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of Health, for their work in the initial identification of the causative organism. The technical assistance of Mr. Paul E. Martineau of the Animal Diseases Research Institute is acknowledged with thanks.

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Congenital Abnormalities in Children Born in Alberta During 1961: A Survey and a Hypothesis

L. J. le VANN, L.R.C.P.(Edin.), L.R.C.S.(Edin.), L.R.F.P. & S.(Glasg.),*
Red Deer, Alta.

ABSTRACT

In Alberta, the provincial average for neonatal congenital physical abnormalities discovered at birth increased from 7.9 per 1000 births in 1959 to 13.8 per 1000 births in 1961.

Drugs taken by mothers during pregnancy were tabulated, including the antiemetic and tranquillizer agents, but no relationship was demonstrated between their use and damage to the fetus.

A significant relation was apparent, however, between the incidence of congenital malformations and the extent of precipitation in the area concerned. In Northern Alberta, where precipitation is highest, 15.5 per 1000 children born in 1961 showed physical defects. In Southern Alberta, where precipitation is lowest, 11.9 children per 1000 births were born with physical defects.

Increases of radioactive dust containing cesium-137, cerium-144 and strontium-90 were associated with above-ground Soviet thermonuclear Arctic explosions during recent years. The hypothesis is advanced that children born in Alberta in 1962 will show a greater incidence of physical deformities than those born in 1961, owing to greater rainfall during 1961 and 1962.

A STUDY carried out in Alberta in 1959 by the author indicated that drugs ingested by expectant mothers may not be responsible for the increased incidence of congenital malformations recently observed in newborn children. The probability that another factor or factors may be involved in this increase became apparent during a two-year survey of the incidence of congenital anomalies in children born in Alberta during the years 1959 and 1961.

In March 1960 the Minister of Health for the Province of Alberta requested information concerning children born with congenital malformations who might eventually require either institutional care or special types of therapy.

At that time no data of this nature were available for Alberta or for any other large area in Canada. In order to obtain such an estimate as quickly as possible, the births registered in Alberta during 1959 were studied.

The survey of birth registrations for 1959 revealed that 37,996 infants had been born in Alberta during that year. Of these, 33,874 were traced and reports were obtained concerning them. Among this group, 257 showed some physical abnormality, a rate of 7.76 births per 1000. This seemed to be a low incidence of abnormalities in the light of other recent data collected in Japan, Birmingham and Sweden.[1] Further analysis of this group was not carried out in 1959.

In 1962, when increasing public attention was focused on malformations attributable to the use of certain drugs, it was decided to carry out a second survey to identify children born with physical deformities during 1961.

In the course of this survey it became apparent that it is possible to determine only gross physical malformations immediately after birth, and even many of the gross abnormalities may not be recognized for weeks or even years. In this category are such disorders as mental retardation, many cardiovascular abnormalities, endocrine and metabolic deficiencies such as cretinism, idiopathic hypercalcemia of infancy, phenylketonuria, Hartnup's disease, also gastrointestinal atresias or hyperplasias,

*Medical Superintendent, Provincial Training School, Red Deer, Alta., and Lecturer in Psychiatry, University of Alberta.

and skeletal anomalies. Even so common a condition as mongolism is frequently not diagnosed at birth. Stillbirths constitute another group which might contain infants with internal organic malformations that are frequently not reported.

Microscopic malformations are rarely discovered at birth and may only be detected considerably later in life, if at all. Therefore, it must be borne in mind that even the best records of neonatal malformations include only a relatively small proportion of such disorders. This consideration lends even greater significance to the figures concerning malformation collected during the surveys described herein.

Of 38,762 births recorded in Alberta in 1961, reports were received on 38,353. In 1961, the average frequency with which children were born with congenital abnormalities was 13.8 per 1000 births for the province as a whole; there were 528 such children. This figure ranged from 15.6 in the northern area of the province to 11.9 in the southern area. Total deformities (several children had multiple deformities) numbered 18.6 per 1000 live births in the northern area compared with 14.0 in the south. The records of only 409 births could not be traced. The births not recorded in our survey were presumed to be those of children born mainly in the colonies of certain religious sects in which mothers are delivered at home rather than in hospitals, together with some births among the Indian and Metis populations.

CLASSIFICATION OF ABNORMALITIES

For the purpose of this study, "malformation" was taken to mean an anatomical aberration or premature cessation of development of a structure.

In classifying the types of physical malformations for this study, we were in a dilemma with respect to the minimum degree of malformation which should be considered significant. There is no doubt that a serious heart lesion constitutes an immediate threat to the newborn child's life, yet who can predict the effect of a hemangioma of the face in terms of eventual psychoneurosis or psychosis? For this reason, it was decided to include all malformations, and no attempt was made to grade them according to their severity. They were all tabulated in accordance with regional anatomical categories.

This survey was based largely on questionnaires, although in some few cases where some ambiguity existed, verbal communication and additional letters were necessary to ensure that the information compiled and used in this communication was correct.

One observation emerging during this study, both in 1959 and 1961, was the fact that congenital malformations were recognized with greater frequency in the northern part of the province than in the southern part. Therefore these deformities were investigated on a regional basis.

GEOGRAPHIC CONSIDERATIONS

Alberta is a large province. In length it extends approximately 850 miles from its northern extremity to the United States boundary. It varies in width: at its northern end it is more than 400 miles wide; at its southern (United States) boundary it tapers to approximately 200 miles.

Its centres of population are separated in such a way that they can be divided into three distinct regions: (1) *Northern area*—demarcated by a transverse line drawn on the map immediately below the city of Edmonton and including the city and all the area north of it. A total of 18,072 births occurred in this area. (2) *Central area*—the total area below Edmonton, extending south to (but not including) the city of Calgary (6,041 births). (3) *Southern area*—the city of Calgary and the remainder of the province south to the United States border (14,240 births). The distribution, by area, of congenital abnormalities that occurred in Alberta in 1961 is shown in Table I.

TABLE I.—CONGENITAL MALFORMATIONS PER 1000 LIVE BIRTHS IN ALBERTA, BY AREA, 1961

Area	*Number of malformations*		*Number of births*		*Births rate per 1000*		*Standard error S E ±*	
Province as a whole	631		38,353		16.5		0.65	
Northern area	337		18,072		18.6		1.01	
Central area	94	294	6041	20,281	15.6	14.5	1.59	0.84
Southern area	200		14,240		14.0		0.98	

The incidence of congenital malformations is shown in the three areas. The difference in malformation rate between the northern and central area is not statistically significant, largely because births in the central area were 1/3 those of the north. The difference between the northern and southern areas is statistically significant, to a 1% confidence level. When the malformations in the central and southern areas are combined and compared with those of the northern area there is also a difference significant to a 1% confidence level.

Association Between the Drugs Ingested by Pregnant Women and Congenital Malformations, by Regions

There seems to be a great human need to attribute the disabilities of mankind to some malign, intervening fate. Drugs have, for many obvious reasons, recently been incriminated in the causation of fetal abnormalities. During the survey it was established that 143 different drugs had been ingested during their pregnancy by women who subsequently gave birth to children with physical deformities. Information concerning all types of drugs was requested in the questionnaire—not only those in the antiemetic group.

One important fact emerged during the present survey: every type of deformity appeared with equal frequency among "unmedicated" mothers as among those mothers who had been "medicated".

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TABLE II.—NUMBER OF MALFORMED INFANTS BORN TO MOTHERS WHO TOOK DRUGS DURING PREGNANCY, COMPARED WITH THOSE BORN TO MOTHERS WHO DID NOT, ALBERTA, 1961

Area	Number of malformed infants born		No. of live births	Rate of malformed infants (per 1000 live births)		Standard error	
No drugs taken during pregnancy							
Province as a whole	344		38,353	9.0		0.48	
Northern area	197		18,072	10.9		0.77	
Central area	55	147	6041	9.1	7.2	1.22	0.59
Southern area	92		14,240	6.5		0.67	
Drugs taken during pregnancy							
Province as a whole	184		38,353	4.8		0.35	
Northern area	84		18,072	4.6		0.50	
Central area	24	100	6041	4.0	4.9	0.81	0.49
Southern area	76		14,240	5.3		0.61	

The antiemetic drugs were the subject of special investigation. Of a total of 55 children with harelip and/or cleft palate, classified under the category "Head and Neck", 11 were born to mothers who had ingested some type of antiemetic* medication. However, the births of 44 other infants with harelip and cleft palate were recorded; the mothers of these infants had taken no (antiemetic) medication.

The relationship of amelia and phocomelia to drug ingestion was also considered. Two mothers who had taken thalidomide during pregnancy gave birth to children with these deformities. On the other hand, 65 malformations of the same or of a similar type relating to the upper and lower limbs were recorded among mothers who had taken no medication of any kind. Indeed, one mother who had taken thalidomide throughout her pregnancy gave birth to a normal child.

*The antiemetics whose ingestion by pregnant women was recorded during this study were as follows: meclizine hydrochloride (Bonamine), trifluoperazine dihydrochloride (Stelazine), dicyclomine, pyridoxine hydrochloride, doxylamine (Bendectin), dimenhydrinate (Gravol), cyclizine hydrochloride (Marzine) and prochlorperazine (Stemetil).

In Table II, the number of malformed infants born to mothers who ingested drugs during pregnancy is compared with those born to mothers who did not ingest drugs.

There is a significant difference between malformations occurring among children born to mothers who had taken no drugs and those occurring among children of mothers who had taken drugs, when the central and southern areas are combined. The reason that the significance of drug ingestion disappears when comparing the northern area and the central area is again largely due to the fact tht the births in the central area were considerably lower than in the northern and southern areas.

Table III indicates the types of abnormalities noted among the births reported in each area. Almost without exception, mothers who took no medication gave birth to an equal number of deformed children, or in the case of some anomalies, a greater number, than mothers who had drugs prescribed for them. The higher incidence of malformations per 1000 births in the northern part of the province than in the southern part is also apparent in this table.

Table IV indicates the geographic distribution—that is, the percentage of the various types of deformities and their regional occurrence per 1000 births. Here again the numbers of malformations are, with few exceptions, higher in the north than in the south.

Investigation of Environmental Factors Associated with the Regional Variation in Incidence of Congenital Malformations in Alberta

During this survey it became apparent that a relationship existed between the incidence of con-

TABLE III.—INCIDENCE OF CONGENITAL MALFORMATIONS AMONG CHILDREN OF MOTHERS WHO DID NOT RECEIVE ANY MEDICATION, COMPARED WITH THE TOTAL ABNORMALITIES OF EACH AREA

Site or nature of malformation	Northern area		Central area		Southern area		Total	
	No drugs	Total malformations	No drugs	Total malformations	No drugs	Total malformations	No drugs	Malformations
Upper limbs	12	23	3	7	5	14	20	44
Lower limbs	33	65	4	15	8	26	45	106
Head and neck (includes facial, oral and nasal deformities)	20	37	8	12	15	36	43	85
Central nervous system (includes hydrocephalus, microcephalus, spina bifida)	28	51	6	9	13	37	47	97
Cardiovascular system	18	27	2	6	9	21	29	54
Urogenital system	28	44	0	5	10	24	38	73
Gastrointestinal system	21	26	4	5	4	7	29	38
Respiratory system	6	7	1	6	1	2	8	15
Blood dyscrasias	2	5	3	3	0	0	5	8
Mongolism	12	28	5	8	5	18	22	54
Others	12	24	11	18	8	15	31	57
Totals	192	337	47	94	78	200	317	631
Rate of malformations per 1000 live births—								
—among mothers who received no drugs	5.7		5.0		3.9		5.0	
—among mothers who received drugs	4.3		5.0		6.1		4.9	

TABLE IV.—GEOGRAPHIC DISTRIBUTION OF MALFORMATIONS

Site or nature of malformation	*Northern area*	*Rate per 1000 births*	*Central area*	*Rate per 1000 births*	*Southern area*	*Rate per 1000 births*	*Total*	*Rate per 1000 births*
Upper limbs	23	1.2	7	1.1	14	0.9	44	1.1
Lower limbs	65	3.5	15	2.4	26	1.8	106	2.7
Head and neck (includes facial, oral and nasal deformities)	37	2.0	12	1.9	36	2.5	85	2.2
Central nervous system (includes hydrocephalus, microcephalus, spina bifida)	51	2.8	9	1.4	37	2.5	97	2.5
Cardiovascular system	27	1.4	6	0.9	21	1.4	54	1.4
Urogenital system	44	2.4	5	0.8	24	1.6	73	1.9
Gastrointestinal system	26	1.4	5	0.8	7	0.4	38	0.9
Respiratory system	7	0.3	6	0.9	2	0.1	15	0.3
Blood dyscrasias	5	0.2	3	0.4	0	0.0	8	0.2
Mongolism	28	1.5	8	1.3	18	1.3	54	1.4
Others	24	1.3	18	2.9	15	1.0	57	1.4
Total malformations per area	337		94		200		631	
Total malformations per 1000 births per area		18.6		15.6		14.0		16.5

genital deformities and the region of the province in which the affected child was born. In the examination of possible environmental factors, which might have a different effect in the northern sections of the province, the factor of precipitation was chosen for initial investigation.

Precipitation as a Factor

In Alberta, precipitation (rainfall, snowfall, etc.) and its runoff are quite different from many other areas in Canada. There is more precipitation in the province's northern regions than in the south. Also, precipitation occurring during the last three months of the year usually accumulates during the winter months, remaining for a further three or four months of the subsequent year as ice or snow, until its runoff in the spring. This usually occurs as much as six weeks later in the northern part of the province than in the south.

The precipitation for the years 1960 and 1961 (a period during which the conception, gestation and birth of the babies studied would have occurred) was compiled, and the average precipitation of these two years was calculated for each geographical area. During each of the years it was higher in the northern than in the southern area.

Fig. 1a indicates the average regional rainfall in inches for the years 1960 and 1961. This figure for precipitation was compared with that for the incidence of malformations per 1000 births (Fig. 1b) in each respective area. This comparison indicated that there was a marked relationship between the extent of precipitation and the frequency of congenital malformations.

Fig. 2a indicates the total number of malformations per 1000 births in the three largest cities in Alberta, each of which had over 1000 births during the year. This figure is significant because it gives the yearly average precipitation in these three cities. There is a direct relationship between levels of precipitation and numbers of malformations per 1000 births in these three major Alberta cities.

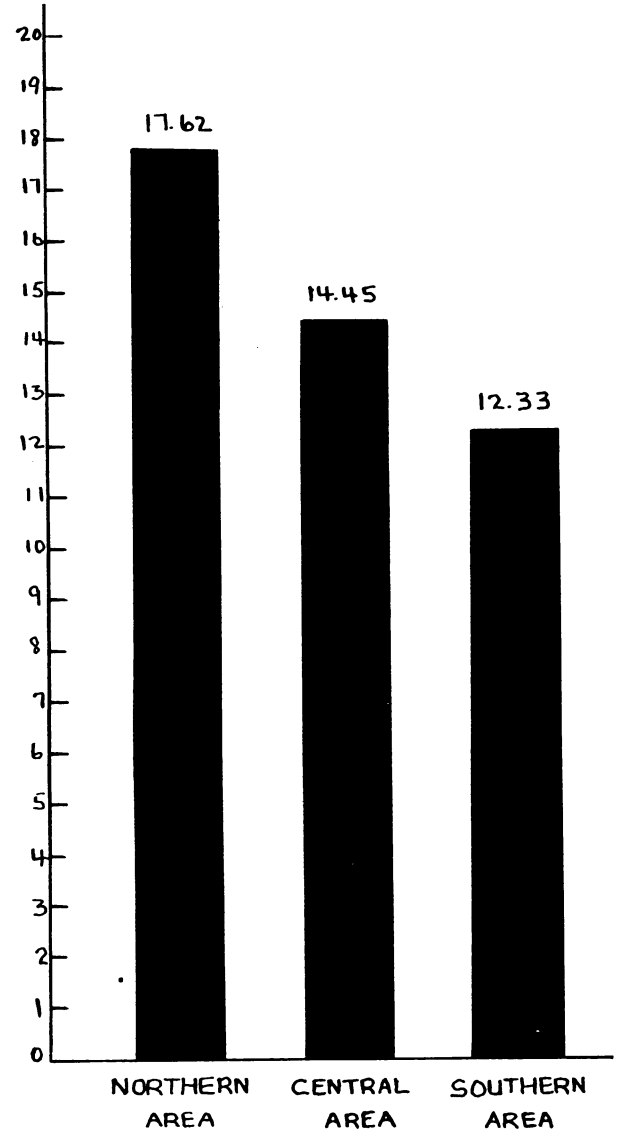

Fig. 1a.—Average precipitation for a two-year period (1960-1961) for the northern, central and southern areas of Alberta.

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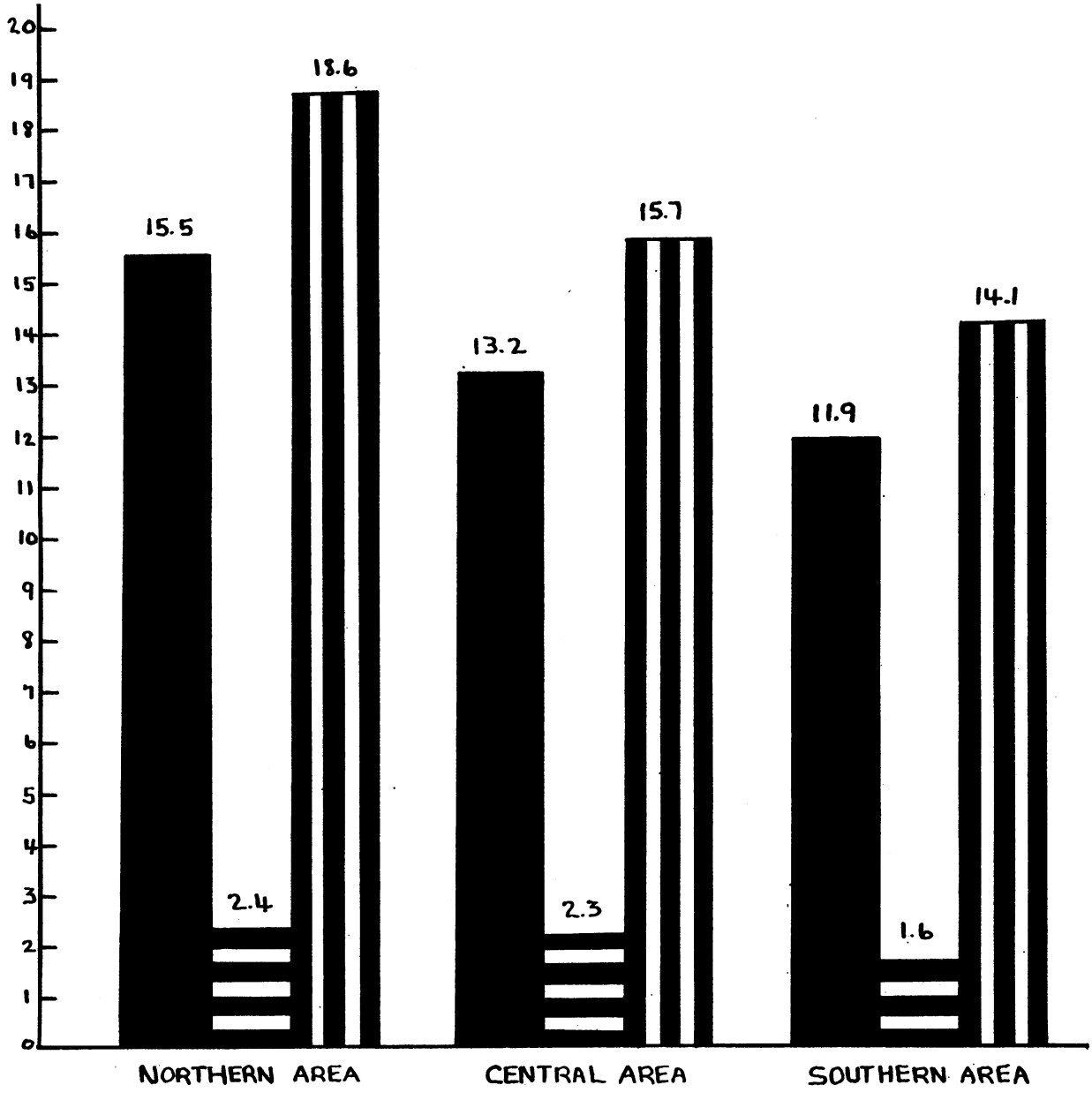

Fig. 1b.—The number of children per 1000 births demonstrating malformations (an organ or other structure showing a developmental fault), for the northern, central and southern areas of Alberta. Black bar-graph represents the number of children per 1000 births born with malformations. Transverse striated bar-graph represents the number of children per 1000 births born with more than one malformation. Vertical striated bar-graph represents total malformations per 1000 births.

Since rain water itself is inert and harmless, and cannot be regarded as the factor producing fetal maldevelopment, a search for other related factors was extended into other scientific fields. In this respect it was recalled that Wiles[2] reported that many plants in Canada have a specific affinity for certain minerals during their growth. Many plants contain so much cesium-137 that they give a high counting rate on prospectors' portable Geiger counters. Because these instruments are not sufficiently sensitive to other types of radiation, they do not distinguish between the γ rays emitted by uranium and those emitted by other radioactive γ-emitters. In this respect Wiles commented: "Certainly it is important to note that radioactivity during or after a rain or snowstorm is to be viewed (by the prospector) with suspicion and may well disappear when the rain or snow runs off. Furthermore, radioactivity which appears only on the surface and does not persist to a depth of more than a few inches, is more than likely attributable to fallout."

The most recent publication[3] of the United Nations Scientific Committee reporting on atomic radiation states: "Although more information is required before firm conclusions can be drawn, there is evidence indicating that embryos are more susceptible to radiation injury than adults, and even low doses may induce both developmental disorders and malignant changes in embryos. Further studies

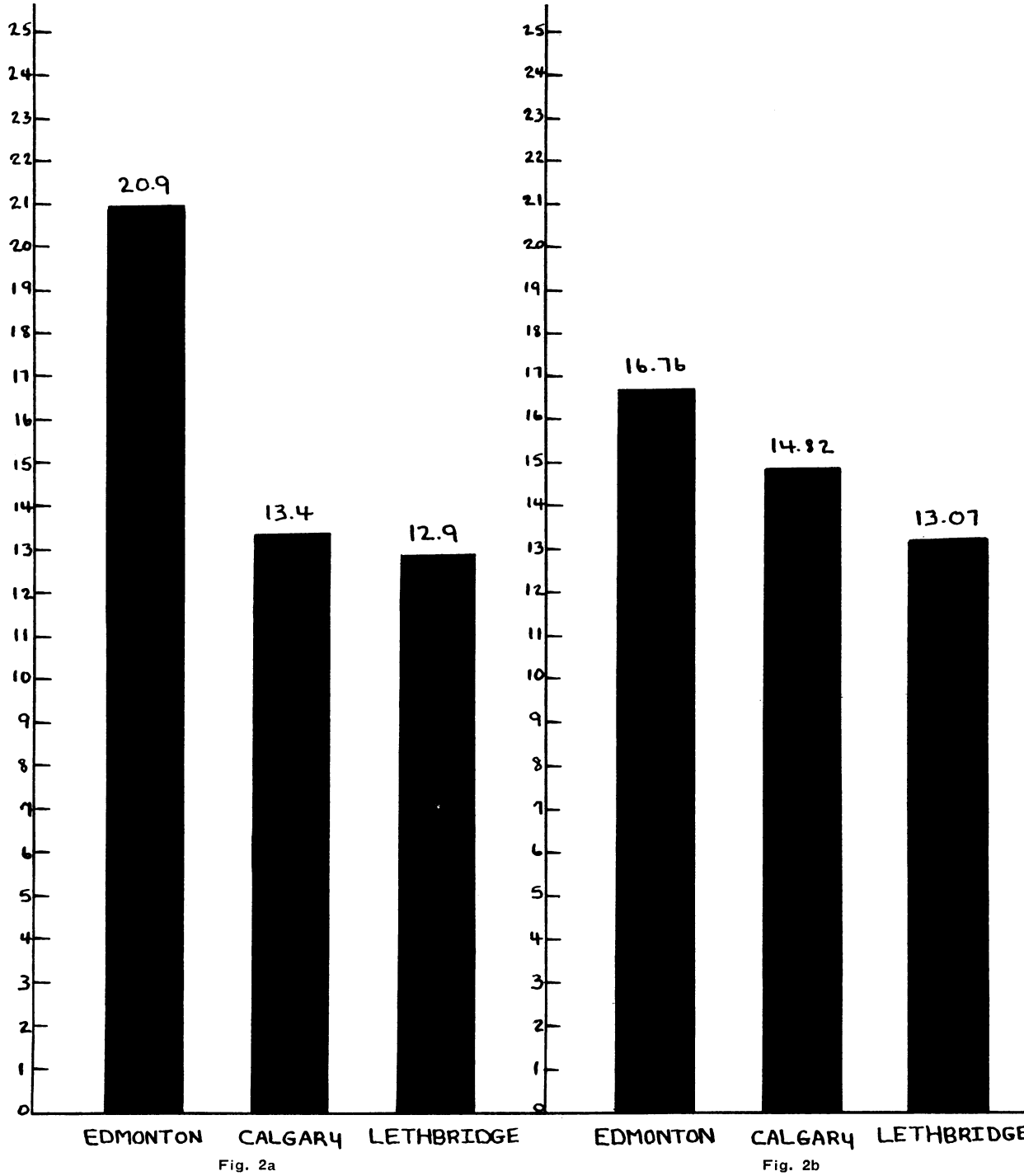

Fig. 2a

Fig. 2b

Fig. 2a.—Total congenital malformations per 1000 births for the three largest cities in Alberta. Fig. 2b.—Average precipitation (snow and rainfall) for 1960-1961 in Alberta.

on the effects of radiation on fetuses exposed *in utero* are therefore crucial."

Among the variety of man-made isotopes produced in increasing amounts as a result of the large number of above-ground explosions of thermonuclear devices are certain isotopes which, by virtue of their long half-life, present serious biological hazards. Of these, strontium-90, cesium-137 and cerium-144 are particularly dangerous. The affinity of strontium-90 for calcium is well known. Cesium has the ability to act as an active metabolite in cellular metabolism, behaving in much the same way as potassium. These elements and cerium are strong gamma emitters.

Because of their long half-lives, these isotopes (strontium-90, 28 years; cesium-137, 33 years, and cerium-144, 282 years) represent a great radiation hazard. It is not unreasonable to assume that any further atomic or thermonuclear explosions carried out above ground will add these isotopes to the stratosphere from whence they can re-enter the atmosphere. They will be carried to earth by

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clouds, rain and snow and will increase the present genetic hazard.

The Department of National Health and Welfare is aware of this danger and has recently started to test previous and present samplings of precipitation and other substances in order to determine the presence of cesium-137. The Department has been most co-operative in making available to us all of the information in their possession that is pertinent to this study.

DISCUSSION

During this survey, the only constant factors recognized to have a relationship to abnormal births were (1) the geographic area where the child was born and (2) the precipitation levels of that area. The hypothesis is advanced that because of the higher levels of rainfall in 1961 and its contamination by radioactive dust, more babies may have been subjected to dangerous man-made radioactive elements *in utero*. Births in 1962 will, if our projection is valid, show even higher rates of abnormalities per 1000 births because of an increased concentration of radioactive dust in the stratosphere, the result of intensive above-ground explosions in the Soviet Arctic and sub-Arctic throughout 1959 and 1962.

Further investigation along the lines suggested by this hypothesis may be impeded by the reaction, within the profession and among the general public, to the sensational treatment given to this complicated subject in the popular press. For example, on certain occasions the author encountered some reticence on the part of the patient's doctor when he was asked for information about the patient's ingestion of certain drugs. Although the fact of the child's deformity, the date of birth and the area of birth were recorded, some physicians refused to give any information concerning the medications that had been prescribed for their patients. They gave as the reason for this refusal the "bad publicity" that might arise.

Comparable studies on the incidence of congenital malformations in our other provinces should be carried out, so that more extensive comparisons can be made. Sequential (yearly) studies would also help to establish trends occurring in the incidence of congenital abnormalities. It is a matter of regret that long-range studies, such as were conducted in Birmingham, England,[1] have not yet been carried out in Canada.

In Canada, studies of this nature are made more difficult because most Provincial Committees on Perinatal Mortality do not yet list all physical malformations on their questionnaires, but confine their records to those inimical to the life of the child.

It is recommended that every birth record should incorporate a tabulation of all the physical abnormalities of the child and that a Central Provincial Register of these anomalies be maintained. A suitable form for this information should accompany all initial requests for birth registration. With modern recording methods such as microfilming, the difficulties experienced previously in carrying out projects of this sort should be largely overcome.

SUMMARY

The incidence of congenital malformations in children born in Alberta in 1961 was 13.8 per 1000 births; this was considerably higher than in 1959 (7.6 per 1000 births).

The ingestion of drugs by the mother during pregnancy does not appear to have made any regular contribution to these malformations.

The direct association between geographic location, high precipitation levels, and the incidence of congenital malformations appears to have been established.

More complete birth records should be kept by all provinces so that a continuing study of the incidence of congenital malformations can be carried out for sequential years, to identify whatever genetic hazards may exist.

The author would like to extend thanks to the Honourable Dr. J. Donovan Ross, Minister of Health for the Province of Alberta, who suggested the initial study in 1960; Dr. Randall R. MacLean, Director of the Division of Mental Health for the Province of Alberta, who acted in a consultant capacity on many occasions; Dr. W. B. Parsons, who read the manuscript and made many valuable suggestions; Dr. S. Orford Smith, who was responsible for organizing the mathematical work which included standard errors as well as the statistical confidence levels; and Mrs. Gail Blades who, in the capacity of research assistant, worked assiduously on the many statistical tables and charts to advance the completion of this study by several months.

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PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

The great physician and surgeon must depend for his diagnosis upon the physical examination and the evidence he extracts, sifts, and weighs in the patient's history. Laboratory methods are of only occasional use, viz. to support or not support clinical findings . . . It is hopelessly futile to attempt anything more than the most elementary teaching in the primary subjects of medicine today. The tried-out subjects of the ages, anatomy, physiology, and chemistry, should have preference as to the length of instruction hours. A student's most precious possessions are his time, his vitality, and a clear mind at the age when the mind is most supple, its curiosity most alert, and its nature most impressionable. It is only by cutting down the time allotted to laboratory subjects that we will be able to find a place to instruct students in all the physical, mental, and nutritional forms of healing. It is high time that there was a readjustment of the programme, and a place, if not a professorship, given to these important subjects.—H. A. McCallum: President's Address to The Canadian Medical Association, London, Ont., June 1913; *Canad. Med. Ass. J.*, 3: 548, 1913.