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# THE INOSITOL CONTENT OF FOETAL BLOOD AND FOETAL FLUIDS

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Inositol is a hexahydroxy*cyclo*hexane and is one of the family of nine isomers. *Meso*-inositol $\left(\text{the } \frac{1\ 2\ 3\ 5}{4\ 6} \text{ isomer}\right)$ would appear to be the predominant isomer met with both in the plant and animal kingdoms, and in this paper inositol will refer to the *meso*-isomer in all cases. In nature it exists in both a free and a combined form (the chief combined form being phosphatides and phytin) from which the free inositol may be liberated by acid hydrolysis for 6 hr with 50%, v/v, HCl (Platt & Glock, 1943), and the resulting inositol estimated as the free substance. The previously determined free inositol subtracted from the value found after hydrolysis (total inositol) gives the combined inositol.

The presence of inositol in foetal blood was first indicated by Offergeld (1906) using a polarimetric method of detection. He found that whereas inositol was present in the human foetal blood it was absent in that of the mother and suggested that its origin was by foetal synthesis. Partridge (1948), using paper chromatography, demonstrated the presence of inositol in a pooled sample of foetal sheep blood; Bacon & Partridge (personal communication) estimated that the sample contained 27 mg/100 ml. of blood.

In the present work investigations have been carried out on the occurrence of free inositol in the maternal and foetal blood and the allantoic and amniotic fluids of several mammalian species in an attempt to ascertain whether there is a correlation of inositol concentration with foetal age, and to obtain further evidence of the suggested foetal synthesis. A preliminary account of these findings has been given by Nixon (1952).

## METHODS

*Inositol determination*

All samples were estimated for inositol by a microbiological technique involving the yeast *Kloeckera brevis*. The turbidity due to the growth of this micro-organism is dependent upon the amount of inositol present, and in its absence no measurable growth occurs. Assays were carried

out in a medium based upon that of Burkholder, McVeigh & Moyer (1944). These authors suggested the possible use of this micro-organism and medium in the estimation of inositol. Emery, McLeod & Robinson (1946) successfully used the method in determining inositol in yeast and liver extracts. Northam & Norris (1952) reported the use of *K. brevis* in the assay of inositol in cereals and cereal products and discussed the statistics of the method.

Woolley (1941) showed that the other isomers of inositol and similar related substances were ineffective substitutes for *meso-inositol* in yeast.

The addition of crystalline *meso*-inositol to human blood, which was subsequently deproteinized and assayed by the method reported here, gave a 100% recovery. Further, it has been shown that cerebrospinal fluid subjected to paper chromatographic separation gives a growth-promoting eluate to *K. brevis* only in the region corresponding in position to that occupied by the inositol control (Nixon 1953).

The composition and preparation of the medium used was as follows:

*Solution I.* Glucose 40·00 g; potassium dihydrogen phosphate 3·00 g; DL-asparagine 4·00 g; calcium chloride ($6H_2O$) 0·98 g; magnesium sulphate 1·00 g; potassium iodide 0·4 ml. of a 0·05% (w/v) solution; ammonium sulphate 4·00 g; dissolved in 750 ml. of glass distilled water.

*Solution II.* Boric acid 0·10 g; zinc sulphate ($7H_2O$) 0·04 g; ammonium molybdate 0·02 g; manganese sulphate ($4H_2O$) 0·04 g; copper sulphate ($5H_2O$) 0·045 g; ferrous sulphate ($7H_2O$) 0·25 g; made up to 1 l. in glass distilled water.

*Solution III.* Thiamine 10 mg, pyridoxine 10 mg, calcium pantothenate 10 mg, nicotinic acid 10 mg, biotin 1 ml. of 1 mg % solution and riboflavin 0·5 mg, made up to 100 ml. with glass-distilled water.

A double-strength medium was made consisting of 750 ml. of solution I, 2 ml. of solution II, and 4 ml. of solution III, the reaction being adjusted with NaOH to pH 5·0 and the volume made up to 1 l. Sterilization was carried out by autoclaving at 15 lb. for 15 min.

Into numbered 25 ml. narrow screw-capped bottles were dispensed 2·5 ml. quantities of the double-strength medium. Volumes of 0·5, 1·0, 1·5, 2·0 and 2·5 ml. of the solution under assay were pipetted into bottles in duplicate and the volumes in each case made up to 5 ml. with glass-distilled water. With each batch of assays a standard curve was obtained using 0·0, 0·25, 0·5, 0·75, 1·0, 1·5, 2·0 and 2·5 ml. of a 2 $\mu$g/ml. inositol solution. All bottles were autoclaved and when cool, planted with 1 drop of freshly prepared suspension of *K. brevis* in 0·9% NaCl solution. Incubation was carried out at 25° C for 72 hr after which the turbidities were measured in a Spekker absorptiometer using a neutral filter (H 508). The amount of inositol present in the varying dilutions was found by interpolation on the constructed standard curve. In an estimation of a solution of known strength the standard deviation of the results was 5% of the mean on twenty estimations. All assays were made on specimens after deproteinization with sodium hydroxide and zinc sulphate.

*Operative technique*

Blood samples were received into vessels containing dry heparin.

*Human.* Samples of foetal blood were withdrawn from the umbilical cord, whilst the maternal blood samples and those of the controls were obtained from the ante-cubital veins.

Except in one case, amniotic fluid was not obtained from the individuals supplying the blood samples since it was essential that the fluid should be as far as possible uncontaminated with extraneous material.

Maternal blood, foetal blood and amniotic fluid samples were obtained from patients in the Maternity Departments of St Mary's and University College Hospitals.

*Sheep.* The animals were Welsh Mountain Sheep of known conceptual age. Laparotomy was carried out according to the technique of Huggett (1927) under spinal anaesthesia with procaine. Maternal blood samples were obtained from the dorsalis pedis artery, foetal blood samples from one of the four vessels of the umbilical cord and amniotic and allantoic fluids by the puncturing of the respective sacs.

*Monkey, cat, rabbit and goat.* No account of the number of foetuses per litter has been taken, since in the case of the rabbit and cat an adequate specimen was only obtained after cardiac puncturing several members of the litter.

*Neonatal blood samples. Cat and rabbit.* Samples were removed by cardiac puncture under ether anaesthesia.

*Plasma samples and haematocrit determinations.* Estimations were made on plasma obtained by centrifuging heparinized blood at 3000 rev/min for 30 min. Haematocrit determinations were also done on heparinized blood under the same conditions as above.

## RESULTS

### *Human material*

*Control bloods and plasma.* The free inositol in the whole blood and plasma of a group of healthy young adult males and non-pregnant females was determined. For whole blood the mean value was found to be 0·59 mg/100 ml., with a range of 0·40–0·84, while for plasma the mean value was 0·47 mg/100 ml. with a range of 0·30–0·64 (Table 1). The values obtained for plasma are in close agreement with the findings of Sonne & Sobotka (1947).

TABLE 1. Inositol concentrations in the adult human whole blood and plasma

| Sex | Whole blood (mg/100 ml.) | Plasma (mg/100 ml.) | Haematocrit value | Calc. corpuscular content (mg/100 ml.) | Ratio: plasma/ corpuscle |
|---|---|---|---|---|---|
| M. | 0·50 | — | — | — | — |
| M. | 0·44 | — | — | — | — |
| M. | 0·84 | — | — | — | — |
| M. | 0·66 | 0·64 | 45·0 | 0·69 | 0·93 |
| M. | 0·48 | 0·32 | 53·4 | 0·62 | 0·52 |
| M. | 0·78 | 0·63 | 47·6 | 0·94 | 0·67 |
| F. | 0·66 | — | — | — | — |
| F. | 0·62 | — | — | — | — |
| F. | 0·66 | — | — | — | — |
| F. | 0·50 | 0·42 | 44·0 | 0·61 | 0·69 |
| F. | 0·58 | 0·50 | 43·2 | 0·69 | 0·72 |
| F. | 0·40 | 0·30 | 45·1 | 0·53 | 0·57 |
| Mean | 0·59 | 0·47 | — | — | — |

Haematocrit values, together with the whole blood and plasma concentration, enabled the corpuscular content of the cells and hence the plasma/corpuscle concentration ratio to be determined. Owing to the small concentrations met with in human blood and plasma, and bearing in mind the limits of accuracy of the microbiological assay technique, the values obtained for the plasma/corpuscle ratio are sufficiently near unity to suggest that free inositol is equally distributed between plasma and corpuscles (Table 1).

*Maternal and foetal bloods and amniotic fluid at term.* The foetal blood had approximately twice the concentration of the maternal blood with means respectively of 1·6 and 0·7 mg/100 ml. The respective ranges were 1·1–2·8 and 0·5–0·8. In the amniotic fluid the concentration lay between the two blood levels with a mean of 1·0 mg/100 ml. and a range of 0·6–1·6 (Table 2).

*Terminated pregnancies.* Six cases of therapeutic abortion between the first and sixth month of pregnancy were examined. Samples of blood were obtained

from only five foetuses, but all gave higher inositol values than full-term foetal blood, although there was considerable individual variation. Pregnancies were terminated either on psychological grounds or because of severe tubercular infection of the mother.

Samples of amniotic fluid were obtained in three of these cases. Two gave results well above the normal range of concentration at full term and the third was at the bottom of the full-term range (Table 3).

TABLE 2. Inositol concentrations in human maternal and foetal bloods and amniotic fluid at full term

| | No. of specimens | Mean (mg/100 ml.) | Range (mg/100 ml.) |
|---|---|---|---|
| Maternal blood | 12 | 0·7 | 0·5–0·8 |
| Foetal blood | 14 | 1·6 | 1·1–2·8 |
| Amniotic fluid | 7 | 1·0 | 0·6–1·6 |

TABLE 3. Terminated human pregnancies, free inositol concentrations

| Foetal age (weeks) | Foetal blood (mg/100 ml.) | Foetal plasma (mg/100 ml.) | Amniotic fluid (mg/100 ml.) | Urine (mg/100 ml.) |
|---|---|---|---|---|
| 4–6 | — | — | 6·1 | — |
| 16 | 5·0 | — | 9·4 | — |
| 16 | 16·0 | — | — | — |
| 18 | — | 11·2 | — | 2·6 |
| 16–20 | 3·4 | 3·4 | 0·7 | 4·2 |
| 22–24 | 5·6 | — | — | 5·4 |

TABLE 4. Human multiple births, free inositol concentrations in mg/100 ml. blood

| | | | |
|---|---|---|---|
| Twins I | 2·1 | 1·9 | |
| Twins II | 3·1 | 2·1 | |
| Twins III | 4·3 | —* | |
| Twins IV | 1·6 | 1·6 | |
| Triplets | 1·5 | 2·1 | 2·2 |

* Foetus dead.

Samples of urine were obtained in three cases direct from the foetal bladder, and in two of these the concentration was of the order of that found in the foetal blood. In the third case it was lower than in foetal blood.

*Multiple births.* The examination of foetal blood from twins at birth appeared to indicate that a higher concentration was present than in singletons (Table 4).

### *Sheep material*

*Singleton pregnancies.* From Table 5 it will be seen that while the maternal blood inositol concentration remains constant throughout the latter portion of the gestation period, and is comparable with the levels found in non-pregnant ewes and rams (mean 1·09 and 1·55 mg/100 ml. respectively), that of the foetal blood shows considerable variation both with the period of gestation and among individuals of similar conceptual age, the mean value obtained for the foetal bloods over the whole period examined being 19·0 mg/100 ml. (range 10·0–31·0 mg/100 ml.)

TABLE 5. Sheep values—free inositol concentrations in singletons

| Sheep no. | Foetal age (days) | Maternal blood (mg/100 ml.) | Foetal blood (mg/100 ml.) | Amniotic fluid (mg/100 ml.) | Allantoic fluid (mg/100 ml.) |
|---|---|---|---|---|---|
| 517 | 43–45 (cal.) | 1·6 | 23·2 | 5·6 | 17·0 |
| 541 | 61 | 1·4 | 27·4 | 5·4 | 9·3 |
| 525 | 72 | 1·0 | 15·8 | 0·6 | 10·8 |
| 504 | 77 | 0·9 | 11·0 | 2·4 | 7·6 |
| 513 | 90–95 (cal.) | 2·0 | — | 12·5 | 14·4 |
| 506 | 96 | 1·4 | 16·0 | 6·0 | 9·0 |
| 522 | 100 | 0·6 | 15·0 | 7·0 | 8·0 |
| 529 | 100 | 1·4 | 10·0 | 5·0 | 5·0 |
| 503 | 106 | 1·4 | 14·0 | 6·0 | 11·0 |
| 531 | 110 | 1·6 | 25·0 | 7·0 | 16·0 |
| 532 | 110 | 1·8 | 10·8 | 6·6 | 8·1 |
| 510 | 110 | 1·6 | 21·4 | 7·7 | 12·3 |
| 527 | 110 | 1·5 | 21·6 | 6·3 | 13·0 |
| 518 | 110 | 2·7 | 22·8 | 6·7 | 16·7 |
| 535 | 111 | 1·3 | 19·8 | 4·0 | 14·0 |
| 509 | 120 | 1·8 | 15·8 | 8·3 | 7·2 |
| 523 | 120 | — | 21·4 | 4·5 | 15·5 |
| 515 | 120 | 2·1 | 16·4 | 7·0 | 13·4 |
| 502 | 130 | 2·2 | 25·4 | — | — |
| 528 | 134 | 1·8 | 31·0 | 20·1 | 20·8 |
| 539 | 134 | 2·0 | 16·0 | 12·4 | 12·8 |
| 512 | 137 | — | 18·4 | 6·4 | 21·9 |
| 514 | 140 | 2·3 | — | 11·2 | 11·0 |
| | Mean | 1·6 | 19·0 | 7·1 | 12·5 |
| | Range | 0·6–2·7 | 10·0–31·0 | 0·6–20·1 | 5·0–21·9 |

*Foetal plasma.* Foetal plasma gave a mean value of 17·9 mg/100 ml. with a range of 11·0–26·4. The plasma/corpuscle concentration ratios were approximately unity, and it would appear that in the foetal sheep, free inositol was in equilibrium between corpuscles and plasma from 100-day gestation onwards (Table 6).

TABLE 6. Inositol concentrations in the whole blood and plasma of the foetal sheep

| Sheep no. | Foetal age (days) | Whole blood (mg/100 ml.) | Plasma (mg/100 ml.) | Haemato-crit | Calc. corpuscular content (mg/100 ml.) | Ratio plasma/ corpuscle |
|---|---|---|---|---|---|---|
| 504 | 77 | 11·0 | 15·0 | 34 | 3·2 | 4·7 |
| 506 | 96 | 16·0 | 20·0 | 39 | 9·7 | 2·1 |
| 522 | 100 | 15·0 | 17·0 | 42 | 12·1 | 1·4 |
| 503 | 106 | 14·0 | 16·0 | 40 | 10·0 | 1·6 |
| 527 | 110 | 21·6 | 26·4 | 38 | 13·7 | 1·9 |
| 518 | 110 | 22·8 | 21·8 | 45 | 24·0 | 0·9 |
| 535 | 111 | 19·8 | 20·0 | 37 | 19·5 | 1·0 |
| 509 | 120 | 15·8 | 15·2 | 41 | 16·6 | 0·9 |
| 515 | 120 | 21·4 | 23·4 | 41 | 18·5 | 1·3 |
| 502 | 130 | 9·0 | 11·0 | 48 | 6·9 | 1·6 |
| 438 | 135 | 13·0 | 11·5 | 45 | 14·9 | 0·8 |

Because of the difficulty in some species of obtaining sufficient blood for determination of inositol in plasma, and the observation that in human and foetal sheep blood the concentration in whole blood and plasma was of the same order all subsequent determinations were carried out on whole blood.

Values obtained for the allantoic fluid appear to follow somewhat those of the foetal blood. The amniotic fluid indicates a similar trend and shows a statistical correlation of concentration of inositol to foetal age ($P < 0{\cdot}01$). The equation of the regression line is given by $y = -2{\cdot}524 + 0{\cdot}0917x$, where $y$ is inositol concentration in mg/100 ml. and $x$ is foetal age in days.

*Twins.* Assays carried out on two sets of twins (Table 7) showed that the foetal blood inositol concentration is higher than that of singletons ($P < 0{\cdot}01$). This result compares with similar observations on human twins referred to above. The inositol levels of the amniotic and allantoic fluids in twins are also higher than for singletons.

TABLE 7. Sheep values—free inositol concentrations in twins

| Sheep no. | Foetal age (days) | Maternal blood (mg/100 ml.) | Foetal blood (mg/100 ml.) | Amniotic fluid (mg/100 ml.) | Allantoic fluid (mg/100 ml.) |
|---|---|---|---|---|---|
| 533 | 120 | 4·2 | 34·2 | 11·3 | 36·0 |
| | | | 37·0 | 22·0 | 60·1 |
| 537 | 134 | 2·0 | 37·2 | 23·3 | 55·2 |
| | | | 25·6 | 29·1 | 80·0 |

TABLE 8. Free inositol concentrations (mg/100 ml.) in some mammalian species

| Species | Foetal age (days) | Maternal blood | Foetal blood | Amniotic fluid | Allantoic fluid |
|---|---|---|---|---|---|
| Monkey | 140? | 0·8 (plasma) | 3·6 (plasma) | 1·8 | — |
| Cat | 47 | 3·4 | 22·6 | 8·2 | 52·6 |
| Cat | 52 | 2·5 | 16·4 | — | 27·2 |
| Rabbit | 9 | 3·2 | — | — | — |
| Rabbit | 20 | 1·7 | — | 30·3 | 161·2 |
| Rabbit | 22 | 3·1 | 13·9 | 19·8 | 139·5 |
| Rabbit | 24 | 1·1 | 16·4 | 18·4 | 191·5 |
| Rabbit | 26 | 2·7 | 9·6 | 23·6 | 67·0 |
| Rabbit | 30 | 0·8 | 3·2 | 1·9 | — |
| Goat | 80 | 0·5 | 34·0 | 7·3 | 8·0 |
| Goat | 138 | — | 11·9 | 2·8 | 17·1 |
| Goat (twins) | 144 | 3·5 | 3·1 | 2·8 | 21·3 |
| | | | 4·2 | 2·5 | 21·2 |

*Monkey, cat, rabbit and goat*

The results summarized in Table 8 confirm the general observation that the inositol concentration in the foetal blood exceeds that in the maternal blood in the same species. The concentration in the allantoic fluid was found to exceed that of the amniotic fluid, and in all cases but one was considerably higher than that of foetal blood. Of particular note is the high concentration in the allantoic fluid of the rabbit.

Only one pair of foetal goat twins was examined, and the blood inositol concentrations were lower than those found in singletons of younger gestation ages. No singleton of comparable age was examined.

*Blood inositol concentrations after birth*

By assaying blood removed by cardiac puncture at various intervals from birth in new-born kittens and rabbits, it was found that the concentration in the blood fell, reaching maternal concentrations within 14 days of birth, as is shown in Figs. 1 and 2. (The low value in the rabbit on the first day was probably due to the inability to obtain an adequate blood sample.)

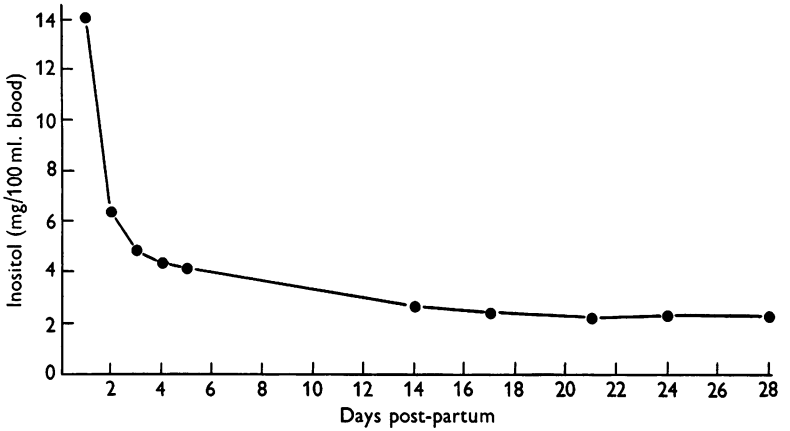


Fig. 1. Kitten. Free inositol concentration in blood obtained at intervals during the first 28 days post-natal life.

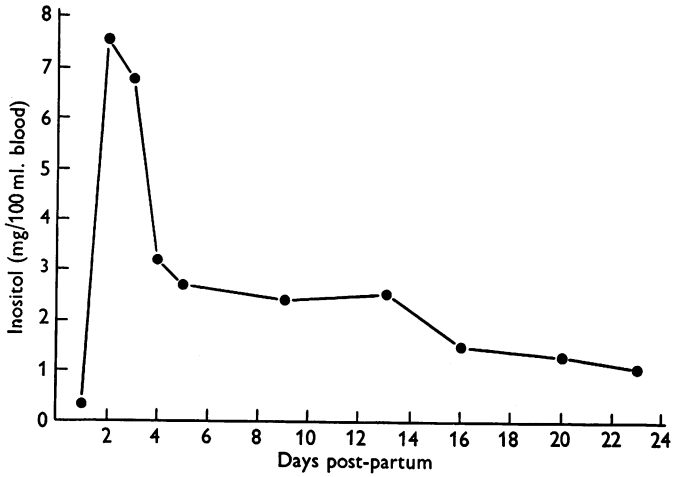


Fig. 2. Rabbit. Change in inositol concentration of rabbit blood during the first 23 days post-natal life.

*Origin of the foetal blood inositol*

Inositol present in the foetal blood could have its origin in three ways: (i) maternal transfer via the placenta; (ii) placental synthesis; (iii) synthesis within the foetus itself.

(i) *Maternal transfer.* The maternal blood inositol concentration of the ewe, when experimentally elevated, was shown to be without any significant effect upon the concentration found in the foetus. Similarly, raising the level in the foetal blood had only slight effect on the concentration present in the maternal blood. These findings are shown in Table 9, which summarizes the results of two experiments in which inositol solutions were injected into a maternal vein and the umbilical vein respectively. From these experiments it is inferred that the placenta, at least in this species, is impermeable to inositol transfer in the direction mother to foetus and negligible in the reverse direction.

TABLE 9. Placental permeability in the sheep towards inositol

| | Ewe to foetus | | Foetus to ewe | |
|---|---|---|---|---|
| Time (min) | Maternal blood (mg/100 ml.) | Foetal blood (mg/100 ml.) | Maternal blood (mg/100 ml.) | Foetal blood (mg/100 ml.) |
| 0 | 2·0 | 21·4 | 1·4 | 10·8 |
| | 10·5 g inositol to ewe | | 6·0 g inositol to foetus | |
| + 30 | 91·8 | 20·1 | 1·5 | 474·0 |
| + 90 | 47·6 | 20·3 | 1·7 | 328·0 |
| +150 | 26·0 | 20·4 | 2·6 | 270·0 |
| +210 | 17·3 | 19·8 | 3·0 | 210·0 |
| +270 | — | — | 2·9 | 182·0 |

TABLE 10. Sheep. Perfusion of placenta *in situ* via the umbilical vessels, the foetus being replaced by a Henry-Jouvelet pump. Foetal age 115 days.

| Time from commencement of experiment (min) | Mg free inositol/100 ml. blood |
|---|---|
| Initial | 7·8 |
| + 15 | 7·4 |
| + 30 | 8·0 |
| + 45 | 8·0 |
| + 60 | 8·0 |
| + 75 | 7·8 |
| + 90 | 7·8 |
| +105 | 7·4 |
| +120 | 7·7 |
| +150 | 7·7 |
| +180 | 7·7 |
| +210 | 6·7 |
| +240 | 6·7 |

(ii) *Placental synthesis.* By substituting a Henry-Jouvelet pump for the foetus and making repeated assays on the circulating blood in the reservoir (primed with maternal blood to give an adequate circulatory volume), it was shown that the concentration of free inositol remained constant over a period of 4 hr (Table 10). The initial value was lower than normal due to dilution by the maternal blood added to the reservoir. The perfusion pressure was maintained throughout the experiment at about 55 mm Hg with a blood flow of about 90 ml./min. The placenta was free from oedema as judged by visual observation and by the constant haemoglobin content of the reservoir blood.

Further evidence that the placenta was undamaged in a physiological sense was obtained by estimating the fructose concentration in the re-circulating blood. This rose from 82 to 144 mg/100 ml. over the 4 hr period, and agreed well with other such experiments (Alexander, Andrews, Huggett, Nixon & Widdas, 1952).

(iii) *Foetal synthesis.* No direct experimental evidence has been obtained on this point.

## DISCUSSION

Inositol is present in the normal adult blood, foetal blood, amniotic and allantoic fluids of all species examined. Pregnancy does not result in a detectable difference in the concentration of inositol found in the adult blood. There is no correlation between the concentration in maternal and foetal bloods, and experimentally increased concentrations in foetal or maternal blood do not result in its demonstrable passage across the placenta. The concentration in the amniotic fluid is on the average higher than in the foetal blood. The same applies to allantoic fluid (in non-primates) when compared with amniotic fluid. Without more knowledge of the physiology and origin of these fluids it is not possible to make deductions as to the significance of these differences in concentration.

Our experiments have shown that the high foetal blood inositol concentration is not due to maternal transfer via the placenta or to placental synthesis. The excess inositol must therefore be produced by the foetus, but the processes involved are not yet known.

Although inositol has been known since 1850 and is widely distributed throughout the plant and animal kingdoms, its function within the living organism, apart from its fairly well-established action as a lipotropic agent (MacFarland & McHenry, 1948), is still undecided. Several facts have emerged within recent years which suggest that it may play some part in the growth of tissues. The concentration in young tissues of both plants and animals is higher than those of the mature organism. Smith (1951) has expressed the view, based upon observations in the micro-organisms *Nematospora gossypii* and *Saccharomyces carlsbergensis*, that inositol may be a structural component of the cells, since he has demonstrated that in these organisms inositol occurs in a form resembling phytin (the Ca-Mg hexaphosphoric acid ester of inositol), also that when grown in a medium deficient in inositol cell division appears to be incomplete. Laszlo & Leuchtenberger (1943) showed that injections of inositol into mice with transplanted carcinomas retarded the growth of the tumour, although Ritchey, Wicks & Tatum (1947) found that in such carcinomas there was a rise in the inositol content when compared with normal tissue. Tatum, Ritchey, Cowdry & Wicks (1946) have, however, found no significant changes in inositol content of methylcholanthrene-induced carcinomas. Inositol has been shown to be capable of removing the metaphase

arrest induced by γ-hexachloro-*cyclo*hexane or colchicine (Chargaff, Stewart & Magasanik, 1948).

SUMMARY

1. The free *meso*-inositol concentrations have been estimated in the maternal and foetal bloods and foetal fluids of man, monkey, sheep, goat, cat and rabbit with the constant finding that the concentration in foetal blood and fluids exceeds that present in the maternal blood of the same species.

2. After birth, the blood concentration of inositol in the cat and rabbit drops, reaching maternal levels within the first 2 weeks.

3. Experiments described have failed to demonstrate placental transfer or placental synthesis of inositol.

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