Digital malformations in the mouse foetus caused by X-radiation during pregnancy

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WITH THREE PLATES

INTRODUCTION

Many investigators have reported experimental malformations caused by different kinds of extrinsic factors acting upon the maternal animal during pregnancy and affecting various parts of the mammalian foetus, but few have described digital malformations in detail. In the author's experiments, digits in mice embryos and foetuses were studied after X-radiation of their mothers during pregnancy. The present paper will deal with:

(a) The relationship between the timing of X-radiation and the incidence of its resulting malformations.
(b) The relationship between dose and the frequency of the malformation, shown by an experiment carried out on the 12th day of pregnancy.
(c) The differences between the ddN- and the CF1-strains.
(d) The development of the digital malformations following irradiation.

MATERIALS AND METHODS

The animals used were mice of the ddN- and the CF1-strain, originally supplied by the Jikkendobutsu Chuo Kenkyujo, 90 days or older and weighing from 22 to 24 g. and kept at a room temperature of about 22–23°C. and 50–60 per cent. humidity. In each case one oestrous female was kept overnight in a cage with a potent male. The next morning the females found with vaginal plugs were considered to be in the 1st day of pregnancy.

For the X-radiation, a therapeutic X-ray machine was used. The beam was produced by the factors; 170 KVP, 10 mA., 40 cm., the filter being 0·5 mm. Al+0·5 mm. Cu, 16 r./min. Six groups of the ddN-strain were exposed to a

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single, whole body X-radiation of 200 r., each group on a different day of pregnancy from the 8th day on.

After killing the mothers on the 19th day of pregnancy, the foetuses were removed and their digits were examined under a low-power microscope. Their ossified skeletal system was then studied after being cleared according to the Dawson method, i.e. clearing tissues with 1 per cent. potassium hydroxide solution and staining the bone with alizarin red S solution. In order to study the cartilages and joints, some major malformations and some suspected ones were examined in serial sections stained with haematoxylin and eosin after being fixed in Bouin's fluid and embedded in paraffin, and others were examined according to Noback's modification of van Wijhe's method (Grüneberg, 1953), i.e. staining the cartilage with methylene blue and clearing the tissues with methyl salicylate.

In another series of experiments, mice of the ddN-strain were exposed to a single, whole body dose of 150 r. or 300 r. to examine the effects of X-ray doses and the results were compared with those treated with 200 r. irradiation. In addition, mice of the CF₁-strain were exposed to a single, whole-body dose on the 12th day of pregnancy to examine the difference between the two strains in their tendency to abnormalities. The results were compared with those from the ddN-mice under similar conditions.

In studying the development of digital malformations foetal and embryonic digits of the ddN-strain were observed externally and microscopically 2, 6, 12, 18, 24, 48 and 72 hr. after X-radiation on the 12th day. After that, they were examined at 1-day intervals until the 19th day of foetal life.

Many terms have traditionally been used to designate digital malformations, although their classification has not yet been established. Moreover, it is difficult to classify the malformations, because foetal bones are not well ossified. Therefore, a detailed classification is avoided in this study.

For example, absence of a part of the digit is termed 'partial ectrodactylism', and it may also be called 'perodactylism' or correspond to the so-called 'spontaneous amputation'. 'Complete ectrodactylism' means 'oligodactylism', but in some cases the ossification of metacarpal or metatarsal bone of the corresponding missing digit may be present or in other cases it is absent. When a digit

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**PLATE 1**

**Ectrodactylism**

Fig. 1. Transitional forms from normal to the 2nd finger missing (19th-day stage, alizarin clearance preparations).

Fig. 2. Developmental process of the 2nd finger missing. Histologic findings. (a) A parallel section to the palmar plane of the right hand plate 24 hr. after 200 r. X-radiation (13th-day stage). The mesenchymal condensation to form the 2nd digital ray is completely absent and the pyknotic nuclei are almost eliminated. (b) 15th-day stage. (c) 17th-day stage. (d) 19th-day stage. The phalanges of the 2nd finger are completely absent. The distal portion of the 2nd metacarpal deviates to radial side and fuses with the 1st metacarpal.
PLATE 1

HIROSHI NOGAMI

(Facing page 638)
is under two-thirds of a normal digit in length, it is called 'brachydactylysm', and a case with completely webbed digits is called 'syndactylysm'. Besides, in this paper, those digits, being both short and webbed, are first distinguished under 'brachydactylysm' and secondly under 'syndactylysm' instead of being called 'brachysyndactylysm'. Some malformed digits which seemed to be 'clindodactylysm' were also observed but they are not included in this classification.

RESULTS

(a) The relationship between the timing of X-radiation and the incidence of corresponding malformations. Malformations of foetal digits clearly showed the highest incidence in the group that was exposed on the 12th day of pregnancy, and most of these malformations were bilateral. The incidence of malformation was much lower in the group treated on the 11th day of pregnancy than in the group treated on the 12th day. In the group treated on the 13th day, the incidence of malformations produced was lower than in the group treated on the 11th day and, moreover, the malformations were all unilateral. Furthermore, all digital malformations found in the group treated on the 13th day were syndactylysm and none of them had fusion of the bone.

Most digital malformations were of the reduction type, i.e. partial and complete ectrodactylisms and the predominant sites were in the 2nd and the 3rd digits.

Polydactylysm and the pedunculated, or the so-called 'floating', digit were detected only in toes. The predominant site of polydactylysm was the 1st toe and that of the pedunculated digit was the 5th toe. It was noticed that malformation manifested itself also in various transitional forms.

There were nine cases of unilateral malformations in the finger on the left side and three cases on the right side, and in the toe there were twenty cases on the left side and twenty-one cases on the right side. The foetuses with malformations of both fingers and toes in each individual were relatively few in number (Table 1).

(b) The relationship between X-ray doses and the frequency of malformations. The results of experiments in which three groups were exposed to X-radiation of 150 r., 200 r. or 300 r. on the 12th day of pregnancy showed that the number

PLATE 2

Polydactylysm

Fig. 3. Reduplication of the 1st toe in the methylene blue clearance preparation on the 19th-day stage. It is the most common type of polydactylysm produced.

Fig. 4. Several cases of polydactylysm manifested in the foot plate on the 14th-day stage.

Fig. 5. A parallel section to the plantar plane of the left foot plate 24 hr. after 200 r. X-radiation, showing the reduplicated 2nd digital ray (13th-day stage).

Fig. 6. Reduplication of the 2nd digital ray on the 14th-day stage.

Fig. 7. The bifid 2nd metatarsal of the left foot on the 19th-day stage.
### Table 1

The relationship between the timing of X-radiation and resulting malformations

<table>
<thead>
<tr>
<th>Day of pregnancy when treated</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>Control</th>
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<td>200 r.</td>
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<td>200 r.</td>
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<td>No. of mice treated</td>
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<td>20</td>
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<td>No. of foetuses examined</td>
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<td>155</td>
<td>162</td>
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<th>Foetuses with finger malformations—Total</th>
<th>8 (6·4%)</th>
<th>113 (81·9%)</th>
<th>5 (3·0%)</th>
<th>0</th>
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<tr>
<td>Bilateral</td>
<td>4</td>
<td>110</td>
<td>0</td>
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</tr>
<tr>
<td>Unilateral</td>
<td>4 (1-3, r-1)</td>
<td>3 (1-3, r-0)</td>
<td>5 (1-3, r-2)</td>
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<td>241</td>
<td>0</td>
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<tr>
<td>Partial</td>
<td>2</td>
<td>30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete</td>
<td>14</td>
<td>211</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brachydactylism</td>
<td>0</td>
<td>49</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Syndactylism</td>
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<td>28</td>
<td>5</td>
<td></td>
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<table>
<thead>
<tr>
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<th>14 (11·2%)</th>
<th>51 (37·0%)</th>
<th>7 (4·5%)</th>
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<tr>
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<td>0</td>
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</tr>
<tr>
<td>Unilateral</td>
<td>11 (1-4, r-7)</td>
<td>23 (1-12, r-11)</td>
<td>7 (1-4, r-3)</td>
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<th>Toe malformations</th>
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<td>90</td>
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<tr>
<td>Partial</td>
<td>6</td>
<td>32</td>
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<td></td>
</tr>
<tr>
<td>Complete</td>
<td>7</td>
<td>58</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brachydactylism</td>
<td>0</td>
<td>16</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Syndactylism</td>
<td>1</td>
<td>8</td>
<td>7</td>
<td></td>
</tr>
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<td>Polydactylism</td>
<td>12</td>
<td>9</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Pedunculated digits</td>
<td>0</td>
<td>8</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

| Foetuses with malformations of both fingers and toes—Total | 4(2·4%) | 47 (34·1%) | 0       |         |

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**Plate 3**

**The pedunculated digit**

**Fig. 8.** The pedunculated 5th toe on the 15th-day stage.

**Fig. 9.** Complete ectrodactylism of the 5th toe on the 15th-day stage.

**Fig. 10.** A transitional form between complete ectrodactylism and the pedunculated digit on the 15th-day stage. Note the rudimentary 5th toe.

**Fig. 11.** The pedunculated 5th toe on the 19th-day stage.

**Fig. 12.** A parallel section to the plantar plane of the 5th toe with pedicle formation. 15th-day stage.

**Fig. 13.** The boxed-in area of Fig. 12. Precartilaginous union is absent at the pedunculated region. There remain traces of the damage in the precartilage concentration.

**Fig. 14.** A parallel section to the plantar plane of the 5th toe missing on the 15th-day stage.

**Fig. 15.** The boxed-in area of Fig. 14. Rudimentary precartilage concentration is observed.

**Fig. 16.** A section of the pedunculated 5th toe on the 19th-day stage. There is no osseous or cartilaginous union in the pedicle.

**Fig. 17.** Ossified terminal phalange, cartilaginous middle and a part of basal phalanges are usually present in the distal portion on the 19th-day stage.
of digital reductions was proportional to the dose, but the tendency to reduction was different for each digit. The 2nd finger was most susceptible to X-ray damage, while the 4th finger was most resistant to it. The order of susceptibility of the other fingers was the 3rd finger, the 5th finger, the 1st finger. In a few cases the 3rd finger was most susceptible and the 2nd finger was next. The
The relationship between X-ray doses and malformations manifested

<table>
<thead>
<tr>
<th>X-ray dose</th>
<th>150 r.</th>
<th>200 r.</th>
<th>300 r.</th>
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<tbody>
<tr>
<td>Day of pregnancy when treated</td>
<td>12</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>No. of mice treated</td>
<td>20</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>No. of foetuses examined</td>
<td>150</td>
<td>138</td>
<td>81</td>
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<tr>
<td>Foetuses with finger malformations—Total</td>
<td>36 (24·0%)</td>
<td>113 (81·9%)</td>
<td>78 (96·3%)</td>
</tr>
<tr>
<td>Bilateral</td>
<td>32</td>
<td>110</td>
<td>78</td>
</tr>
<tr>
<td>Unilateral</td>
<td>4 (l-3, r-1)</td>
<td>3 (l-3, r-0)</td>
<td>0</td>
</tr>
<tr>
<td>Finger malformations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ectrodactylism</td>
<td>19</td>
<td>241</td>
<td>294</td>
</tr>
<tr>
<td>Partial</td>
<td>6</td>
<td>30</td>
<td>57</td>
</tr>
<tr>
<td>Complete</td>
<td>13</td>
<td>211</td>
<td>237</td>
</tr>
<tr>
<td>Brachydactylism</td>
<td>47</td>
<td>49</td>
<td>7</td>
</tr>
<tr>
<td>Syndactylism</td>
<td>23</td>
<td>28</td>
<td>4</td>
</tr>
<tr>
<td>Foetuses with toe malformations—Total</td>
<td>10 (6·7%)</td>
<td>51 (37·0%)</td>
<td>78 (96·3%)</td>
</tr>
<tr>
<td>Bilateral</td>
<td>6</td>
<td>28</td>
<td>71</td>
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<tr>
<td>Unilateral</td>
<td>4 (l-2, r-2)</td>
<td>23 (l-12, r-11)</td>
<td>7 (l-3, r-4)</td>
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<tr>
<td>Toe malformations</td>
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<tr>
<td>Ectrodactylism</td>
<td>10</td>
<td>90</td>
<td>339</td>
</tr>
<tr>
<td>Partial</td>
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<td>32</td>
<td>74</td>
</tr>
<tr>
<td>Complete</td>
<td>7</td>
<td>58</td>
<td>265</td>
</tr>
<tr>
<td>Brachydactylism</td>
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<td>16</td>
<td>3</td>
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<tr>
<td>Syndactylism</td>
<td>5</td>
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<td>7</td>
</tr>
<tr>
<td>Polydactylism</td>
<td>2</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Pedunculated digits</td>
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<td>8</td>
<td>6</td>
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<tr>
<td>Foetuses with malformations of both fingers and toes—Total</td>
<td>8 (5·3%)</td>
<td>47 (34·1%)</td>
<td>75 (92·6%)</td>
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</table>

The incidence of individuals with bilateral malformations in fingers or toes and digital malformations both in the fore- and hind-limbs was proportional to X-ray doses employed (Table 2). A similar tendency was also observed in the incidence of foetuses whose conditions in the stage of the ossification or the form of the ossification in the skeleton between digits on the right and left side in one individual were not parallel.

(c) Strain differences between the ddN- and the CF1-mice under similar conditions. The differences in the tendency to manifest digital abnormalities between the ddN- and the CF1-strain were clear. Digital malformations vary in total
Digital malformations in the mouse foetus

TABLE 3

The strain differences between the ddN- and the CF1-mice

<table>
<thead>
<tr>
<th>Strain</th>
<th>ddN</th>
<th>CF1</th>
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<tr>
<td>Day of pregnancy when treated</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>X-ray dose</td>
<td>200 r.</td>
<td>200 r.</td>
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<tr>
<td>No. of mice treated</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>No. of foetuses examined</td>
<td>138</td>
<td>186</td>
</tr>
</tbody>
</table>

Foetuses with finger malformations—Total
- Bilateral: 110
- Unilateral: 3 (l-3, r-4)

Finger malformations
- Ectrodactylism: 241
  - Partial: 30
  - Complete: 211
- Brachydactylism: 49
- Syndactylism: 28

Foetuses with toe malformations—Total
- Bilateral: 28
- Unilateral: 23 (l-12, r-11)

Toe malformations
- Ectrodactylism: 90
  - Partial: 32
  - Complete: 58
- Brachydactylism: 16
- Syndactylism: 8
- Polydactylism: 9
- Pedunculated digits: 8

Foetuses with malformations of both fingers and toes—Total
- Bilateral: 47 (34.1%)
- Unilateral: 53 (28.5%)

number and even in kind in the two strains treated under similar experimental conditions (Table 3, Text-fig. 3).

(d) The development of digital malformations in the embryo and foetus following irradiation. No digital ray could be observed externally in the hand or foot plate in the early hours of the 12th day of foetal age. Localized foci of cellular necrosis, causing digital malformations, were already evident in the primordia of the digital bud 2 hr. after X-radiation on the 12th day and such necrotic cells were detectable in profusion after 6 hr. The pyknotic nuclei were almost eliminated but the concentration of the precartilage primordia to form a digital ray became
abnormal 24 hr. after X-radiation. The prospective pattern of digital malforma-
tion could already be detected externally before the cleft between digits was
marked, i.e. by the developmental stage 24 hr. after X-radiation.

![Graph showing incidence of abnormalities in each digit.]

**DISCUSSION**

The critical stage for digital malformations in mice of the ddN-strain is found
to be at the beginning of the 12th day of foetal life. The critical stage for syndactyl-
ism seems to be somewhat later and polydactylism involving the 1st toe somewhat
earlier.

Russell (1950, 1954) stated that digital malformations in the mouse foetus had
a peak in sensitivity to X-radiation of 200 r. on day 11½, which corresponds to the
Digital malformations in the mouse foetus

12th day in the present work. Neifach (1960) also reported that the periods of greater sensitivity were between the 11th and the 12th days when mice embryos were exposed to X-rays.

In genetic studies on digital malformations in the mouse, Bagg (1929) reported that abnormalities were detectable between days 12 and 13, while Grüneberg (1960, 1961, 1962) stated that oligosyndactylism was detectable in the 11-day stage as reduction of foot plate and syndactylism in the 12- or 12\(\frac{1}{2}\)-day stage.

These results suggest that the timing of gene action in a hereditary abnormality can be estimated by producing a similar abnormality by extrinsic factors. Another example is exencephalia in mice (Murakami & Katsunuma, 1955).

Asling, Nelson, Wright & Evans (1955), who considered that the manifestation of abnormalities depended on the stage at which the disturbance occurred rather than on the specific disturbing agent, based this conclusion on their experiments producing skeletal abnormalities in foetal rats by a maternal nutritional deficiency. On the other hand, Nishimura (1959), who subjected pregnant mice to a number of injurious chemical agents, reported that the critical stage for certain skeletal malformations differed according to the agent employed.

In an experiment inducing skeletal malformations in the mouse foetus of the ddN-strain by maternal hypoxia during pregnancy, Murakami, Kameyama & Nogami (1962) found that digital malformations were produced in the group treated between days 10 and 11, especially in the 10-day group, but not in the 12-day group.

These reports suggest that the critical stage for malformations differs with the kind of extrinsic agent employed. But the question of whether an injurious extrinsic agent affects the primordia directly or indirectly cannot be disregarded.

It is noticed that ectrodactyly increases remarkably in proportion to X-ray dose, while the incidence of brachydactyly and syndactyly decreases in malformed digits.

Such findings suggest that a lower dose generally produces brachy- and syndactyly, while a higher dose usually causes ectrodactyly (Text-fig. 4). Brachydactyly and syndactyly seem to be due to the lesion not so severe as to induce ectrodactyly.

It may be presumed that ectrodactyly is produced by a disturbance of formation or differentiation of the digital ray, and partial or complete missing of the digit will depend upon the extent of damage in the digital bud.

Streeter (1930) found that intra-uterine amputations were not due to constricting bands, but were due to focal deficiencies in the foetal tissues. He believed these to be due to an abnormal constitution of the germ plasm, but in the author’s experiments, the extrinsic factors that impair the embryos can also cause such changes.

Polydactyly and the pedunculated digit occur only in toes and they often occur in conjunction with ectrodactyly in the same foot. It seems that their bifid or constricted digital ray is due to the reproductive activity of the digital
primordia after being partially arrested in development at the apical or the circumscribed areas of the digital bud tissues.

There is a great deal of variation in the extent of these digital malformations. They manifested themselves also in various transitional forms. The results described above may suggest the difficulty of classification of digital malformations.

The tendency to reduction was different for each digit and the 4th digit was most resistant to X-ray damage. Forsthoefel (1963) found that this is the first digit to be laid down. These results present one of the interesting aspects of the

![TEXT-FIG. 4. Relationship between X-ray doses and finger malformations (ddN strain).](image)

relationship between developmental progression and the sensitivity of each digit.

Kalter & Warkany (1957) reported that incidence and kind of abnormalities varied with the genetic constitution of animals involved. Besides, in the author's experiments, tendency to manifest special malformations seems to be varied in
each individual even in the same strain. The relationship between genetic constitution and individual sensitivity for teratogenic environmental agents is worth study.

Warkany & Nelson (1942) and Warkany, Nelson & Schraffenberger (1943) stated that skeletal malformations caused in rats by maternal nutritional deficiency were induced during the cartilaginous or precartilaginous stage. Grüneberg (1953) concluded that the abnormalities of the skeleton of ch/ch mice were preceded by abnormalities of the mesenchymal condensations and the cartilage and the bone were only secondarily involved.

It was observed by Hicks, Brown & D’Amto (1957) that the mesenchymal tissues in the limb bud were severely damaged by X-radiation. Neifach (1960) reported that the mechanism of reduction of digits in mouse embryos following X-ray irradiation might be explained by the selective damage of definite areas of the limb anlage.

Murakami, Kameyama & Nogami (1963) believed manifestation of digital malformations in the mouse foetus caused by X-radiation depended primarily on cellular necrosis in the digital primordia on the 12th day of developmental stage. The pattern of digital malformations seems to be determined according to the region and degree of such necrotic changes. A digital bud with vaguely outlined precartilage concentrations of the mesenchyme is about to be represented in the hand and foot plates at this special period.

It might correspond to the stage in human embryo from the end of the 4th week to the beginning of the 5th week (Otis & Brent, 1954).

But the mechanism forming digital malformations does not usually depend primarily on such necrotic changes. Hereditary abnormalities of digits in the mouse (Bagg, 1929), resulting from the X-ray mutation, were caused by a blister-like bleb in the epithelium of the foot plate which interfered with the further digital differentiation.

However, it is noteworthy that the causes of digital malformations need not necessarily be a primary lesion of the primordium itself for polydactyly involving the first toe was detected in the group treated on the 8th-day stage. This indicates that it was induced by disturbance in development of some embryonic region before the appearance of the primordia. Russell (1954) also described such a case. This suggests an effect—indirect or inductive—on the cells ancestral to the digits.

SUMMARY

1. Six groups of mice of the ddN-strain were exposed to a single, whole body X-radiation of 200 r. on the different days between the 8th and the 13th day of pregnancy. Others were exposed to 150 r. or 300 r. on the 12th day of pregnancy. Mice of the CF1-strain were also exposed to 200 r. on the 12th day of pregnancy. Embryonic and foetal digits were examined both externally and microscopically 2, 6, 12, 18, 24, 48 and 72 hr. after X-radiation. After that they were examined
at 1-day intervals until the 19th day of foetal age. Their ossified skeleton was studied by the Dawson method and their cartilaginous one was studied by Noback’s modification of van Wijhe’s method.

2. The critical stage for digital malformations in the ddN-mouse was presumed to be in the beginning of the 12th day of embryonic stage. Digital rays with precartilage concentrations of the mesenchyme became obvious at this period.

3. The incidence of digital malformations was proportional to the X-ray dose employed. Most malformations were of the reduction type, i.e. partial or complete ectrodactyly.

4. The number of digits missing was proportional to the X-ray dose. The 2nd and the 3rd digits were most susceptible, while the 4th digit was most resistant. It was noticed that each malformation manifested itself also in various transitional forms.

5. Differences between the ddN- and the CF1-strain in their tendency to manifest digital abnormalities were observed.

6. Localized foci of cellular necrosis were already evident in the primordia of the digital bud 2 hr. after X-radiation and the pyknotic nuclei were almost eliminated after 24 hr.

7. The prospective pattern of malformations could already be detected externally before the cleft between the digits became marked.

RÉSUMÉ

Malformations digitales provoquées sur le foetus de souris par les rayons X pendant la gestation

1. Six groupes de souris de la lignée ddN ont été exposés à une seule irradiation totale de 200 r., aux rayons X, intervenant entre les 8e et 13e jours de la gestation. D’autres ont été exposés à des doses de 150 ou 300 r. le 12e jour de la gestation. Des souris de la lignée CF1 ont aussi été exposées à une dose de 200 r. le 12e jour de la gestation.

Les doigts des embryons et des foetus ont été examinés à la fois extérieurement et microscopiquement 2, 6, 12, 18, 24, 48 et 72 h. après l’irradiation. Ils ont été ensuite examinés à intervalles d’une journée jusqu’au 19e jour de la gestation. Leur squelette osseux a été étudié par la méthode de Dawson et leur squelette cartilagineux à l’aide de la modification de Noback de la méthode de Van Wijhe.

2. On a pensé que le stade critique pour les malformations digitales de la souris ddN se trouvait au début du 12e jour de l’âge embryonnaire. Des rayons digitaux avec des concentrations précartilagineuses du mésenchyme deviennent visibles à cette époque.

3. La présence de malformations digitales a été proportionnelle à la dose de rayons X employée. La plupart des malformations étaient du type ‘réductionnel’, c’est-à-dire ectrodactylyme partiel ou complet.

4. Le nombre de doigts manquants a été proportionnel à la dose de rayons
Digital malformations in the mouse foetus

X. Les 2ème et 3ème doigts étaient les plus sensibles, tandis que le 4e était le plus résistant. On a noté que chaque malformation se manifestait aussi sous diverses formes de transition.

5. On a observé des différences entre les lignées ddN et CF₁ quant à leur tendance à manifester des anomalies digitales.


7. L’allure présomptive des malformations pouvait déjà être décelée extérieurement avant que la fissuration entre les doigts ne devienne marquée.

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REFERENCES


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