tively globular body. In Figure 2 of a second meiotic metaphase polar view, nearly 38 elements can be clearly counted. Whereas the largest element in this plate is comparable in size to some of the smaller mammalian chromosomes, some of the smallest elements are at the limit of the effective resolution in a light microscope.

Counting chromosomes in nine second meiotic plates showing discrete elements without any apparent scattering or clumping, has revealed numbers between 38 and 42.

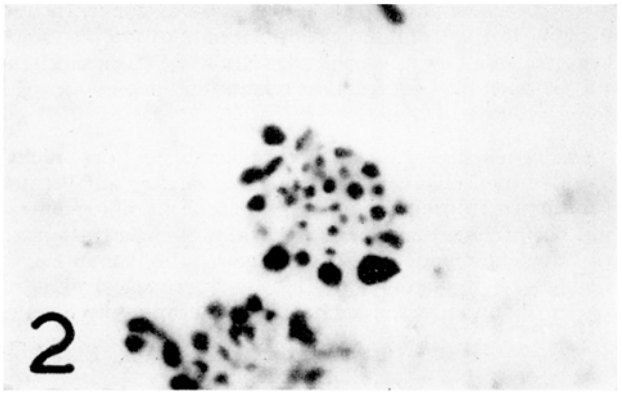

Fig. 2
Meiotic metaphase II plate showing nearly 38 elements. ×3250 approx.

Due to the extremely small size of some of the elements in the meiotic divisions, it is not possible to say with certainty what constitutes the exact haploid number in the present species. As a number of plates show between 38 and 42 elements, and in some of the best plates from both the meiotic divisions either 41 or 42 elements could be counted, it appears probable that either of these two numbers represents the haploid set.

The present author is of the view that variations in the haploid chromosome number recorded are caused by the clumping of some of the smaller elements. Evidence from the second meiotic divisions of the present material does not support the observations of NEWCOMER and BRANT[8] and NEWCOMER[1], who described that 'there is a marked reduction in number and volume of the chromosomoids and by the second metaphase and anaphase they have virtually disappeared' in the domestic fowl.

Handling of the avian material with some improved prefixation treatment-squash techniques[6] has convinced the present author that the so called avian microchromosomes are in no way non-chromosomal. Evidence from the present material, and that of some other birds[4,5,7], strongly suggests that there is no decrease in the number of the smaller elements with the progress of meiosis and that they retain their individuality throughout the mitotic and the meiotic cycle and do not act as mere reserves of DNA for the larger elements.

Résumé. Les chromosomes méiotiques des testicules des petites alouettes de l'Inde (*Alauda gulgula gulgula*) ont été examinés après prétraitement avec la solution hypotonique de Ringers. Dans chacune des deux métaphases méiotiques, on en a compté un nombre variant entre 38 et 42. Dans certaines des meilleures plaques, on a compté 41 ou 42 éléments. Il n'est pas possible de savoir avec précision le nombre haploïde exact, à cause des dimensions extrêment petites de quelques éléments. L'auteur pense que la variation en nombre provient de l'agglutination de quelques petits chromosomes[9].

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Zoology Department of the Punjab University, Chandigarh (Punjab, India), November 24, 1962.

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[9] I am thankful to Dr. G. P. SHARMA, F.N.I., for his kind supervision and help during my tenure as a research fellow in his department.
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Histamine Formation in Bone Marrow

Histamine formation by decarboxylation of histidine has been demonstrated isotopically in tissues of all mammalian species so far investigated, in contrast with results obtained by a non-isotopic method which SCHAYER[1] and KAHLSON[2] have refuted as inadequate to the purpose. In the rat, the level of histidine decarboxylase is singularly high in some tissues characterized by a high rate of cell multiplication or cell renewal, such as tissues of the embryo, gastric mucosa, wound and granulation tissue of healing skin wounds (for references see KAHLSON[2]). In the mouse Landschütz I ascites tumour, a high correlation between histidine decarboxylase level and mitotic index was found[3].

The bone marrow was examined in this respect since this tissue is a site of high rate of cell multiplication. Bone marrow was obtained from the humerus, femur and tibia of rats, the age and sex of which are noted in the Table. In each of the three last experiments of the Table, tissue from two rats was pooled. Histidine decarboxylase activity was determined by incubating samples of bone marrow with 40 µg ^{14}C-histidine and measuring the amount of ^{14}C-histamine formed, expressed as counts per

Histidine decarboxylase activity in rat bone marrow

Age in days	Sex	Amount of tissue incubated g	Cpm/g
41	♂	0.07	30000
43	♀	0.11	20000
45	♀	0.08	26000
46	♀	0.10	21000
48	♀	0.11	40000
52	♂	0.17	21000
54	♀	0.13	24000
63	♀	0.06	58000
76	♂	0.16	26000
140	♀	0.18	25000
140	♀	0.23	31000

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min per g tissue (cpm/g). With the ^{14}C-histidine used, 1 µg ^{14}C-histamine formed corresponded to about 5000 cpm.

For comparison with the values for bone marrow, the histamine-forming capacities of several adult rat tissues, as determined in this laboratory, are given in approximate figures (cpm/g): liver (embryonic) 150000; liver 50; skin 50; stomach 30000; granulation tissue 2000; wound tissue 1500; lung 1000.

Because of the very high rate of histamine formation and the great combined mass of the bone marrow, a substantial proportion of the total-body histamine formation resides in this tissue. The present study, which so far has not included a cytological examination of the number and type of cells actually in mitosis, supports previous evidence from this laboratory of a possible relationship between histamine-forming capacity and certain types of rapid tissue growth. It remains to be seen to what extent the activity is confined to basophil granulocytes, as these cells have been shown to contain histidine decarboxylase in man[4,5].

Zusammenfassung. Das Knochenmark der Ratte hat ein hohes Vermögen zur Histaminbildung durch Dekarboxylierung von Histidin.

G. Kahlson and Elsa Rosengren

Institute of Physiology, University of Lund (Sweden), January 24, 1963.

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Drug Induced Skeletal Malformations in the Rat

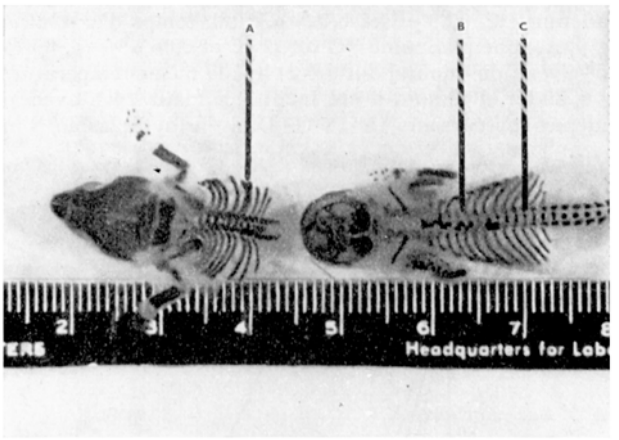
Various animal experiments[1-11] on the teratogenic action of thalidomide have been reported. To date, gross malformations have only been observed in the rabbit[1,3,5,6,8,9] and in the mouse[6,10]. No positive findings, other than increased mortality and reabsorption sites[4,6], or comparative studies of other hypnotic agents, have been reported in the rat.

Groups of 15 and 20 Sprague–Dawley rats (Charles River Breeding Laboratories) were placed on a diet (Purina Laboratory Chow) containing thalidomide (1% and 2%), phenobarbital (0.16%), methaqualone (0.8%), and glutethimide (0.4%) for three days prior to mating. Both male and female animals received the test agent. When about two weeks pregnant, the female animals were removed and permitted to deliver. They received the treatments for the full gestation period. Stillborn and animals dying up to seven days were carefully examined for defects and preserved. The survivors were weaned.

One hundred and three pregnant animals were studied and of 233 dead offspring, 137 were examined for skeletal malformations.

Offspring mortality was highest in the phenobarbital (78%) and thalidomide groups (29% and 42% respectively) as compared to the controls (6%). Mortality was less with methaqualone (23%) and glutethimide (18%). Litter size was decreased in the phenobarbital and thalidomide treated groups suggesting uterine reabsorption.

Examination of the alizarin red stained skeletons[12] revealed abnormalities of a kind observed with other teratogens[13]. These included multiple occurrence of double vertebral centra (Figure).This was highest with methaqualone (9/9), thalidomide 2% (30/48) and phenobarbital (20/25) and lowest with glutethimide (4/17). Extra ribs were observed on the first lumbar vertebrae (L 1) in eight animals on methaqualone and in two animals each on phenobarbital and thalidomide 1%. In the thalidomide 2% group three animals showed a marked branching and fusion of the ribs (Figure). Another common finding in the thalidomide treated animals was 'scrambled' sternabrae in 22 instances (Figure). With phenobarbital, 5 similar malformations were observed. In the skull, inhibition of ossification, manifest by abnormally wide sutures between the cranial bones, was observed. This was common to all the phenobarbital-treated animals but only occurred in 2 animals each on thalidomide 2% and glutethimide. Control animals showed minor deviations—one offspring had a single vertebral malformation and an extra ossification centre on L 1. Further indication of the drug effect was obtained by examination of a second litter from the same mothers on a drug-free diet. Mortality in the second litter was not different from controls and skeletal malformations were either absent (e.g. phenobarbital) or markedly reduced both in incidence and severity. These results confirm the induction of malformations produced by the agents tested.



Alizarin red stained skeleton of 1 day old Sprague-Dawley rats. (a) branched and fused ribs, (b) 'scrambled' sternabrae and (c) double vertebral centra. Scale in cm.

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