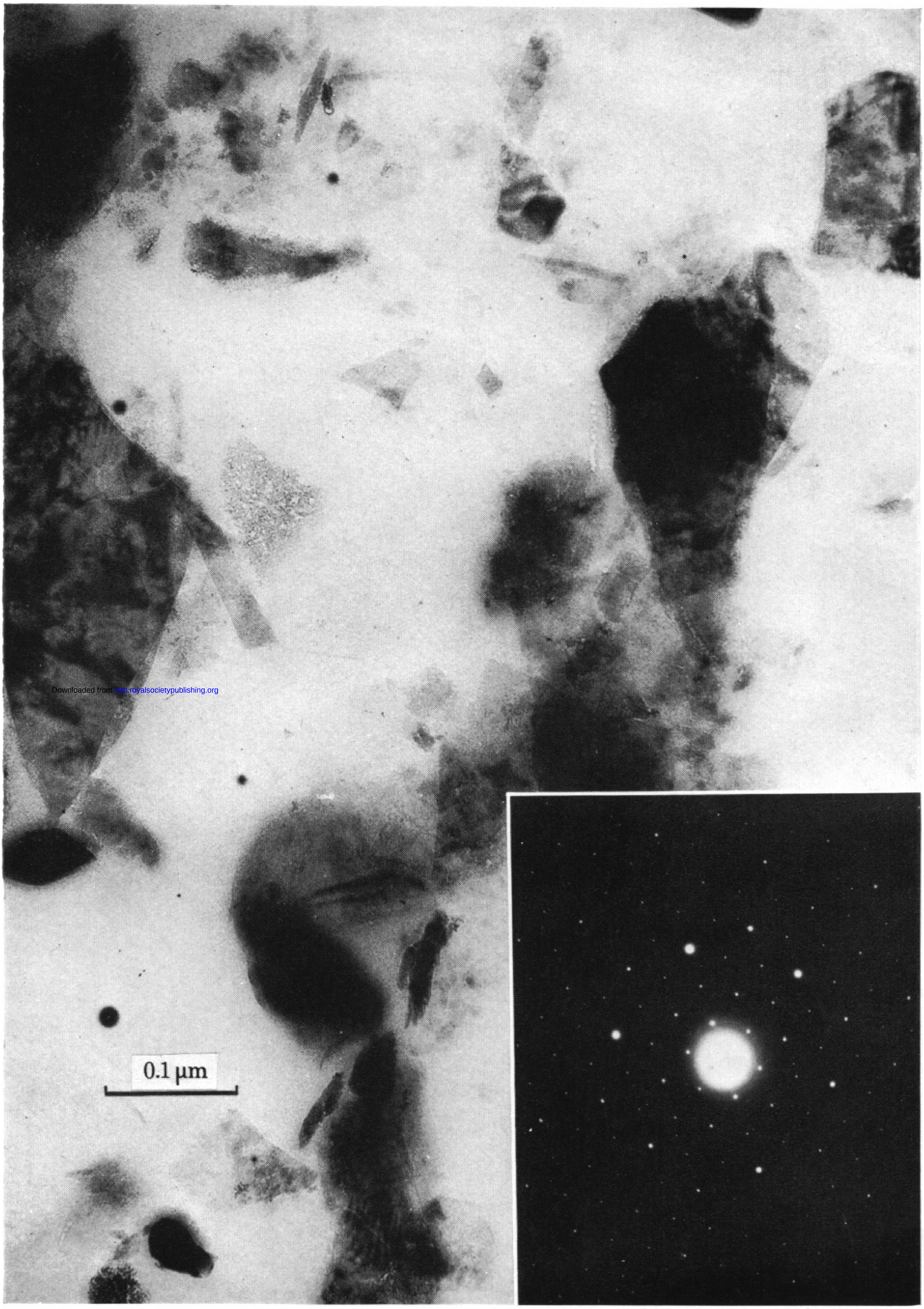

FIGURE 17. An electron micrograph of particles in suspension in Dainyor water. The particles were dried down onto collodion-filmed grids and examined at an electron-optical magnification of $\times$ 30000. The final magnification after photographic enlargement is indicated by the calibrating mark. The smallest particles detectable were about 10 nm in thickness. A selected-area diffraction pattern from a single larger particle is shown inset; the pattern is typical of clay minerals.