animals were removed to cold only 15 min after the injection the mortality figures decreased significantly ($p < 0.05$). The mortality levels of 2 control groups showed that 5% had died before 15 min, 21% before 18 min, 37% before 20 min, 53% before 25 min and 74% before 30 min after the injection. Thus it seemed that if an intoxicated mouse was taken into cold a few min before it would otherwise die, it could survive.

The effect of diazepam and practolol on the toxicity of fenfluramine is described in Table II. It can be seen that a diazepam dose of only 0.2 mg/kg decreased the toxicity of fenfluramine significantly ($p < 0.01$). Practolol, on the other hand, had a less important effect. Only a very high practolol dose (5 mg/kg) could decrease the toxicity of fenfluramine. Neither the practolol nor the diazepam dose of 0.2 mg/kg had a clearly noticeable effect on the behaviour phenomena caused by fenfluramine. A diazepam dose of 0.5 mg/kg slightly decreased the convulsions and the jumping attacks. A diazepam dose of 2 mg/kg abolished the convulsions and motor activity.

Discussion. The results established indicate that cold treatment efficiently decreases the fenfluramine toxicity in mice. According to YEHUDA and WURTMAN[7], the toxic fenfluramine dose (50 mg/kg i.p.) raises the rat's temperature at room temperature but causes a 7–8 degrees' (°C) sudden fall at a temperature of 4 °C. It is unclear whether a mere decrease in temperature, or any secondary change caused by it, protects smaller mammals against the toxicity of fenfluramine. It is quite possible that cold treatment in fenfluramine poisoning decreases also man's and especially a child's temperature, or at least prevents it from rising dangerously high.

Only high doses of practolol decrease the toxicity of fenfluramine. Thus it may have no clinical use. On the other hand, diazepam doses, which are equal to human doses, decrease the toxicity of fenfluramine very efficiently. In these tests diazepam was administered after the fenfluramine injection but before the toxic symptoms appeared. These results suggest that diazepam and cold treatment given as early as possible decrease the toxicity of fenfluramine also in men and especially in children.

Zusammenfassung. Kaltbehandlung und i.v. Injektion von Diazepam reduzierten die Toxizität des Fenfluramins bei der Maus beträchtlich.

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Placental Transfer of Fluoride During Methoxyflurane Anaesthesia for Cesarean Section

After the discovery of the prophylactic action of systemic fluoride against dental caries, several studies on the placental transfer of this halide have been carried out. Placental transfer of fluoride has been shown to occur in animals and in humans[1–4]. It is known that the maternal fluoride concentration is dependant on the fluoride content of water and food[5,6]. It was also demonstrated that increased feeding of fluoride to animals and humans causes a rise of F^- concentration in maternal and fetal blood[7]. BAWDEN et al.[8], who administered radiofluoride (18 F) to pregnant ewes, found a relatively low fetal blood plasma radiofluoride level compared to the maternal concentration. ERICSSON and MALMNÖ[9] obtained similar results in their 18 F studies with rabbits as well as in women submitted to therapeutic abortions. However, ARMSTRONG[10] in a series of patients undergoing Cesarean section, found that the fluoride concentration in maternal and fetal blood were quite similar. This result was confirmed in a recent similar study by SHEN and TAVES[11].

The situation seems to be different in the presence of high maternal fluoride levels. For instance, GEDALIA[12] found that the cord fluoride values of babies, born in fluoridated areas, was consistently lower than the mother fluoride levels, whereas this was not the case when the mothers had not been submitted to fluoride supplements (water or tablets).

In a recent study, FRY and TAVES[13] reported on measurements of fluoride containing metabolites in maternal and cord blood associated with Methoxyflurane (MOF) analgesia during labor.

Already during anaesthesia, a metabolic break-down of MOF takes place[14]. This break-down into inorganic fluoride and an organic acid-labile fluoride, presumably methoxydifluoracetic acid, starts within 10 to 15 min after the administration of the anesthetic[13,15]. Thus, high fluoride blood concentrations can be demonstrated, presumably responsible for the observed nephrotoxicity after MOF anaesthesia[16]. FRY and TAVES[13] reported that during analgesia with MOF, the maternal serum inorganic

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Table I. Serum fluoride levels in mother and child after MOF anaesthesia

Case No.	Operating time (min)	F^- mother (mol/l)	F^- child (mol/l)
1	3	—	1.55
2	6	1.05	0.775
3	7	4.0	2.45
4	8	3.0	3.88
5	8	3.88	2.6
6	9	4.13	3.33
7	10	8.0	5.75
8	11	12.0	—
9	11	2.3	1.33
10	11	4.54	3.33
11	11	5.6	2.88
12	13	—	2.45
13	13	6.4	2.49
14	14	2.42	1.11
15	15	—	4.63
16	15	—	4.38
17	18	9.5	4.63
18	18	—	1.55
19	19	3.06	0.25
20	21	—	1.38
21	23	12	3.1

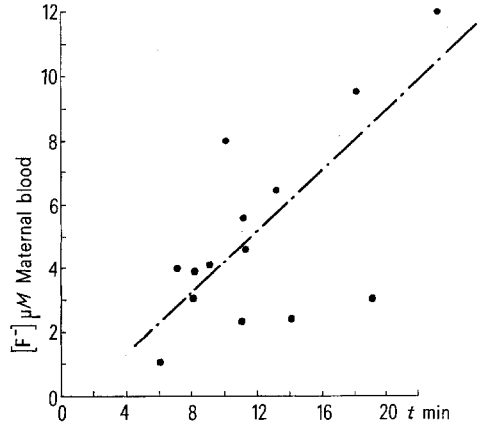

Fig. 1. Correlation between the maternal F^- concentrations and the time of anaesthesia till child birth ($r = 0.59$; $p < 0.02$).

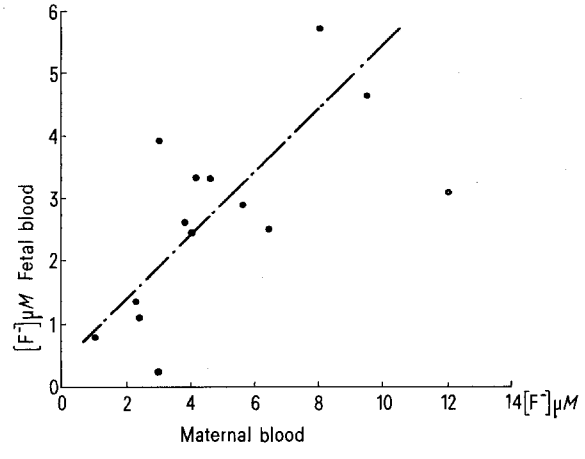

Fig. 2. Correlation between the maternal and fetal F^- concentration ($r = 0.77$; p 0.01).

fluoride rose 5- to 10-fold in the 10 to 15 min before delivery, but the cord blood showed less than 25% of that increase.

In our hospital, we use MOF, because of its high analgesic potency, already in the first part of anaesthesia for Cesarean section, i.e. until childbirth[17,18]. In view of the somewhat conflicting results reported above, it was of interest to study the placental transfer of inorganic serum fluoride produced in abundance by the break-down of MOF during general anaesthesia for Cesarean section: this was performed by simultaneous measuring of inorganic F^- in maternal arterial blood, in cord blood and, for the first time, in the urine of the newborn. In addition, the time sequence of the mother fluoride concentration during MOF anaesthesia was monitored.

Material and methods. 21 cases of Cesarean section were chosen at random from the daily routine. After premedication with 0.5 mg atropine and preoxygenation, anaesthesia was induced with thiopental 4 mg/kg on average not exceeding 250 mg in the total. Intubation was performed with 100 mg Succinylcholin for all patients and relaxation was continued with a drip of Succinylcholin until childbirth. Ventilation was carried out with a gas mixture of N_2O-O_2 at a rate of 8 l/min. To this gas flow 0.2 vol. % MOF were added and the patients manually ventilated. The time of induction as well as the time of childbirth were noted. The radial artery of the mother was canulated. At the moment of birth 10 ml arterial blood were drawn from the mother as well as blood between 2 clamps from the umbilical cord vein. Inorganic fluoride was estimated in the maternal and the cord blood by using a fluoride electrode (Orion). The first 12-h urines of the newborn were also collected for fluoride analysis.

Results. The time of anaesthesia lasted from 3 to 23 min, with an average of 12.25 min. A significant correlation ($r = 0.59$: $p < 0.02$) was found between the F^- concentration in the maternal arterial blood of the patients and the time of anaesthesia (Figure 1).

In cases where the anaesthesia had lasted only 10 min, the F^- concentration in the maternal blood sample was around 4 μmol/l; it reached values as high as 12 μmol/l when the anaesthesia lasted 20 min or more. Interestingly, the serum fluoride concentration in the umbilical vein of the newborn showed a similar trend and a positive significant correlation ($r = 0.77$: $p < 0.01$) was found between the fluoride levels in the maternal and the fetal blood (Figure 2).

However, as shown numericaly in Table I, it is important to point out that the fluoride concentration of the newborn blood was always about $^1/_2$ that of the maternal blood. In the first 12 h urines of the newborn no increased fluoride concentration could be found (Table II).

Discussion. Two different situations arise when considering the problem of F^- transfer through the placenta.

First, in the presence of low maternal F^- blood levels, most of the investigators agree that the placenta does not constitute a barrier to the passage of the halide[3,6,10]. The results of the investigation with 18 F^9 seem to contradict this statement. However, one must remember that in the radiofluoride studies the results have not been given in the form of fluoride specific activity, and could therefore not take into account the ion exchange taking place at different rates in the maternal and fetal skeleton.

Second, when mothers are exposed to high fluoride intake, a significant difference has generally been reported between the maternal and the fetal fluoride concentra-

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Table II. Maternal and fetal blood concentrations of F^- and urinary concentrations of the newborn after anaesthesia with methoxyflurane (in μM).

	F^- blood maternal	F^- blood fetal	F^- urines newborn	Time of anaesthesia (min)
Mean value	5.66 (15)	2.70 (20)	4.26 (20)	12.25 (21)
SD	3.91	1.45	3.20	5.23
$S\bar{x}$	1.01	0.325	0.775	1.16

Number of cases in parenthesis.

tions[13,19]. The findings of the present study support this observation, since the mean cord fluoride concentration in our 21 cases was $^1/_2$ that of the maternal blood. Further, the urine of the newborn did not contain any measurable amount of the halide. As previously postulated[12], two mechanisms could explain the difference between the levels of F^- in the mother and the baby: the uptake of the halide by the rapidly growing skeleton of the fetus and the uptake by the zones of calcification often found in the human placenta[20].

Finally, some consideration should be given to the problem of safety. As pointed out by FRY and TAVES[13], it would appear questionable to start using a new anaesthetic, when little is known about its metabolism. In this connection, it is somewhat reassuring to note that the present results confirm that, throughout anaesthesia, till extraction of the child, the cord fluoride values were well below those usually considered as dangerous[21]. Our mean fluoride value for the mothers (5.6 µmol/l) represents a very modest increase in F^- concentration and is much lower than those capable of impairing renal function[22,23].

Résumé. Le passage diaplacentaire de F^- libéré par le métabolisme du méthoxyflurane pendant l'anesthésie pour césarienne a été dosé dans le sang maternel et foetal. Le taux sanguin du cordon en F^- était la moitié du taux sanguin artériel de la mère à la naissance de l'enfant. On n'a pas trouvé un taux élevé en F^- dans les urines, du nouveau-né pendant les 12 premières heures de vie.

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Chromosome Damage Induced by Gentamicin in Mouse L-cells

Many mammalian cell cultures, growing in the presence of antibiotics, are frequently contaminated by mycoplasma[1,2]. Such unsuspected infections can be an important source of artefacts in many experiments and might therefore result in the misinterpretation of experimental results. Presence of mycoplasma can alter macromolecular synthesis, cellular morphology and growing rate of cell-cultures, and was also shown to induce chromosomal aberrations and to modify sensitivity to viruses and drugs[2]. In studies performed in our laboratory[3] on the physico-chemical properties of virions (L-cell virus) produced by different L-cell sublines, such contamination was found to depress the amount of uridine-^{3}H-labelled L-cell virus and to cause a degradation of viral RNA to low-molecular weight species.

Several methods have been recommanded to eradicate mycoplasma contamination from tissue cultures. They include[1,2,4] heating treatment or the use of specific antisera, chemical compounds or antibiotics such as kanamycin, tetracyclines, tylosin, erythromycin or lyncomycin. Recently gentamicin, a broadspectrum antibiotic derived from *Micromonospora purpurea*, has been reported[5] to be very effective against several species of mycoplasma and to allow elimination of such contaminations. Since many antibiotics are known[6] to induce chromosome aberrations in cell cultures, treatment with gentamicin was now studied for such effects.

Material and methods. The effects of gentamicin were studied on a L-cell strain maintained in our laboratory for electron microscopic and physicochemical studies on L-cell virions. The karyological characteristics of this L-cell strain, published elsewhere[7], can be summarized as follows: the average number of chromosomes is around 60 including 17 non-acrocentric chromosomes. There is no statistically significant correlation between the total number of chromosomes per cell and the number of non-acrocentric chromosomes.

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