forearm did not change with the infusion of either insulin or proinsulin.

The subjects were five healthy, nonobese males who had no family history of diabetes mellitus. Five proinsulin and two subsequent single-component insulin infusions were carried out in these individuals. The dose of proinsulin was calculated to be equivalent to the maximum molar weight of insulin used in past forearm experiments (100 μU kg^{-1} min^{-1} or 6.4×10^{-10} mmole kg^{-1} min^{-1} (*3*).

From experiments with glucagon-free insulin (300 to 400 μU/ml final plasma concentration) the following metabolic effects have been noted: (i) Insulin blocked lipolysis in adipose tissue and unmasked ongoing uptake of FFA by muscle. (ii) Efflux of K^+ was blocked in muscle, but there was a much lesser effect on adipose tissue. (iii) Glucose uptake was increased up to 12-fold in muscle and 6-fold in adipose tissue (*6*).

In this study, net maximum or net mean maximum alterations from the basal state were used as an index of the hormones' biologic action; that is, arteriovenous concentration differences in a given bed minus the mean basal arteriovenous concentration differences in that bed (Table 1). Positive changes represent an increased uptake of a given substance in comparison with the basal state for that tissue; negative changes represent an output of a substance relative to the basal state.

A comparison of the effect of proinsulin alone with the effect of single-component insulin in equimolar concentrations in the same individuals demonstrated a decreased biologic potency of proinsulin. The relative arteriovenous concentration differences for FFA, K^+ concentration, and glucose were less, with one exception, for proinsulin than insulin. Proinsulin had as little as 6 percent of the effect of insulin upon increasing glucose uptake across the deep bed in one subject (Table 2). In one of the two individuals (E.K.) studied with both insulin and proinsulin, proinsulin had a greater effect than single-component insulin upon differences in arterial and venous amounts of FFA in adipose tissue. This raises the possibility that proinsulin's effect upon differences in arterial and venous concentration of FFA in adipose tissue may be equivalent to or greater than the effect of insulin.

In general, proinsulin had more effect upon the superficial venous bed (predominantly fat) than upon the deep bed (predominantly muscle). This was true for both FFA and glucose, whereas effects on K^+ were approximately equal (Table 1). This pattern of tissue sensitivity contrasts sharply with present and past forearm experiments with insulin (Table 2). These observations may be pertinent to states in man where proinsulin constitutes a greater proportion of total immunoreactive insulin than normal (*7*, *8*).

S. E. FINEBERG
THOMAS J. MERIMEE
Boston University Medical Services,
Boston City Hospital,
Boston, Massachusetts 02118

References and Notes

1. D. F. Steiner, D. Cunningham, L. Spigelman, B. Atten, *Science* **157**, 697 (1967); D. F. Steiner, O. Hallund, M. B. Rubenstein, S. Cho, C. Bayliss, *Diabetes* **17**, 725 (1968); P. T. Grant and K. B. M. Reid, *Biochem. J.* **109**, 32P (1968); R. E. Chance and R. M. Ellis, *Arch. Int. Med.* **123**, 229 (1969).
2. Porcine proinsulin CT-1649-8A and single-component porcine CT-1651-8A insulin were obtained from Dr. R. Chance (Lilly Research Laboratories). We thank Drs. Chance and J. Galloway of Lilly Laboratories.
3. R. Andres, M. A. Baltzan, G. Cader, K. L. Zierler, *J. Clin. Invest.* **41**, 108 (1962).
4. R. Andres, G. Cader, K. L. Zierler, *ibid.* **35**, 671 (1956); M. A. Baltzan, R. Andres, G. Cader, K. L. Zierler, *ibid.* **41**, 116 (1962); R. Andres, K. L. Zierler, M. Anderson, W. N. Stainsby, G. Cader, A. S. Ghrayyib, J. L. Lillienthal, Jr., *ibid.* **33**, 482 (1954).
5. T. J. Merimee, D. A. Lillicrap, D. Rabinowitz, *Lancet* **1965-II**, 668 (1965).
6. K. L. Zierler and D. Rabinowitz, *Medicine* **42**, 385 (1963).
7. A. H. Rubenstein, S. Cho, D. F. Steiner, *Lancet* **1968-I**, 1353 (1968).
8. R. Gorden and J. Roth, *Arch. Int. Med.* **123**, 237 (1969).
9. Supported in part by PHS training grant AM 054456-04, PHS grant 1 RO1 AM 13565-01, and by a grant from the American Diabetic Association.

10 October 1969; revised 1 December 1969

Somatic Association in Avena sativa L.

Abstract. *Root tip cells of hexaploid oats* Avena sativa *L. were examined at mitotic metaphase, and distances between homologous as well as between nonhomologous chromosomes were measured and their frequency distributions compared. Nonhomologous chromosomes were scattered at random in the cells studied. In contrast, the mean distance between homologous chromosomes was significantly shorter. There is a tendency for somatic association of homologs in this species.*

Association of homologous chromosomes in somatic cells has been reported for a number of organisms (*1*, *2*). Recently, Feldman *et al.* (*1*) measured the distances between members of pairs of homologous and between nonhomologous chromosomes in root tip cells of common wheat and found that the homologous chromosomes were not distributed at random but were associated with one another. In addition, Feldman (*3*) presented evidence that genes, located on chromosome 5B, 5D, and 5A, regulate this somatic association.

In *Avena sativa* L. a number of chromosomes can be easily identified by karyotype in somatic cells. Thus it is possible to determine whether the phenomenon of somatic association is also present in this species.

For this purpose the distances between members of chromosomes pair 21 and between members of a pair of homologous telocentrics were measured. Chromosome 21 is the shortest of the complement and easily distinguished (Fig. 1). In addition, the distances between the telocentrics and chromosomes 21 were scored. The telocentrics were not identified but were not chromosome 21 since the 21 bivalents always formed at meiosis, the telocentrics pairing together to form an open bivalent. The telocentrics could be differentiated from chromosome 21 by their terminal centromeres in somatic metaphase.

Distances between the midpoints of telocentrics, distances between centromeres of the chromosomes 21, and distances between the midpoints of the telocentrics and the centromeres of the chromosomes 21 were taken in the same cell. The distance between the two chromosomes farthest apart in the cell concerned was also taken to mini-

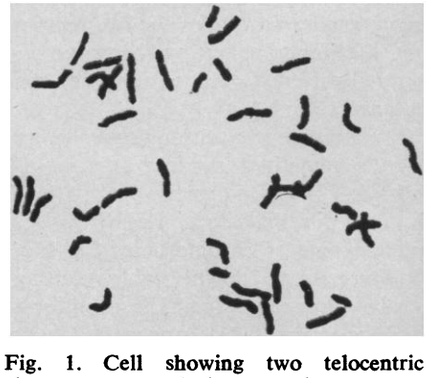

Fig. 1. Cell showing two telocentric chromosomes and the two chromosomes 21 (shortest of the complement).

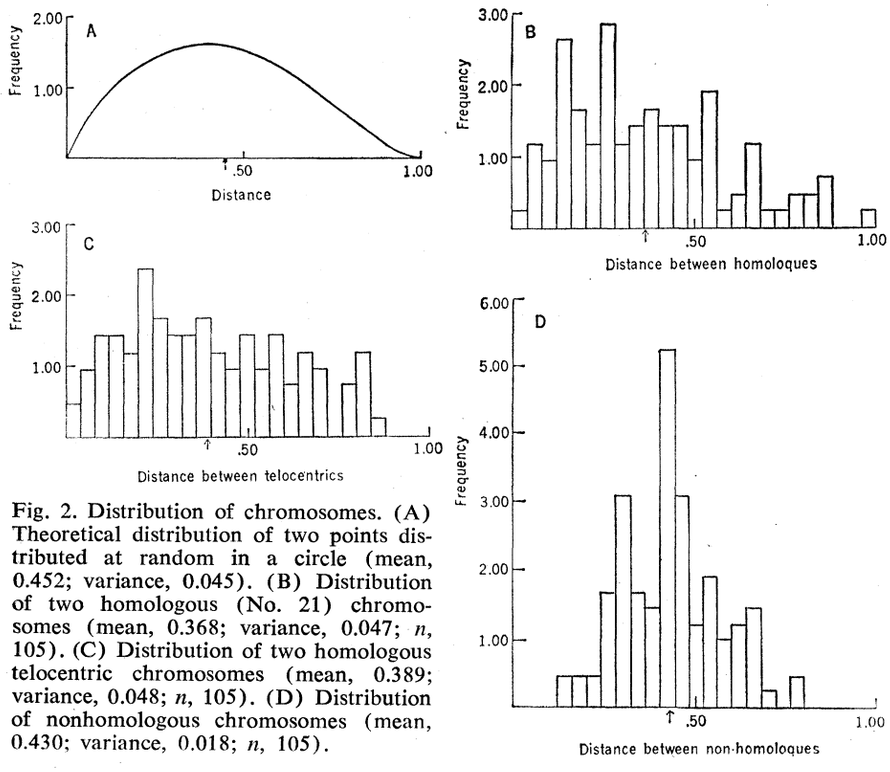

Fig. 2. Distribution of chromosomes. (A) Theoretical distribution of two points distributed at random in a circle (mean, 0.452; variance, 0.045). (B) Distribution of two homologous (No. 21) chromosomes (mean, 0.368; variance, 0.047; n, 105). (C) Distribution of two homologous telocentric chromosomes (mean, 0.389; variance, 0.048; n, 105). (D) Distribution of nonhomologous chromosomes (mean, 0.430; variance, 0.018; n, 105).

mize the differences due to squashing.

If we consider the nonhomologous chromosomes as two points distributed at random in an area, the expected frequency distribution can be calculated by the substitution of a series of values from 0 to 1 in Hemmersley's formula (Fig. 2A). The mean and variance of such an expected distribution were 0.452 and 0.045, respectively. The Wilcoxon matched pairs signed-ranks test was used for the statistical comparisons of these distributions of homologous and nonhomologous chromosomes (*4*).

The frequency distribution for nonhomologous chromosomes was not significantly different from the expected frequency distribution ($P < .05$). The mean and variance were 0.430 and 0.018, respectively. The close fit to the theoretical curve verifies the assumption that the nonhomologous chromosomes were distributed at random in the flattened cell.

The homologous chromosomes were not distributed at random (Fig. 2, B and C). The frequency distributions obtained for the telocentrics (Fig. 2C) and the pair of chromosomes 21 (Fig. 2B) were skewed to the right, resulting in a lower mean value. The mean and variance were 0.368 and 0.047 and 0.389 and 0.048, respectively, for the homologs of chromosome 21 and the telocentrics. The frequency distributions for homologs were significantly different from the frequency distribution for nonhomologous chromosomes ($P < .05$). Furthermore, the frequency distribution for homologous chromosomes 21 did not differ significantly from the frequency distribution of the pair of telocentrics.

There is association of the homologs of chromosome 21 and of the telocentrics in somatic cells of *Avena sativa*. It is probable that such attractions apply to all the homologous chromosomes of the oat complement. Somatic association appears to be a more widespread phenomenon in plants and animals than previously thought although its cytological and physiological significance is still obscure.

J. P. DUBUC
R. C. MCGINNIS
Department of Plant Science, University of Manitoba, Winnipeg 19

References and Notes

1. M. Feldman, T. Mello-Sampayo, E. R. Sears, *Proc. Nat. Acad. Sci. U.S.* **56**, 1192 (1966).
2. Y. Kitani, *Jap. J. Genet.* **38**, 244 (1964); M. P. Maguire, *Chromosoma (Berlin)* **21**, 221 (1967); S. G. Smith, *Can. J. Res.* **20D**, 221 (1942); L. Schneiderman and C. A. B. Smith, *Nature* **195**, 1229 (1962); E. B. Wagenaar, *Chromosoma (Berlin)* **26**, 410 (1969).
3. M. Feldman, *Proc. Nat. Acad. Sci. U.S.* **55**, 1447 (1966).
4. S. Siegel, *Nonparametric Statistics* (McGraw-Hill, New York, 1956).
5. Supported by National Research Council of Canada. We thank M. Feldman for suggestions and for reading the manuscript.

5 November 1969

Cerebral Hemorrhage in Relation to Birth Asphyxia

Abstract. *The brains of monkeys and guinea pigs asphyxiated at birth, completely resuscitated, and killed at various times thereafter revealed no petechial hemorrhages. However, when postnatal distress and other factors leading to a moribund state occurred, the brains revealed petechial hemorrhages.*

Postmortem examinations of human infants who die soon after birth sometimes reveal petechial cerebral hemorrhages. Pathologists generally believe that asphyxia is the cause of these hemorrhages. Some medical examiners, especially in France, entertain the possibility of homicide by suffocation when an infant is discovered dead in its crib with its face up and its brain contains petechial hemorrhages. Whether asphyxia at birth is actually the cause of cerebral hemorrhages cannot be established in human subjects, but experiments in animals have shed light on the question.

The subjects of the present research were guinea pig and monkey (*Macaca mulatta*) fetuses of known gestational age and newly born infant monkeys. Cesarean sections were performed under local anesthesia, usually near term. Either the fetus with its placenta and membranes was removed intact or the fetal membranes were opened, a small rubber bag containing saline solution was slipped over the fetal head, and the umbilical cord was clamped. These techniques induced asphyxia, the duration of which was varied from less than 5 minutes to more than 21 minutes, resuscitation becoming necessary in monkeys asphyxiated for 8.5 minutes or more.

Events accompanying asphyxia at birth are as follows: The blood Po_2 quickly approaches zero, Pco_2 rises, and pH declines. Initially there is a brief tachycardia and a few rhythmical respiratory movements following which the fetus executes some mass movements and then enters into primary apnea which, in the absence of anesthesia, lasts less than a minute. The heart rate promptly slows, but blood pressure at first increases and then gradually declines. With exhaustion of oxygen from the blood, glycogen stores are called upon for tissue respiration and the fetus begins to gasp at two to four gasps per minute, which end, on the average, 8.5 minutes after the start of asphyxiation. Secondary, or termi-