# CYTOTOXIC EFFECT OF NICKEL CHLORIDE ON THE SOMATIC CHROMOSOMES OF SWISS ALBINO MICE *MUS MUSCULUS*

P. K. MOHANTY
*Department of Zoology Utkal University, Vani Vihar, Bhubaneswar 751 004, India.*

## ABSTRACT

People are often exposed to nickel and nickel salts by industries as well as through effluents. Sub-lethal doses of nickel chloride treatment and its effects on bone-marrow chromosomes of Swiss albino mice *Mus musculus* show various chromosomal anomalies. Hence, restricted exposure to nickel is suggested for minimizing human health hazards.

## INTRODUCTION

MUTAGENIC study using various chemicals has been reported on plants[1–4] and in some animals[5–12]. Significant work on the effects of a number of agents has been undertaken on the chromosomes of mammalian tumour and normal cells *in vivo* and *in vitro* conditions[13–17]. The effect of nickel chloride on plants like *Pisum* is well known[18,19]. The present investigation on the effect of nickel chloride on mice is to understand the general nature of nickel poisoning.

## MATERIALS AND METHODS

Laboratory bred Swiss mice *M. musculus* (10–12 weeks old) were used as experimental animals and bone-marrow chromosomes constituted the materials for investigation. The effect of different doses of nickel chloride (24 mg, 12 mg and 6 mg/kg body weight) with 3 different exposures (6, 24 and 48 hr for each dose) was studied on the mice. In chronic treatment the highest dose of 24 mg/kg body weight was divided into 5 equal parts and the individual mouse was injected with each fraction 5 times at intervals of 24 hr and the animals sacrificed 24 hr after the last injection. For all the treatments the chemical was administered intraperitoneally.

Cytological preparations of bone-marrow cells were carried out following the conventional technique[20]. For all treated experiments parallel controls were prepared by injecting with equal volumes of distilled water.

## RESULTS

Qualitatively, the chemical induced general physiological effects like corrosion , chromatin and centromeric stretching (figure 2). Quantitative scoring indicates chromatid gaps (figure 1) and breaks (figures 3 and 4), exchange of chromatid (figure 5) and centromeric fission (figure 6).

Biometrical aspects show that all the doses induced the highest effect after 24 hr of exposure (table 1) and irrespective of the dose and hour of acute exposures, the highest frequency of aberration (4.33%) was induced by the dose of 12 mg/kg body weight after 24 hr exposure (table 1).

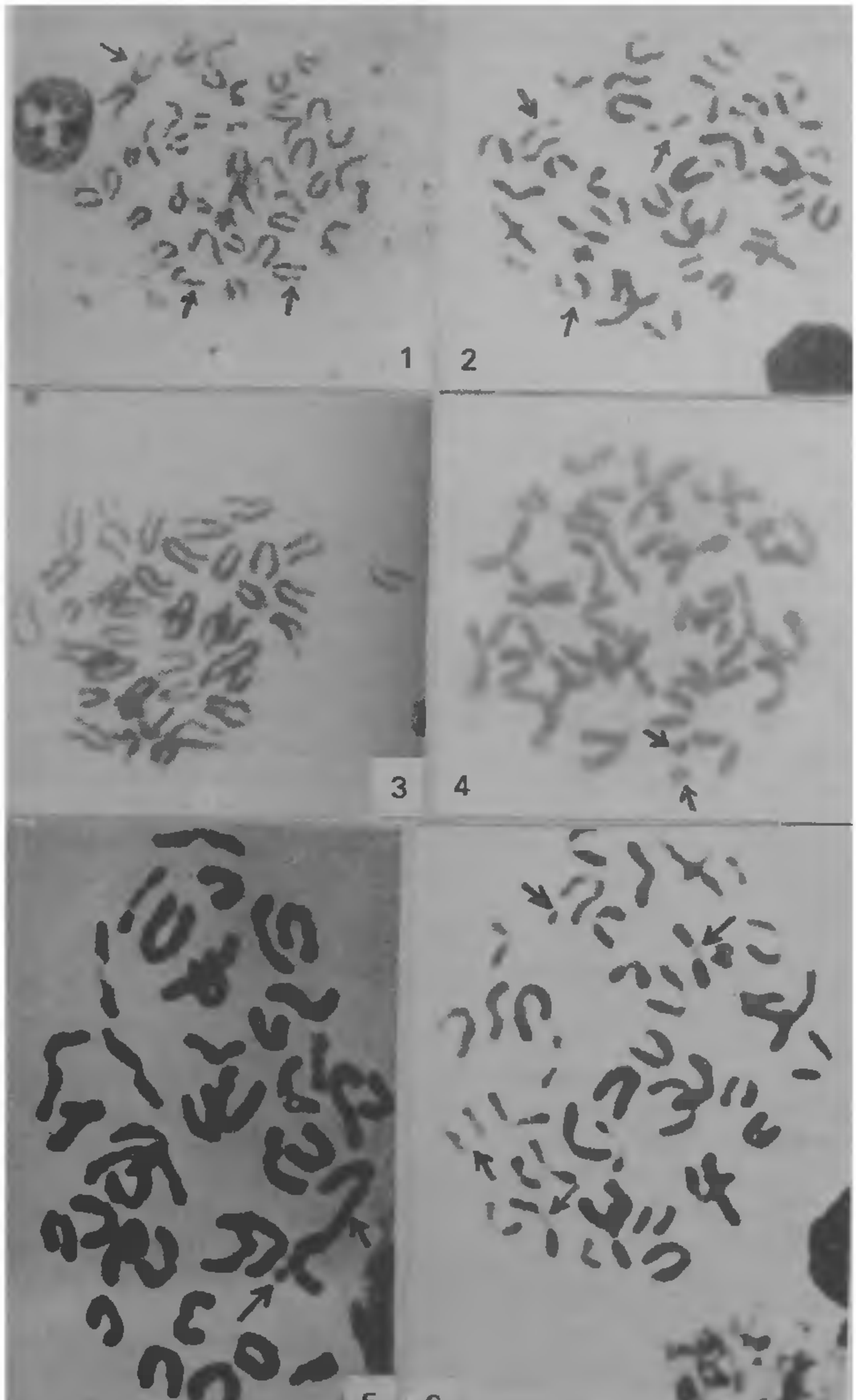
Considering the frequency of gaps and breaks, it is evident that a greater number of gaps is induced rather than breaks (table 2).

The combined distribution of gap and break points obtained from all the treatments in bone-marrow cells was analysed to determine the localized effects produced by the chemical. The chromatid arms were divided into three distinct regions viz proximal, middle and distal. The total chromosomal complement was divided into 5 groups according to the size[21] and these groups were further arranged into 3 different sizes to evaluate the frequency of gaps and breaks in respective sizes. Results (table 2) indicate that the distal end of long-sized chromosomes is comparatively more susceptible to nickel chloride. Considering the initial action on the protein moiety of the chromatids, it is clear that the distribution of gaps is greater than breaks irrespective of the dose and hour of treatment (tables 1–3). Also, larger size chromosomes are more affected to gaps and breaks (table 3). Statistical evaluation by '*t*-test' shows that aberrations induced by all the acute doses differ significantly from the control (table 1).

## DISCUSSION

It is clear that a number of metallic salts are potential chromosome-breaking materials[22]. It is also apparent that the distribution of gaps and breaks is non-random. Since the distal portion of the mouse

chromosomes is weaker in nature[23], any disturbance could lead to a break in these places more often than any other part of the chromosomes. This is because those points are broken when treated with chemicals of different nature having other specific type of action.




**Figures 1–6. 1.** Chromatid gap during 6 hr with 12 mg/kg; **2.** Centromeric stretching and chromatid break during 24 hr with 6 mg/kg; **3.** Chromatid break (single terminal) during 48 hr with 12 mg/kg; **4.** Chromatid breaks (double terminal) during 24 hr with 24 mg/kg; **5.** Chromatid exchange during 120 hr with chronic treatment; and **6.** Centromeric stretching and fission during 48 hr 12 mg/kg.

**Table 1** *Frequency of chromosomal aberration in bone-marrow cells of mice induced by Nickel chloride treated intraperitoneally*

| Dose mg/kg | Exposure time (hr) | No. of cells studied | Chromatid | | Fragment | Exchange | Centromeric fission | Total | % of Aberration ± S.E. | *t*-value |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Gap | Break | | | | | | |
| 6 | 6 | 300 | 3 | 2 | 1 | 1 | – | 7 | 2.33 ± 0.32 | |
| | 24 | 300 | 6 | 4 | – | – | – | 10 | 3.33 ± 0.32 | 6.11* |
| | | | | | | | | | 2.66 ± 0.32 | |
| 12 | 6 | 300 | 5 | 3 | – | 1 | – | 9 | 3.00 ± 0.57 | |
| | 24 | 300 | 7 | 4 | 2 | – | – | 13 | 4.33 ± 0.66 | 7.03* |
| | 48 | 300 | 6 | 3 | – | 1 | 1 | 11 | 3.66 ± 0.32 | |
| 24 | 6 | 300 | 5 | 3 | – | – | – | 8 | 2.66 ± 0.32 | |
| | 24 | 300 | 7 | 4 | – | – | 1 | 12 | 4.00 ± 0.99 | 6.25* |
| | 48 | 300 | 5 | 4 | 1 | – | – | 10 | 3.33 ± 0.57 | |
| Chronic 5 × 4.8 | 120 | 300 | 5 | 4 | 2 | 2 | 1 | 14 | 4.66 ± 0.87 | |
| Control (pooled) | | 900 | 4 | 2 | – | – | – | 6 | 0.66 ± 0.57 | |

*$P < 0.01$ (significant at 0.01% level); *$P$ - calculated from $t$-table).

**Table 2** *Region-wise frequency distribution of gaps and breaks*

| Region of the chromosomes | Nature of aberration | |
|---|---|---|
| | Gap | Break |
| Proximal | 4 | 3 |
| Middle | 31 | 9 |
| Distal | 19 | 22 |

**Table 3** *Size-wise frequency distribution of gaps and breaks*

| Size of the chromosome according to length | No. of chromosomes | Nature of aberration | |
|---|---|---|---|
| | | Gap | Break |
| Long size | 6 pairs | 36 | 19 |
| Medium size | 10 pairs | 13 | 11 |
| short size | 4 pairs | 5 | 4 |

As to the mechanism of chromosomal aberration induced by nickel chloride, it can be envisaged that nickel chloride dissociated in solution could induce a change in the ionic environment of the cell. A change in ionic environment may affect the chromosome structure[24].

The higher frequency of aberrations with chronic treatments could also be due to prolonged change in the ionic environment. In single administration, the metabolism of the chemical could lead to an early recovery in the ionic balance. One line of approach[25] states that internal factors, rather than external, cause spontaneous breakage and a difference in the metabolic set-up in immature tissues causes spontaneous mutation.

The author is grateful to Dr S. P. Bhunya for guidance.

31 January 1987; Revised 11 August 1987

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# ANNOUNCEMENTS

## SECOND NATIONAL SYMPOSIUM ON RECENT DEVELOPMENTS IN APPLIED ANALYTICAL CHEMISTRY

On the occasion of the Diamond Jubilee Celebration of the Institution of Chemists (India), the above symposium will be held during February 13–14, 1988 at the Indian Institution of Chemical Biology (CSIR) Calcutta. Last date for submission of Abstracts of papers on recent developments in analysis of minerals, silicates, foods, drugs, water, sewage and effluent, biochemicals, oils, soaps, fuels, gases, soils, fertilizers, forensic materials, leathers, textiles, environmental materials, radio-isotopes, etc. is 1st December 1987 and last date for becoming a Delegate is 15 December 1987 (Late Delegate—6 February 1988). Details and registration forms may be had by writing to the Hony. Secretary, Institution of Chemists (India), 11/4 Dr Biresh Guha Road, Calcutta 700 017.

## INTERNATIONAL SYMPOSIUM ON RECENT ADVANCES IN MALE REPRODUCTION

The above Symposium is organised by the University of Hyderabad in association with the Indian Society of Andrology during July 12–14, 1988 at Hyderabad.

The main topics of the Symposium are: 1. Inhibin — basic aspects and molecular biology of Inhibin, 2. Maturation of spermatozoa, 3. Androgen binding protein — new developments, 4. Role of new peptides in testis function, 5. Methods for the regulation of fertility — including immunological aspects, 6. New developments in the mechanism of action of androgens, 7. Regulation of steroidogenesis in testis.

Any one interested in participating in the Symposium is requested to contact the secretariat. Abstracts (200 words) for free communications along with registration fee must reach by 31 January 1988. The list of speakers will be given in the second circular.

Further information may be had from: Prof. P. R. K. Reddy, School of Life Sciences, University of Hyderabad, Hyderabad 500 134.