ON THE INFLUENCE OF FORMIC ALDEHYDE UPON THE METABOLISM OF CHILDREN.

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FORMIC aldehyde, the simplest possible aldehyde, is a substance possessed of considerable biological and chemical interest. Its biological interest consists in the fact that it has long been regarded as forming the first product of plant assimilation, and has recently been actually demonstrated as such in plants[1]. The ease with which this substance undergoes polymerisation resulting in the formation of sugars, under the influence of simple reagents, justifies the assumption that formic aldehyde is an essential link in the building-up of complex carbohydrates by plants. In addition to this it has recently been requisitioned as the only possible source of proteid anabolism[2]. Its interest to the physiological chemist is that it combines energetically with proteids, and to a less extent with carbohydrates, effecting considerable alteration of their physical and physiological properties. This behaviour seems to be directly antagonistic to the biological *rôle* ascribed to the substance above. This apparent anomaly of the same substance being both a poison and an essential physiological constituent of living cells is discussed by Loew[3]. It seems to depend upon the fact

[1] Pollaci, *Boll. chim. farmac.*, 1899, xxxviii. p. 1601.

[2] Loew, *Die chemische Energie d. lebenden Zellen*, pp. 67, 86, etc. and R. Hebert, *Ann. Argronom.* xcviii. p. 416. [3] *loc. cit.* p. 66.

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that what may be termed the biological formic aldehyde is present in small quantities (dilute solutions) and is quickly used up, owing to the ease with which it polymerises or forms innocuous compounds. This last property has an immediate bearing upon the subject of this inquiry in so far as it may serve to explain the results obtained by the administration of small quantities of formic aldehyde to man in his food. It is in this connection that formic aldehyde is of interest to us, and the importance of this subject is in our opinion sufficient to justify us in reviewing somewhat exhaustively the results of other observers with regard to the chemical and physiological properties of this substance.

Hofmann[1] discovered formic aldehyde (CH_2O) in 1869. It is a gas, soluble in water, and obtainable commercially as a 40 % solution which is known as formaline or formol. It has an irritating and pungent odour, and is easily converted into a polymeric solid modification. Its disinfectant action was first pointed out by Loew[2] and has subsequently engaged the attention of numerous workers, amongst whom may be mentioned Trillat, Aronson, Blum, etc. Their results are mostly of interest to bacteriologists, and are outside the subject of our inquiry. The literature so far as it concerns us may be classified as follows: (I) chemical action of formic aldehyde upon proteids, (II) influence of formic aldehyde upon digestions *in vitro*, (III) experiments upon animals.

Chemical Action of Formic Aldehyde upon Proteids.

The action of formic aldehyde upon native proteids is, in general, to render them insoluble. Egg and serum albumin are however exceptions. The compounds which formic aldehyde forms with them are soluble and non-coagulable by heat[3]. The reaction between formic aldehyde and the proteids is explained by assuming an interaction between the aldehyde and the amido groups of the proteid molecule: there is however no proof of this. The insoluble compounds are resistant to

[1] *Berichte d. deutsch. chem. Ges.* 1869, p. 152.

[2] Loew, *München. med. Wochenschr.*, 1888, p. 412.

[3] In this regard it may be mentioned that Trillat (*Compt. rend. Acad. d. Sc. Paris*, 1892, T. CXIV. p. 1279) states that formic aldehyde coagulates albumin as well as blood. Subsequently Blum (*Zeitschr. für physiol. Chemie*, 1896, p. 137) found that formic aldehyde prevents the coagulation by heat, of serum and egg albumin in aqueous solution, a fact which has been confirmed by Benedicenti and all later observers. See also L. Schwarz, *Zeit. f. phys. Chemie*, 1901, XXXI. p. 460.

the action of the digestive enzymes[1]. By the action of steam the formic aldehyde is easily split off, the proteids reformed possessing their original digestibility. (Blum[2], Bach[3], Benedicenti[4], Beckmann[5], Mosso and Paoletti[6], Foulerton[7], Riche[8].)

According to Lepinois[9] a 1 °/₀ solution of formic aldehyde preserves thyroid glands without affecting either their digestibility or the solubility of the active principle—(iodo-thyrin).

The evidence concerning the action of formic aldehyde upon albumoses and peptones is somewhat conflicting[10].

According to Beckmann[11], gelatine peptone and egg albumin peptone are unaffected by formic aldehyde, whereas hemialbumose is rendered insoluble. Trillat without giving any experimental data makes the statement that formic aldehyde renders insoluble all proteid substances not coagulable by heat. This generalisation would of course include albumoses and peptones[12]. Lepierre[13] worked on the action of formic aldehyde upon the products of partial peptic digestion isolated by himself, viz. hetero-, proto-, and deutero-albumoses, and peptones, also upon commercial peptones the composition of which he previously examined in the usual manner. According to him there was no action in the cold, and even at 100° C., working with a 14 °/₀ formic aldehyde solution, only in some cases did precipitation take place, usually (commercial peptones) no change occurred. From subsequent examination of the resulting solutions, concerning which no details are given, he enunciates a theory according to which formic aldehyde causes a "progressive regression" of the simpler products of proteid digestion back again to the more complicated ones, viz. of peptones to deutero-albumoses, of deutero-albumoses back to proto-albumoses, which finally

[1] Hehner (*Analyst*, XXII. 1897) said in a discussion on formic aldehyde that he had seen the results of certain experiments which showed that the soluble compound formed by formic aldehyde and egg albumin was digested more easily than egg albumin itself.

[2] *Zeitschr. f. physiol. Chemie*, 1896, XXII. p. 137.

[3] *Moniteur Scientifique*, XI. p. 157.

[4] *Du Bois-Reymond's Archiv*, 1897, p. 210.

[5] *Forschungs-Berichte über Lebensmittel-Unters.*, etc., III. p. 324.

[6] *Giorn. d. r. Accad. di med. di Torino*, 1895.

[7] *Lancet*, II. 1899, p. 1579.

[8] *Journ. Pharm. Chim.* VI. p. 197.

[9] *Bull. Soc. Chim.*, 1899, T. IX. p. 76.

[10] Loew (*loc. cit.*) observed that pure peptone gave no precipitate with formic aldehyde, whilst commercial peptones (Witte) yielded immediately a precipitate in the cold; this he regards as being due to the presence of albumoses (propeptone).

[11] *loc. cit.*

[12] *Bull. Soc. Chim.* 1898, p. 1017.

[13] *Compt. rend. Acad. d. Sc. Paris*, T. CXXVIII., p. 789.

are precipitated. This observer states further that the compounds formed by formic aldehyde and the proteids are digestible, but less rapidly than the corresponding original proteid, and that these compounds could be reconverted into the original easily digestible proteids by the action of superheated steam.

Influence of Formic Aldehyde upon Digestions in Vitro.

The work done in this connection may be divided into that which concerns itself with the action of the digestive enzymes in the presence of formaldehyde, with their action upon formalised food, and with the effect of formic aldehyde upon the enzymes themselves. The digestions can be considered in this regard *seriatim*.

Salivary Digestion. Rideal and Foulerton[1] estimated the amount of maltose formed from arrow-root starch by saliva alone and in the presence of formic aldehyde in different proportions. Taking the control as 100, they found that ptyaline in the presence of 1 in 100,000 formic aldehyde converted 99·8 %, in the presence of 1 in 10,000, 89·0 %. Foulerton[2] tested the progress of starch conversion in the presence of formic aldehyde and found that dilute solutions, 1 in 40,000 to 1 in 1,000, had a retarding but not an inhibitory action.

The relative convertibility of previously formalised starch into sugar by means of ptyaline has so far as we are aware only been investigated by Bliss and Novy[3]. These observers found that a 1 % starch paste previously kept for 5 days at 35° C. with formic aldehyde (1 in 100) behaved with ptyaline exactly as fresh starch paste.

The same investigators showed that formic aldehyde in the strength of 1 in 1,000 exerts very little action upon ptyaline itself, unless the mixture is allowed to stand for several days or is kept at 35°—40° C. With stronger solutions of formic aldehyde the effect is more marked, the ferment being destroyed by the action of 1 in 1,000 for 9 days at 40° C.

Rennet. Pottevin[4] observed that formic aldehyde added to milk retarded its coagulation by rennet, and that rennet itself (*loc. cit.*) was rendered inactive by strong solutions of formic aldehyde.

[1] *Public Health*, 1899, p. 554.
[2] *Lancet*, 1899, II. p. 1432.
[3] *Journ. of Experimental Med.*, 1899, IV. p. 74.
[4] *Ann. de l'Inst. Pasteur*, 1897, p. 807.

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Bliss and Novy also examined the action of rennet upon formalised milk and found that milk which had been subjected to the action of formic aldehyde, 1 in 1,500, behaved in this respect very similarly to normal milk. (Normal milk coagulated in 15 minutes, this formalised milk in 20 minutes.) Milk which had been acted upon by formic aldehyde, 1 in 1,500 for 1 hour, behaved identically with normal milk.

Foulerton's[1] experiments with rennet show that formic aldehyde added to milk in the proportion of 1 in 40,000, whether at the same time as the enzyme or 48 hours before, has practically no influence upon the process of coagulation. With higher proportions up to 1 in 5,000 coagulation was retarded, but not prevented. This was also the case to a more marked degree with solutions of 1 in 1,000. These results with higher proportions do not correspond with those of Bliss and Novy detailed above. The discrepancy in the results of these two observers is probably to be explained by the variations in milks and rennets used. It will be noted that the behaviour of the control milks was not identical (coagulation in 15 minutes Bliss and Novy, and 30 minutes Foulerton).

Halliburton[2] observed that strong solutions of formic aldehyde delayed rennet action, more dilute solutions acted similarly but to a less marked degree. Freudenreich[3] observed that formic aldehyde in the form of vapour had a destructive influence upon rennet, but that in solution in the strength of 1 in 500 it had no appreciable action upon its milk-coagulating power.

With regard to the action of formic aldehyde upon the rennet ferment itself Bliss and Novy[4] found that it had no apparent effect upon this ferment, even when present in the proportion of 1 in 50.

Peptic Digestion. Symons[5] found that formic aldehyde did not influence peptic digestion.

According to Mayberry and Goldsmith[6], when pepsin was allowed to act upon fibrin in the presence of formic aldehyde the amount of fibrin digested diminished with the increasing percentage of

[1] *Lancet*, 1899, II. p. 1578.
[2] Halliburton, *Brit. Med. Journ.*, 1900, II. p. 2.
[3] Freudenreich, *Centralbl. f. Bakteriologie*, Abth. II. 1898, p. 309.
[4] *loc. cit.*
[5] *Journ. of American Chem. Soc.*, 1897, XIX. p. 744.
[6] *Ibid.* p. 889.

formic aldehyde. Taking the control as 100 they found that, when formic aldehyde was present in the proportion of 1 : 2,000, 97·74 %, of the fibrin was digested, when present in the proportion 1 : 1,000, 94·34 %[1].

Rideal and Foulerton[2] concluded from carefully executed quantitative experiments that the addition of formic aldehyde immediately before digestion in the proportion of 1 : 50,000 had no appreciable effect. Their quantitative results were as follows. When formic aldehyde was added in the proportion of 1 : 50,000 immediately before digestion, the amount digested in unit time was 97·63 %, taking the control as 100.

With regard to *previously formalised* proteid they found that (taking again the control as 100) 91·45 % was digested in the case of fresh beefsteak previously formalised for 24 hours with 1 : 100,000, 90·38 % when the strength used was 1 : 50,000, 85·25 % when the formic aldehyde was increased to 1 : 10,000. From these results they conclude that formic aldehyde has no influence on the digestibility of the food after contact with it for 24 hours prior to the action of the enzyme.

These conclusions have been criticised by Hehner[3] and in a subsequent paper Foulerton[4] modifies them considerably, and infers that in addition to any possible effect which formic aldehyde may have on the action of the enzyme, it also renders food itself less digestible.

Bliss and Novy[5] found that the digestion of fibrin by pepsin, both previously formalised for 24 hours, proceeded normally when the strength of formic aldehyde was 1 : 2,500, and even when it was increased to 1 : 100 the fibrin was eventually digested.

Halliburton[6] made a series of experiments on the relative digestibility of fibrin previously treated with formic aldehyde (for from two to three days with 1 : 100 to 1 : 2000). He found that previous formalisation with 1 : 2,000 for two days delayed gastric digestion 20 minutes, for three days for 30 minutes. Formalisation with a 1 % solution did not prevent digestion, the latter becoming complete in 24 hours.

[1] The results of Mayberry and Goldsmith were re-calculated by us, from the average of their experiments (taking the average of the three control experiments as 100).

[2] *Public Health*, 1899, p. 554.

[3] *Brit. Food Journ.*, 1899, p. 132.

[4] Foulerton, *Lancet*, 1899, pp. 1432 and 1577.

[5] *loc. cit.*

[6] *Brit. Med. Journ.*, 1900, II. p. 2.

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Loew[1] was the first to study the action of *formic aldehyde on pepsin* and found that when this enzyme was exposed to strong solutions for one day it lost its activity.

Bliss and Novy[2] subsequently found that pepsin is not affected by a 1 °/₀ solution of formic aldehyde, even when the mixture has stood for four weeks. Even a 5 °/₀ solution acting for three weeks has no effect on pepsin. Contrary results by others are explained as being due to an alteration of the fibrin by the aldehyde, before the pepsin could act.

Pancreatic Digestion. Symons[3] found that when formic aldehyde was added to the digestive mixture in the proportion of 1 : 2,000, it had a distinctly retarding influence on pancreatic proteolysis (fibrin), whilst 1 : 300 completely inhibited digestion.

Rideal and Foulerton's[4] results showed that when formic aldehyde was added in the proportion of 1 : 50,000 to milk immediately before its artificial digestion with commercial pancreatin 97·0 °/₀ of casein was digested, taking the amount digested in the control experiment as 100.

With regard to *previously formalised* milk the same authors found that 94·1 °/₀ casein was digested when milk formalised to the extent of 1 : 50,000 was acted upon by commercial pancreatin (taking as before the amount digested in the control as 100).

Bliss and Novy working with commercial pancreatin and fibrin found that fibrin previously formalised for 24 hours with 1 in 1,000 formic aldehyde was digested much more slowly than fresh fibrin, but that its total digestion did eventually take place. The same observers working with *fresh pancreatic extract* found that when fibrin was formalised for 24 hours with 1 in 1,000 there was no influence upon its digestibility, whilst when 1 in 500 was used there was a slight retarding influence.

Halliburton[5] studied the effect of previous formalisation upon the digestibility of fibrin by means of commercial pancreatin and found that whereas the digestion of fresh fibrin was completed in 30 minutes that of fibrin previously formalised by an exposure to formic aldehyde solution 1 in 2,000 for two days required 95 minutes for its completion. In the case of formalisation with stronger solutions no signs of digestion occurred within 24 hours.

Loew[6] observed that when a *solution of trypsin* was treated with

[1] *loc. cit.* [2] *loc. cit.* [3] *loc. cit.*
[4] *loc. cit.* [5] *loc. cit.* [6] *loc. cit.*

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formic aldehyde a precipitate occurred. The action of formic aldehyde upon the pancreatic enzyme has been carefully studied by Bliss and Novy[1]. They found in the case of commercial pancreatin (Parke Davis) that solutions of formic aldehyde in the strength of from 1 in 1,000 to 1 in 100 acting for 24 hours completely destroyed its proteolytic activity. In the case of freshly prepared pancreatic extract the influence was not so marked, a strong extract, previously formalised for 24 hours, with 1 in 1,000, digested formalised fibrin (1 in 1,000) normally; when the ferment solution was previously formalised with 1 in 500 there was a distinct retardation in the case of the *strong extract, and absolute destruction of proteolytic power* in the case of the weak extract.

Amylolytic Ferment of Pancreas. Rideal and Foulerton[2] tested the activity of the amylolytic ferment of two samples of commercial pancreatin in the presence of formic aldehyde. They found that when formic aldehyde was added immediately before digestion, so that it was present in the digestive mixture in the proportion of 1 in 50,000, 91·8 % maltose was produced in the case of Extract No. I and 84·00 % in the case of Extract No. II. When the formic aldehyde was present in the proportion of 1 in 10,000, 91·5 % and 83·0 % maltose were produced respectively. The amount produced under normal conditions was taken as 100.

Halliburton[3] made a few experiments with regard to starch conversion by means of commercial Liq. Pancreaticus (Benger) in the presence of formic aldehyde and found that the strongest solution of formic aldehyde caused a retardation of total conversion amounting to five minutes, the weakest a retardation amounting to two minutes. Bliss and Novy[4] made some observations upon the amylolytic power of previously formalised freshly prepared pancreatic extracts. From their results it follows that formic aldehyde has very little influence upon them. Amylopsin previously formalised for 24 hours with 1 in 1,000 was not affected, even 1 in 500 exerted but little action[5].

Experiments upon Animals.

The symptoms produced by formic aldehyde consist in strong local irritation. The animals become restless and exhibit clonic convulsions and opisthotonus. They finally pass into a condition of coma, during which the respiration is quick and irregular in rhythm, the cause of

[1] *loc. cit.* [2] *loc. cit.* [3] *loc. cit.* [4] *loc. cit.*

[5] "Lipase" seems unaffected by formic aldehyde. Kastle and Loewenhart, *Am. Chem. Journ.* xxiv. No. 6.

death being asphyxia. According to Benedicenti[1] formic aldehyde is a blood poison, converting haemoglobin into haematin.

The toxicity of formic aldehyde upon higher animals seems to be relatively low and differs considerably according to the animal.

Trillat[2] gives the lethal dose per kg. body weight for guinea-pigs as 0·8 g. when injected *sub cutem*, whilst 0·53 and 0·66 produced no effect; 0·038 g. per kg. guinea-pig, injected into a vein was also without result.

Berlioz and Trillat[3] found the toxic dose for dogs (intravenous) to be 0·07 g. pro kg. and for rabbits (intravenous) 0·09 g. pro kg.

Aronson[4] found 0·24 g. pro kg. body weight to be lethal for rabbits, and according to Pottevin[5] larger doses than 0·25 g. pro kg. *sub cutem* and 0·03 g. pro kg. intravenous are lethal for the same animal. 0·016 g. injected into the veins of rabbits for four days in succession produced no effect.

According to Mosso and Paoletti[6] 0·32 g. pro kg. proved lethal for dogs, whilst 0·22 g. produced serious symptoms.

Bruni[7] found that 0·28 g. pro kg. killed a dog to which the same dose had been administered *per os* the day before.

When *administered by the mouth* the results obtained are somewhat conflicting.

Blum[8] gave to a rabbit weighing 1,500 g. 0·72 g. formic aldehyde in two doses in the form of a 1·2 % and of a 2·4 % solution. The animal refused food for a day. He also administered 1·5 c.c. of a 40 % formalin solution, that is 0·6 g. formic aldehyde, to a hare. The hare took its food normally after two days.

U. Mosso and Paoletti[9] gave to a dog 0·04 g. formic aldehyde in the form of a 1 in 250 solution. Vomiting ensued. Subsequently they gave 0·022 g. formic aldehyde in the form of a 1 : 500 solution. No vomiting occurred, but symptoms referable to an action of the drug upon the central nervous system. A dose of 0·011 g. in the same dilution produced no effect.

Bruni[10] found that 0·032 g. of a 1 : 1,000 solution had no effect upon a dog weighing 7·2 kg., and that 0·28 g. formic aldehyde in the form of

[1] *Arch. f. (Anat.) Phys.*, 1897, p. 210.
[2] *loc. cit.*
[3] *Compt. rend.* 1892, T. cxv. p. 291.
[4] *Berliner klin. Wochensch.* 1892, p. 751.
[5] *Ann. de l'Inst. Pasteur*, 1894, p. 807.
[6] *Giorn. d. r. Accad. di med. di Torino*, 1895.
[7] *Ann. di Farmacoterapia e Chimica*, 1899, p. 339.
[8] *Münchener med. Wochensch.* 1893, p. 602.
[9] *loc. cit.*
[10] *loc. cit.* p. 338, et seq.

1 : 500 solution caused vomiting in a dog weighing 14 kgs. After 50 minutes no further disturbances occurred.

Some experiments have been made with regard to the general effect of doses of formic aldehyde continued for some time upon animals.

Rideal and Foulerton[1] fed cats three months old for a period of several weeks on milk containing formic aldehyde to the extent of 1 in 50,000, 1 in 25,000, and 1 in 20,000, and in two cases noted an increase in weight, while in one case the weight remained constant. They further fed one rabbit in the same way, estimating the amount of nitrogen in the food and the excretions, and found that the animal gained in weight and that although there was some increase in the excretion of nitrogen, the nitrogen balance remained positive. These observers however give no control experiments. Reviewing these experiments in a later article[2] Foulerton concludes that these observations were not sufficiently numerous to allow of any stress being laid upon them either one way or the other.

Annett published some experiments[3] on young kittens three or four weeks old extending over several weeks. These he fed on milk containing formic aldehyde 1 in 50,000, 1 in 25,000, and 1 in 12,500. Control experiments were made on a smaller number of kittens, fed on normal milk. The quantity of milk taken by each kitten is not given, therefore no data are available with regard to the quantity of formic aldehyde consumed by each kitten. These experiments and the conclusions drawn from them have been criticised at length by Liebreich[4] and Rideal[5], who have pointed out that the results were so irregular[6] in comparison to the number of animals experimented upon, that no important conclusions could be drawn from them.

Rideal further pointed out that cows' milk as such is an unsuitable food for kittens of that age and that six kittens fed on undiluted fresh cows' milk all died. Rideal in the same paper published a series of observations upon kittens five weeks old fed with 70 c.c. of cows' milk per diem formalised to the extent of 1 in 5,000; he noticed under these conditions no injurious action but an increase in body weight.

In this connection some experiments have been made by A. D. Hall and H. S. Hammond in collaboration with ourselves at the South Eastern

[1] *loc. cit.* [2] *Lancet*, 1899, II. p. 1582.

[3] *Lancet*, 1899, II. p. 1284.

[4] Liebreich, *Lancet*, 1900, I. p. 13. [5] Rideal, *Lancet*, 1900, I. p. 228.

[6] *E.g.* he obtained three deaths in the case of the 1 in 50,000 milk, none with the 1 in 25,000, and two with the 1 in 12,500.

Agricultural College, Wye. These observations will be published fully elsewhere; they showed that the continuous administration for six weeks of from ·8 to 1·6 grammes daily of formic aldehyde with a mixed diet had no effect upon the live weight of young sucking-pigs. The initial weight of the pigs varied from 25 to 58 lbs., and the quantity of formic aldehyde given amounted to a concentration of from 1 in 185 to 1 in 730 of the total food.

Concerning *the fate of formic aldehyde* in the animal body the results of various observers are not in accord.

Trillat (*loc. cit.*) found that guinea-pigs' urine underwent no fermentative change after they had been injected with formic aldehyde. According to Aronson (*loc. cit.*) the urine of rabbits after the administration of large doses of formic aldehyde has a reducing action upon ammoniacal silver nitrate and gives Schiff's reaction for aldehydes. Blum (*loc. cit.*) could not find formic aldehyde in the urine of rabbits after doses of 0·6 g., but obtained traces of formic acid.

Quite recently Filippi and Martoleni[1] have studied the fate of formic aldehyde in the body after injection. The object of the research seemed to be to determine whether the results of Albertoni[2] concerning acetic aldehyde, namely, its complete excretion as such without oxidation, were true for formic aldehyde. They seem unaware of the fact that these results have not been confirmed by Reizenstein[3]. They quote Perando[4] as having found that formic aldehyde is completely oxidised in the body, to formic acid, and call into question his methods. From their own experiments they conclude that formic aldehyde after its administration in apparently very large doses could be found in all the organs of the body; the colour reaction upon which they relied being most marked in the intestines, lungs and kidneys. No mention is made as to its presence in the urine.

Among the compounds of formic aldehyde easily decomposable into the original substance, Pohl[5] has examined the fate in the body of the sodium sulphite compound $\left(HCH\begin{smallmatrix}OH\\SO_3Na\end{smallmatrix}\right)$. After the administration of 5 g. of this substance to a dog, no aldehyde reaction could be obtained in the urine, but there was a very slight increase in the amount

[1] *Ann. Farmacoterapia e Chimica*, 1900, p. 195.

[2] *Albertoni e Lussana*, Padua, 1875. Albertoni, *Arch. Italiennes de Biologie*, 1888.

[3] *Dissertation, Würzburg*, 1894.

[4] Perando, *Boll. di R. Acc. med. di Genova*, Vol. XI. No. 9.

[5] *Arch. f. exper. Path. u. Pharm.*, 1893, p. 281.

of formic acid normally present. The fate of the ammonium compound of formic aldehyde (hexamethylentetramine or urotropin) is discussed by Nicolaier[1] in his original communication. His results have subsequently been confirmed by other observers. Urotropin appears rapidly in neutral or alkaline urines as such, and in acid urines as formic aldehyde.

With regard to *the fate of formic aldehyde* in the body the observations of Pohl (*loc. cit.*) are of interest. He found that the fresh organs of warm-blooded animals, especially the liver, can oxidize formic aldehyde to formic acid. Jacobi[2] isolated a pure ferment from the liver of oxen, possessing very strongly the power of oxidizing aldehydes, especially salicylic aldehyde.

Action on Man. Very little is known concerning the action of formic aldehyde on man, either in therapeutic or poisonous doses. A case of poisoning is recorded by Andés[3] in which a "spoonful" of a 40 °/₀ formic aldehyde solution was taken by mistake. Ammonium acetate and an emetic were administered immediately and complete recovery took place in two days. No general symptoms other than those referable to shock were recorded.

Another case is mentioned in the *Medical Press*[4], where a youth took about 2·5 g. of formic aldehyde in the form of a 4 °/₀ solution. Vomiting occurred and death 29 hours afterwards from heart-failure. A post-mortem examination showed "that the oesophagus was slightly inflamed and escharotic changes were visible in the stomach."

Trillat[5] gave 5 g. of the polymerised solid modification of formic aldehyde to patients without any poisonous symptoms. Aronson records similar experiences with paraformaldehyde.

The ammonium compound (urotropin) mentioned above is used extensively in medicine.

Quite recently[6] 50 c.c. of a 1 in 2,000 solution of formic aldehyde have been injected intravenously as a means of treatment in pulmonary tuberculosis, without any symptoms of poisoning occurring. The injections were continued over a considerable time.

1 *Centralbl. f. med. Wiss.*, 1894, p. 897, and *Deutsche Med. Wochenschr.*, 1895, p. 541.

2 *Zeitschr. f. physiol. Chemie*, 1900, p. 133.

3 *Journ. de Pharm. et Chim.*, 1899, T. x. p. 10.

4 *Medical Press*, 1899, p. 309.

5 *Journ. de Pharm. et Chim.* 1894, p. 540.

6 Reported in *Brit. Med. Journ.* from Dr Maguire's *Harveian Lectures*, Nov. 24th, 1900.

Critical Review of Literature.

In this connection we do not purpose considering formic aldehyde from either a therapeutical, bacteriological or toxicological standpoint, but from the standpoint of its possible use as a food-preservative. This limitation of our point of view brings us at once to a limitation of material and quantity. Material in so far as we have only to consider milk, and quantity in so far as only those experiments are relevant in which formic aldehyde is used in quantities not in excess of those necessary for its action as a preservative. In this regard the strong solutions are at once excluded owing to their taste, and because they are unnecessary[1].

From a careful consideration of the results of various workers we are inclined to accept 1 in 25,000[2] as the maximum quantity which can possibly come in regard in this connection, but as it will be seen from the context we took for the purpose of our own experiments a higher proportion (1 in 10,000 and 1 in 5,000).

If we consider the literature, keeping these limitations in mind, the following points are to be emphasised :—

From the experiments made to ascertain the chemical action of formic aldehyde upon the proteids generally, the conclusion may be drawn that compounds of a more or less definite composition are formed, and that the digestibility of these compounds is less than that of the original proteids. All these experiments however relate to compounds produced by the action of an excess of formic aldehyde, none being recorded with dilution approximating to that of the above adopted standard. Taking in regard the complex nature of milk and the excess of chemical compounds capable of combining with formic aldehyde in it, in proportion to the very small amount of formic aldehyde added, it does not seem to be justifiable to draw *a priori*

[1] By the assistance of a number of observers we were able to convince ourselves that formic aldehyde in the strength of 1 in 2,000 imparted to milk in the cold a characteristic taste. If the milk were warmed to drinking temperature 1 in 5,000 could be easily detected.

[2] *Vide* Droop Richmond and Harrison, *Analyst*, 1900, p. 116.

It is further interesting in this connection to observe, assuming Benedicenti's figures to be correct (*loc. cit.* p. 243), that milk could fix owing to its 3 % of casein 0·0036 % formic aldehyde, whilst 1 in 25,000 formic aldehyde corresponds to 0·004 %. There seems to be a relation between the fixing of the formic aldehyde by the casein and its power as a preservative as the time during which this amount will keep milk sweet corresponds approximately to the time required for the proteid to fix all the formic aldehyde.

conclusions as to the effect of formic aldehyde upon the digestibility of the proteid constituents of milk, from the mere chemical data above.

With regard to the chemical reactions between formic aldehyde and the products of partial or complete proteid digestion, we must bear in mind again that so far as we know these reactions only take place at unphysiological temperatures[1], and with relatively concentrated solutions of formic aldehyde.

If we direct our attention to the digestion experiments *in vitro* with formic aldehyde, we come to the conclusion that speaking generally under the conditions of these experiments, formic aldehyde has a retarding effect upon the digestion of food by the various enzymes concerned. In the case of peptic digestion this effect is less marked (according to some observers there is no effect) than in the case of pancreatic. The general value of these conclusions is however in our opinion somewhat lessened by the following considerations. All experiments have been made with commercial pepsin or trypsin, except the later pancreatic digestions of Bliss and Novy, from which it is manifest that the difference between the digestibility of formalised and fresh proteid is far less marked in the case of fresh trypsin than in that of commercial. These observers found that, in the case of freshly prepared pancreatic juice, fibrin formalised with 1 in 1,000 formic aldehyde was as digestible as fresh fibrin. Since we have no experimental data with regard to fresh pepsin we cannot tell how this latter would have behaved in the presence of formic aldehyde.

No digestion *in vitro* following physiological sequence has been carried out, in no case has the residue of the gastric digestion of a formalised food been subjected to pancreatic digestion. No quantitative experiments as far as we are aware have been made concerning the most important point under consideration, viz. the gastric digestion of formalised milk.

It has been pointed out by many critics[2] that conclusions from experiments *in vitro* can only be applied to living animals if at all with great caution, since the conditions which obtain in the living stomach are much more complicated, and impossible to imitate *in vitro*. To mention one of the more gross objections we may point out that no attempt is made in experiments *in vitro* to imitate even the mechanical

[1] Lepierre, *loc. cit.* Compare also Schwarz, *loc. cit.*

[2] Rubner, *Leyden's Handb. der Ernährungs-Therapie*, Vol. I. p. 114. Hammarsten, *Lehrb. der physiol. Chemie*, 1895, p. 247, etc.

conditions which obtain in the living stomach, which effect both a continuous churning of the food with the digestive juice, and a continuous removal of the products formed. Further, from the purely biological standpoint, according to the interesting experiments of Pawlow[1], the food seems by virtue of its relative digestibility to have an influence upon the nature of the secretion produced by the stomach to digest it. In addition, a possible stimulant action on the part of formaldehyde must not be overlooked, so far as concerns the secretion of the enzymes and their quality, apart from a possible stimulant action upon their activity. That formic aldehyde seems to have a stimulating action upon certain enzymes may be concluded from the experiments of Macfadyen, Morris and Roland[2] on Buchner's zymase, from those of Weigel and Merkel[3] upon diastase, and from those of Kastle and Loewenhart upon "lipase[4]."

With regard to the experiments on animals, only those interest us in which the formic aldehyde was given by the mouth; even in these the formic aldehyde was in no case given with food, but in a free state in water, and when any effect was produced at all the drug was present in a concentration and in an amount far in excess of that in which it would be given as a preservative in food. So far as concerns the effect of formic aldehyde when given to animals admixed with food, for long periods, the results are conflicting, but, on the whole, seem to show that formic aldehyde in moderate doses has little or no influence upon the growth, weight, and general health of even young animals.

It will be seen from the above criticism that although we are provided with a copious indirect literature, no conclusions, in the absence of direct observations upon man, can be drawn concerning the possible effect upon him of the addition of small doses of formic aldehyde to his food. It was clear to us that the only way to fill this gap in the literature was to make such observations, and the kind of observation best calculated to give exact and definite data for conclusions was in our opinion a series of metabolic experiments.

[1] Pawlow, *Die Arbeit der Verdauungsdrüsen*, 1898.

[2] *Berichte der deutsch. chem. Gesellsch.*, 1900, p. 2782.

[3] *Forschungsberichte über Lebensmitteln*, etc., 1895, p. 91.

[4] *loc. cit.*

Methods.

Our experiments were conducted upon the same three children (*A*, *B* and *C*) who served for our research "On the Influence of Boric Acid and Borax upon the General Metabolism of Children" (*Journ. of Hygiene*, vol. I. p. 168), and the methods employed (*loc. cit.* pp. 172—175 etc.) were identical.

The following table shows the percentage composition of the foods used:—

TABLE I.

SHOWING THE PERCENTAGE COMPOSITION OF FOODS.

——	Specific gravity	Water %	Fat %	Total carbohydrates %	Nitrogen %	Phosphoric acid %	Ash %
				Lactose			
Milk I	1·0329	86·55	4·50	4·92	0·49	0·29	0·69
,, II	1·0331	86·92	3·85	4·03	0·58	0·28	0·70
,, III	1·0320	87·36	3·50	5·21	0·49	0·24	0·69
,, IV	1·0329	87·76	3·37	4·81	0·51	0·23	0·64
				Dextrose			
Bread I ...	—	36·10	0·51	47·47	1·48	0·36	—
,, II ...	—	40·13	0·11	39·21	1·50	0·18	—
,, III ...	—	35·77	0·24	55·48	1·32	0·19	—
,, IV ...	—	29·83	0·23	59·13	1·78	0·27	0·89
,, V ...	—	34·42	0·11	60·80	1·55	0·19	0·89
				Lactose			
Butter I ...	—	12·46	86·44	0·36	0·02	—	0·65
,, II ...	—	12·82	85·44	0·21	0·13	—	0·72
,, III ...	—	12·89	85·31	0·40	0·12	—	0·61
,, IV ...	—	12·68	86·00	0·14	0·11	—	0·50
Meat I ...	—	75·00	5·38	—	2·95	0·41	—
,, Veal II ...	—	74·13	0·78	—	3·79	0·55	—
,, III ...	—	72·12	6·31	—	3·08	0·51	—
,, IV ...	—	72·60	6·67	—	3·23	0·53	1·00
,, V ...	—	69·04	7·12	—	3·52	0·46	1·07
,, VI ...	—	74·48	4·62	—	3·74	0·46	1·00
				Dextrose			
Apple I	—	70·08	—	25·20	0·04	0·04	0·35
,, Compote II	—	56·66	—	37·66	0·05	0·05	0·38
,, ,, III	—	69·86	—	30·25	0·05	0·04	0·33
				Dextrose			
Toffee	—	1·06	2·20	18·24	0·03	—	—

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OBSERVATION I. CHILD A.

The child was a healthy boy aged 2½ years, weighed 14·6 kilos, and remained in good health throughout the whole observation. He consumed daily as follows, 200 g. of bread, 550 c.c. of milk, 20 g. of butter, 30 g. of meat, 50 g. of apple compote, 10 g. of sugar, 50 c.c. of water, 5 g. of toffee. This diet was very well taken and adhered to throughout the experiment. The whole observation extended over 28 days, seven days being taken for a fore period, and seven days for an after period; during the intermediate 14 days formic aldehyde was administered. In the first seven days of this intermediate period formic aldehyde was given in the morning and evening milk in such quantity that it was present in the proportion of 1 in 10,000: the actual quantity given per day was 0·05 g. formic aldehyde in 500 c.c. of milk. The formic aldehyde was added to the milk in the morning about 7.30 a.m.: 250 c.c. of the milk were taken at about 8.30 a.m., and 250 c.c. at 5 p.m.: it will be seen therefore that we not only gave freshly formalised milk, but milk which had been exposed to the action of formic aldehyde for a considerable time. The whole food per diem weighed approximately 900 g., it therefore follows that the total food and drink during the first week of the formic aldehyde period was formalised to the extent of 1 in 18,000. During the second formic aldehyde period the dose of formic aldehyde was doubled, viz. 0·10 g. per diem, equal to 1 in 5,000 in milk, and 1 in 9,000 in total food and drink. The increased dose, viz. 0·05 g., was occasionally given with the meal at dinner and occasionally in the milk. The analytical results obtained throughout the observation are recorded in the following table:

Table II.

Showing the Influence of Formic Aldehyde

PERIOD	—	Date	Dose	URINE						
			g	Quantity c.c.	Reaction	Specific gravity	Total sulphuric acid g	Ethereal sulphuric acid g	Uric acid g	Nitroge[n] g
FORE PERIOD		2 IV		375	Acid	1·0220	0·8925	0·0533	0·1823	5·07
		3 ,,		375	,,	1·0235	0·8925	0·0533	0·1823	5·35
		4 ,,		410	Amphoteric	1·0200	1·0016	0·0538	0·2337	5·22
		5 ,,		340	Acid	1·0250	0·8305	0·0446	0·1938	5·55
		6 ,,		330	,,	1·0230	0·8061	0·0433	0·1881	5·13
		7 ,,		375	Amphoteric	1·0225	0·9160	0·0492	0·2137	5·05
		8 ,,		320	Acid	1·0242	0·8841	0·0533	0·2160	5·60
	Total	7 days		2,525			6·2233	0·3508	1·4099	36·97
	Average	*1 day*		*360*		*1·0229*	*0·8890*	*0·0501*	*0·2014*	*5·28*
FIRST FORMIC ALDEHYDE PERIOD		9 IV	0·05	270	Acid	1·0269	0·7460	0·0449	0·1822	4·82
		10 ,,	0·05	315	,,	1·0260	0·8703	0·0524	0·2126	5·30
		11 ,,	0·05	320	,,	1·0259	0·8841	0·0532	0·2160	5·42
		12 ,,	0·05	320	,,	1·0260	0·8841	0·0532	0·2160	5·43
		13 ,,	0·05	405	,,	1·0179	0·8925	0·0550	0·2157	4·75
		14 ,,	0·05	320	,,	1·0270	0·7052	0·0435	0·1704	5·55
		15 ,,	0·05	270	,,	1·0289	0·5950	0·0367	0·1438	4·80
	Total	7 days	0·35	2,220			5·5777	0·3380	1·3567	36·07
	Average	*1 day*	*0·05*	*317*		*1·0255*	*0·7968*	*0·0484*	*0·1938*	*5·15*
SECOND FORMIC ALDEHYDE PERIOD		16 IV	0·1	325	Acid	1·0260	0·7162	0·0441	0·1731	5·19
		17 ,,	0·1	445	,,	1·0175	0·9860	0·0604	0·2370	4·96
		18 ,,	0·1	315	,,	1·0235	0·9131	0·0494	0·2126	5·19
		19 ,,	0·1	300	,,	1·0240	0·8697	0·0470	0·2025	5·01
		20 ,,	0·1	310	,,	1·0262	0·8986	0·0487	0·2092	5·08
		21 ,,	0·1	270	,,	1·0266	0·7827	0·0423	0·1822	5·33
		22 ,,	0·1	295	,,	1·0293	0·8552	0·0463	0·1991	5·83
	Total	7 days	0·7	2,260			6·0215	0·3382	1·4157	36·59
	Average	*1 day*	*0·1*	*323*		*1·0247*	*0·8602*	*0·0483*	*0·2022*	*5·22*
AFTER PERIOD		23 IV		355	Acid	1·0269	0·8516	0·0494	0·1679	5·47
		24 ,,		295	,,	1·0272	0·7077	0·0410	0·1395	5·09
		25 ,,		370	,,	1·0215	0·8875	0·0514	0·1750	4·89
		26 ,,		370	Amphoteric	1·0230	0·8875	0·0514	0·1750	5·28
		27 ,,		350	Acid	1·0200	0·8396	0·0487	0·1655	4·47
		28 ,,		415	Amphoteric	1·0200	0·9396	0·0624	0·2428	6·01
		29 ,,		345	,,	1·0200	0·7811	0·0419	0·2018	4·86
	Total	7 days		2,500			5·8946	0·3562	1·2675	36·07
	Average	*1 day*		*360*		*1·0227*	*0·8421*	*0·0509*	*0·1810*	*5·15*

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TABLE II.

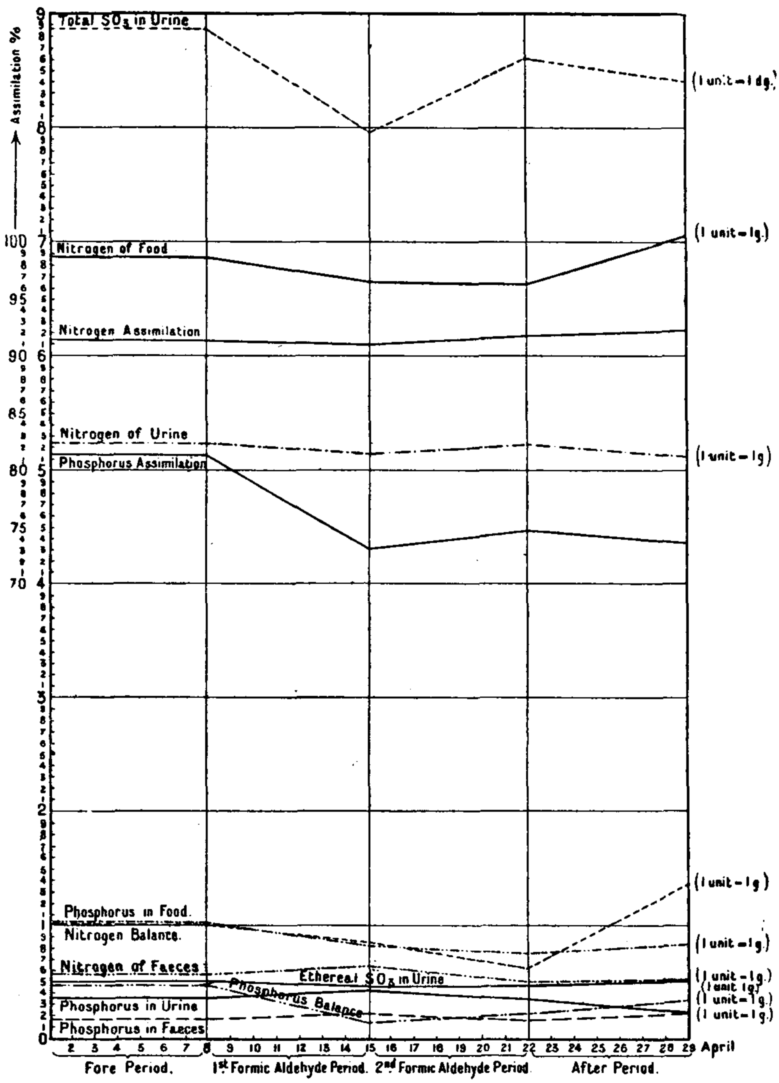
UPON THE GENERAL METABOLISM OF CHILD A.

FAECES				Nitrogen of food	Balance	Body weight	PHOSPHORUS				FAT		
Moist	Dry	Water %	Nitrogen				Urine	Faeces	Food	Balance	Faeces	Food	Balance
g	g		g	g	g	kg	g	g	g	g	g	g	g
65	9·0	86·2	0·56	6·56	+0·93	14·61	0·4436	0·1809	1·10	+0·48	2·40	44·77	+42·37
49	9·2	81·2	0·58	6·81	+0·88		0·4436	0·1809	1·16	+0 54	2·45	47·02	+44·57
64	12·5	85·9	0·78	6·81	+0·81		0·3805	0·2440	1·18	+0·55	3·33	47·02	+43·69
—	—	—	—	6·85	+1·30		0·3155	—	1·02	+0·70	—	44·84	+44·84
68	14·5	78·7	0·84	6·60	+0·73		0·3062	0·2779	0·96	+0·44	3·81	38·82	+35·01
60	11·5	80·8	0·66	7·41	+1·70		0·3480	0·2255	0·96	+0·39	3·02	40·74	+37·72
59	12·4	77·3	0·72	7·16	+0·84	14·39	0·4838	0·2365	0·96	+0·24	3·26	40·74	+37·48
365	69·1		4·14	48·20	+7·19	− *220g.*	2·7212	1·3457	7·34	+3·34	18·27	303·95	+285·68
52	*96*	*81·7*	*0·59*	*6·88*	*+1·02*	*Loss*	*0·3887*	*0·1922*	*1·05*	*+0·48*	*2·61*	*43·42*	*+40·81*
51	11·4	77·7	0·68	7·16	+1·66	14·39	0·4082	0·2463	0·90	+0·25	2·97	40·48	+37·51
64	11·0	82·8	0·65	7·16	+1·21		0·4762	0·2376	0·90	+0·19	2·86	40·74	+37·88
41	8·4	79·6	0·49	6·79	+0·88		0·4838	0·1816	0·90	+0·23	2·19	40·74	+38·55
88	15·0	82·9	0·90	6·53	+0·20		0·4838	0·3242	0·79	−0·02	3·91	38·79	+34·88
—	—	—	—	6·32	+1·57		0·4957	—	0·79	+0·29	—	38·79	+38·79
76	15·2	80·0	0·88	6·33	−0·10		0·3917	0·3085	0·79	+0·09	3·76	38·79	+35·03
115	15·5	86·5	0·89	6·33	+0·64	14·61	0·3304	0·3147	0·79	+0·14	3·83	38·79	+34·96
435	76·5		4·49	46·62	+6·06	+ *220g.*	3·0698	1·6129	5·86	+1·17	19·52	277·12	+257·60
62	*10·9*	*82·6*	*0·64*	*6·66*	*+0·87*	*Gain*	*0·4385*	*0·2304*	*0·84*	*+0·17*	*2·79*	*39·59*	*+36·80*
—	—	—	—	6·33	+1·14	14·61	0·3978	—	0·79	+0·39	—	38·79	+38·79
—	—	—	—	6·38	+1·42		0·5447	—	0·79	+0·25	—	38·90	+38·90
82	20·0	75·6	1·17	6·38	+0·02		0·3238	0·4615	0·79	+0·00	5·14	38·90	+33·76
55	11·2	79·6	0·66	6·38	+0·71		0·3084	0·2585	0·79	+0·22	2·87	38·90	+36·03
70	13·7	80·4	0·80	6·38	+0·50		0·3186	0·3162	0·79	+0·16	3·52	38·90	+35·38
—	—	—	—	6·38	+1·05		0·2773	—	0·79	+0·51	—	38·90	+38·90
65	15·5	76·2	0·91	6·39	−0·35	14·72	0·3033	0·3577	0·78	+0·12	3·98	39·04	+35·06
272	60·4		3·54	44·62	+4·49	+ *110g.*	2·4739	1·3939	5·52	+1·65	15·51	272·33	+256·82
39	*8·6*	*77·9*	*0·51*	*6·37*	*+0·64*	*Gain*	*0·3534*	*0·1991*	*0·79*	*+0·23*	*2·22*	*38·90*	*+36·69*
57	14·8	74·0	0·87	7·31	+0·97	14·72	0·1974	0·3326	0·86	+0·33	4·08	39·02	+34·94
54	10·8	80·0	0·63	7·31	+1·59		0·1640	0·2427	0·86	+0·45	2·98	39·02	+36·04
61	13·2	78·4	0·77	7·39	+1·73		0·2057	0·2966	0·86	+0·36	3·64	38·31	+34·67
48	12·0	75·0	0·67	6·92	+0·97		0·2057	0·2882	0·78	+0·29	3·04	37·32	+34·28
—	—	—	—	6·92	+2·45		0·1946	—	0·78	+0·59	—	37·46	+37·46
—	—	—	—	6·92	+0·91		0·2922	—	0·78	+0·49	—	37·46	+37·46
106	14·9	85·9	0·84	6·92	+1·22	15·00	0·2429	0·3579	0·78	+0·18	3·78	37·46	+33·68
326	65·7		3·78	49·69	+9·84	+ *280g.*	1·5025	1·5180	5·70	+2·69	17·52	266·05	+248·53
47	*9·4*	*80·0*	*0·54*	*7·09*	*+1·40*	*Gain*	*0·2146*	*0·2168*	*0·81*	*+0·38*	*2·70*	*38·01*	*+35·50*

The results expressed in the above table are graphically represented in the following curves:

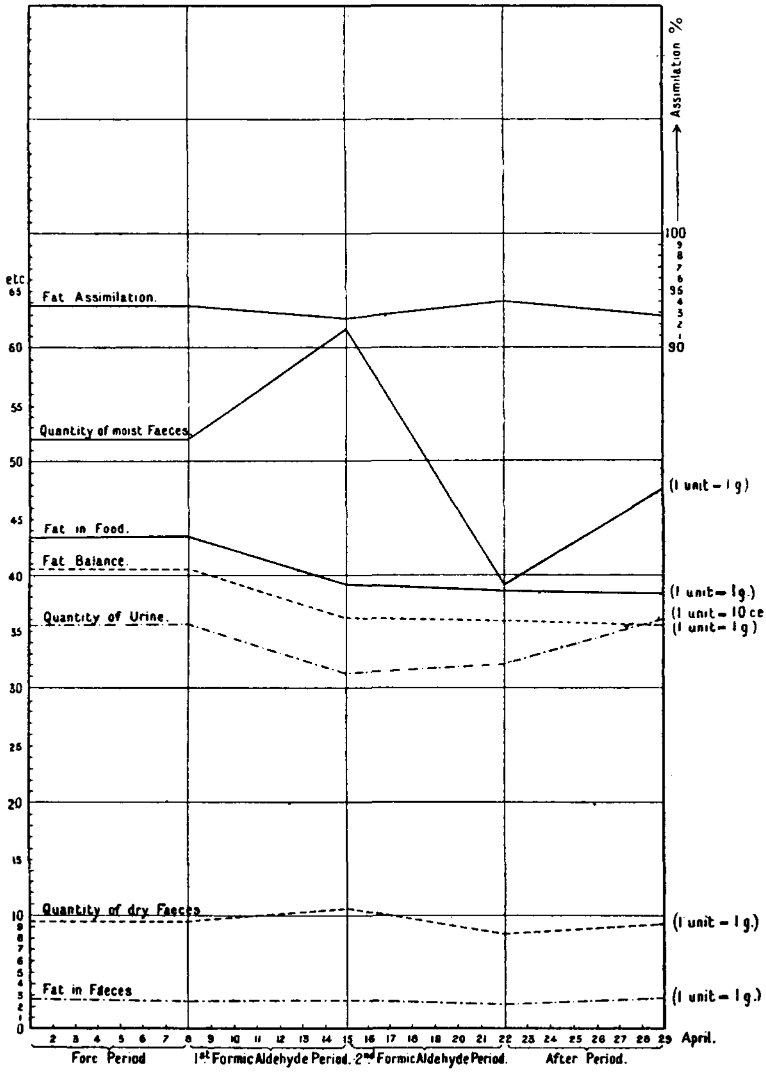
CURVE I.,

showing the influence of formic aldehyde upon nitrogen and phosphorus metabolism, etc.



CURVE II.,

showing the influence of formic aldehyde upon fat assimilation and quantity of faeces and urine.



Referring to the tables and curves relating to the *first observation*, we will classify our remarks under the following headings:

Nitrogen Metabolism.

In the fore period the daily quantity of nitrogen taken in the food was 6·88 g., of which 0·59 g. was not assimilated, being lost with the faeces, corresponding to 8·58 %. The assimilation of nitrogen in the fore period amounted therefore to 91·42 %.

With the urine 5·28 g. of nitrogen were excreted, and if this be subtracted from the amount assimilated we obtain a daily balance of + 1·02.

To avoid repetition we give the results with regard to the nitrogen balance and assimilation during the different periods in tabular form:

—	Fore period	First F.A. period	Second F.A. period	After period
Nitrogen of Food	6·88	6·66	6·37	7·09
,, ,, Urine	5·28 }	5·15 }	5·22 }	5·15 }
,, ,, Faeces	0·59 }	0·64 }	0·51 }	0·54 }
Balance	+1·02	+0·87	+0·64	+1·40
Assimilation %	91·42	91·22	91·99	92·38
Nitrogen % in dry Faeces ...	6·1	5·9	5·9	5·8

From these results we are justified in drawing the conclusion that the formic aldehyde had no appreciable influence upon proteid metabolism in the case of this child. If with the necessary restrictions we regard the nitrogen excreted in the faeces as an index of the digestibility of the food, we find that in this case the addition of formic aldehyde to the proteid constituents of the food has been without influence in this direction. This is best seen from the average percentage of nitrogen in the faeces in the several periods. The assimilation and the balance are likewise not affected.

Phosphorus Metabolism.

The daily average of phosphorus in the food in the fore period was 1·05 g., of which 0·1922 were lost, being excreted in the faeces. Phosphorus was therefore assimilated to the extent of 81·70 %. The relative excretion, etc. of phosphorus in the four periods we give in tabular form:

—	Fore period	First F.A. period	Second F.A. period	After period
Phosphorus of Food	1·05	0·84	0·79	0·81
,, ,, Urine	0·3887	0·4385	0·3534	0·2146
,, ,, Faeces	0·1922	0·2304	0·1991	0·2168
Balance	+0·48	+0·17	+0·23	+0·38
Assimilation %	81·70	72·57	74·80	73·24
Phosphorus % in dry Faeces ...	2·0	2·1	2·3	2·3

From these figures it will be seen that the absolute quantity of phosphorus in the urine in the first formic aldehyde period is slightly increased (·05 g.), in the second formic aldehyde period it falls, however, slightly below the fore period value and in the after period still further. As at the same time the assimilation of phosphorus as measured by the phosphorus excreted in the faeces is somewhat lessened, it would seem that during the first period formic aldehyde tended to stimulate phosphorus metabolism. The absolute changes are however so small that they can only be regarded as indicating what might be the possible effect of formic aldehyde in larger doses.

Fat Assimilation.

The daily average of fat in the food during the fore period was 43·42 g., of this 2·61 was lost, being excreted with the faeces, leaving a balance of + 40·81 g. The assimilation therefore amounted to 93·99 %. These results and those of the following periods are recorded in tabular form:

—	Fore period	First F.A. period	Second F.A. period	After period
Fat in Food	43·42	39·59	38·90	38·01
,, Faeces	2·61	2·79	2·22	2·70
Fat balance	+40·81	+36·80	+36·69	+35·50
Assimilation %	93·99	92·96	94·30	92·90
Fat % in dry Faeces	27·1	25·6	25·8	28·7

From these figures it will be seen that the quantity of fat in the faeces during the formic aldehyde periods did not increase, if anything decreased, in proportion to the faeces. The fat assimilation and fat balance remained unaffected.

In connection with the fat in the faeces, we estimated the *lecithin*

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according to the method described above. The results expressed as a percentage of total fat are as follows:

—	Fore period	First F.A. period	Second F.A. period	After period
Lecithin in grammes of 100 g. fat	15·08	11·31	13·16	4·28

As we enter into this subject later, we would only point out here that formic aldehyde seemed to have an influence in diminishing the excretion of lecithin by the faeces, and that this influence extended into the after period.

Having considered the most important factors in metabolism as investigated by us and drawn the conclusion that formic aldehyde had little if any influence upon them, we turn our attention to certain other factors which although of minor importance ought not to be overlooked.

On referring to the chief table (Table II)[1] it will be seen that the total *quantity of urine* in the first formic aldehyde period decreased, whilst the quantity of faeces and especially their percentage of water increased. In the second formic aldehyde period the quantity of urine increased slightly, whilst the quantity of faeces and their water percentage decreased. It would thus seem that formic aldehyde had a tendency to produce a retention of water by the body. A rise in the specific gravity of the urine occurred *pari passu* with its diminution of volume.

If we regard the *uric acid* figures during this observation we shall see that the average excretion of uric acid during the first formic aldehyde period underwent a very slight diminution along with the total nitrogen, and this would justify us in concluding that the urea and ammonia varied in the same direction. The analytical figures so far as concerns the average total *sulphuric acid* excretion show that formic aldehyde exerted upon it a barely appreciable effect, suggesting in connection with the nitrogen figures above, if we draw conclusions from them at all, that formic aldehyde exerted a slightly inhibitory action upon the breaking up of proteids in the body. Even these conclusions can only be applied to the first formic aldehyde period taken as a whole.

[1] In these remarks throughout the entire paper we refer to the average daily excretion in question.

The strongly antiseptic properties of formic aldehyde render an inquiry as to its effect upon intestinal putrefaction, as measured by the quantity of ethereal sulphates in the urine, of interest. If we refer to the absolute figures in Table II we are forced to the conclusion that the slight diminution of ethereal sulphates which occurred during both formic aldehyde periods is not sufficient to indicate any inhibitory effect upon intestinal putrefaction[1]. This seems to show that when formic aldehyde is taken with the food in these proportions, it does not in healthy children occur as such in the intestines.

So far as concerns body-weight, it will be observed that there was a slight increase in the two formic aldehyde periods, which seems however to be due not to an increased flesh formation or fat retention, but to a retention of water as indicated by the diminished excretion of water in the urine or faeces.

The results relevant to the observations made above are summarised in the following table:

TABLE II A.

—	Nitrogen assimilation, %	% N. of dry faeces	Phosphorus assimilation, %	% P. of dry faeces	Fat assimilation, %	% Fat of dry faeces	$\frac{A}{B}$ *	$\frac{N}{SO_3}$ †
Fore period ...	91·42	6·1	81·70	2·0	93·99	27·1	16·7	6·1
First F.A. period	91·22	5·9	72·57	2·1	92·96	25·6	15·5	6·4
Second F.A. period	91·99	5·9	74·80	2·3	94·30	28·8	16·9	6·1
After period ...	92·38	5·8	73·24	2·3	92·90	28·7	15·5	6·1

* $\frac{A}{B} = \frac{\text{Inorganic } SO_3}{\text{Ethereal } SO_3}$.

† $\frac{N}{SO_3} = \frac{\text{Nitrogen of Urine}}{SO_3 \text{ of Urine}}$.

OBSERVATION II. CHILD B.

The child was a healthy boy aged 5 years, weighing 17·2 kilos, and remained in good health throughout the whole observation. He consumed daily 250 g. of bread, 600 c.c. of milk, 20 g. of butter, 50 g. of meat, 50 g. of apple compote, 10 g. of sugar, 50 c.c. of water, and 5 g. of toffee. The duration and arrangement of the observation was as in Child A. The formic aldehyde was administered in an identical manner and dose, but as in this case the total food was slightly increased, the proportion of formic aldehyde in it was slightly less. The analytical results obtained throughout this observation are recorded in the following table:

[1] The ratio of total sulphuric acid to actual sulphuric acid is likewise not affected; further, as has been pointed out by many observers, this ratio is of no special importance.

Table III.

Showing the Influence of Formic Aldehyde

Period	—	Date	Dose g	Urine: Quantity c.c.	Reaction	Specific gravity	Total sulphuric acid g	Ethereal sulphuric acid g	Uric acid g	Nitrogen g
Fore period		2 IV.		340	Acid	1·0220	0·7782	0·0623	0·1122	4·58
		3 ,,		360	,,	1·0195	0·8240	0·0659	0·1188	4·92
		4 ,,		390	,,	1·0225	1·0600	0·0819	0·1346	6·03
		5 ,,		150	,,	1·0290	0·4076	0·0315	0·0518	2·61
		6 ,,		540	,,	1·0260	1·4674	0·1135	0·1863	9·76
		7 ,,		360	,,	1·0260	0·9783	0·0756	0·1242	6·09
		8 ,,		390	,,	1·0249	1·1890	0·0750	0·1082	6·82
	Total	7 days		2,530			6·7045	0·5057	0·8361	40·81
	Average	*1 day*		*361*		*1·0245*	*0·9578*	*0·0772*	*0·1194*	*5·83*
First formic aldehyde period		9 IV.	0·05	300	Acid	1·0295	0·9146	0·0577	0·0833	6·02
		10 ,,	0·05	325	,,	1·0300	0·9908	0·0625	0·0902	6·82
		11 ,,	0·05	335	,,	1·0280	1·0210	0·0644	0·0929	6·73
		12 ,,	0·05	365	,,	1·0240	1·1130	0·0702	0·1013	5·63
		13 ,,	0·05	345	,,	1·0252	0·9736	0·0627	0·0647	5·78
		14 ,,	0·05	270	,,	1·0300	0·7619	0·0490	0·0506	5·27
		15 ,,	0·05	335	,,	1·0305	0·9453	0·0608	0·0628	6·55
	Total	7 days	0·35	2,275			6·7202	0·4273	0·5458	42·80
	Average	*1 day*	*0·05*	*325*		*1·0282*	*0·9600*	*0·0610*	*0·0779*	*6·12*
Second formic aldehyde period		16 IV.	0·1	345	Acid	1·0220	0·9736	0·0627	0·0647	5·17
		17 ,,	0·1	410	,,	1·0215	1·1570	0·0745	0·0769	5·82
		18 ,,	0·1	395	,,	1·0226	1·1755	0·0729	0·1185	6·01
		19 ,,	0·1	380	,,	1·0245	1·1131	0·0702	0·1140	6·73
		20 ,,	0·1	280	,,	1·0280	0·8332	0·0517	0·0840	5·35
		21 ,,	0·1	380	,,	1·0255	1·1131	0·0702	0·1140	6·29
		22 ,,	0·1	275	,,	1·0293	0·8183	0·0508	0·0825	5·59
	Total	7 days	0·7	263			7·1838	0·4530	0·6546	40·96
	Average	*1 day*	*0·1*	*323*		*1·0247*	*1·0262*	*0·0647*	*0·0935*	*5·85*
After period		23 IV.		395	Acid	1·0276	0·8998	0·0536	0·0593	6·18
		24 ,,		495	,,	1·0180	1·1276	0·0672	0·0743	5·49
		25 ,,		410	,,	1·0275	0·9337	0·0557	0·0615	7·39
		26 ,,		535	,,	1·0190	1·2184	0·0726	0·0803	6·41
		27 ,,		480	,,	1·0210	1·0934	0·0652	0·0720	6·55
		28 ,,		560	,,	1·0190	1·2710	0·0795	0·0420	7·38
		29 ,,		455	,,	1·0200	1·0330	0·0646	0·0341	6·62
	Total	7 days		3,330			7·5769	0·4584	0·4235	46·02
	Average	*1 day*		*476*		*1·0216*	*1·0824*	*0·0655*	*0·0605*	*6·57*

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Table III.

upon the General Metabolism of Child B.

Faeces: Moist g	Faeces: Dry g	Faeces: Water %	Faeces: Nitrogen g	Nitrogen of food g	Balance g	Body weight kg	Phosphorus: Urine g	Phosphorus: Faeces g	Phosphorus: Food g	Phosphorus: Balance g	Fat: Faeces g	Fat: Food g	Fat: Balance g
85	19·5	77·1	1·24	7·15	+1·33	17·21	0·8092	0·3918	1·14	−0·06	4·87	45·85	+40·98
7	2·2	68·6	0·14	7·40	+2·34		0·8568	0·0454	1·20	+0·30	0·56	48·10	+47·54
56	13·0	76·8	0·85	7·40	+0·52		0·5413	0·2681	1·20	+0·39	3·33	48·10	+44·77
112	21·5	80·8	1·24	7·44	+3·59		0·2082	0·5215	1·07	+0·34	5·59	45·00	+39·41
—	—	—	—	7·19	−2·57		0·7495	—	1·01	+0·26	—	38·98	+38·98
57	15·4	73·0	0·89	8·01	+1·03		0·4994	0·3736	1·01	+0·14	4·01	40·90	+36·89
—	—	—	—	9·17	+2·35	17·27	0·5974	—	1·05	+0·45	—	40·96	+40·96
317	71·6		4·36	53·76	+8·59	*Total Gain*	4·2618	1·6004	7·68	+1·82	18·36	307·89	+289·53
45	*10·2*	*77·4*	*0·62*	*7·68*	*+1·23*	*+60g.*	*0·6088*	*0·2286*	*1·09*	*+0·26*	*2·62*	*43·98*	*+41·36*
9	3·0	66·7	0·22	8·82	+2·58	17·27	0·4596	0·0798	1·04	+0·50	0·71	43·72	+43·01
39	8·0	79·5	0·57	8·82	+1·43		0·4979	0·2128	1·04	+0·33	1·90	43·72	+41·82
126	31·7	74·8	2·28	8·37	−0·64		0·5132	0·8432	1·04	−0·32	7·54	44·04	+36·50
—	—	—	—	8·06	+2·43		0·5592	—	0·92	+0·36	—	41·92	+41·92
81	17·5	78·4	0·58	7·84	+1·48		0·4982	0·4449	0·92	−0·02	4·16	41·92	+37·76
—	—	—	—	7·85	+2·58		0·3899	—	0·92	+0·53	—	41·92	+41·92
75	20·0	73·3	0·67	7·85	+0·63		0·4838	0·5085	0·92	−0·07	4·75	41·92	+37·17
330	80·2		4·32	57·61	+10·49		3·4018	2·0892	6·80	+1·32	19·06	299·16	+280·07
47	*11·5*	*75·7*	*0·62*	*8·23*	*+1·49*		*0·4859*	*0·2984*	*0·97*	*+0·19*	*2·72*	*42·73*	*+40·01*
—	—	—	—	7·85	+2·68		0·4982	—	0·92	+0·42	—	41·92	+41·92
100	24·5	75·5	0·80	7·95	+1·33		0·5920	0·6229	0·92	−0·29	5·82	42·10	+36·28
—	—	—	—	7·95	+1·94		0·5799	—	0·92	+0·34	—	42·10	+42·10
54	9·0	83·3	0·53	7·95	+0·69		0·5579	0·2384	0·92	+0·12	2·25	42·10	+39·85
85	21·6	74·6	1·26	7·95	+1·34		0·4110	0·5722	0·92	−0·06	5·41	42·10	+36·69
19	5·3	72·1	0·31	7·95	+1·35		0·5579	0·1404	0·92	+0·22	1·33	42·10	+40·77
57	15·7	72·5	0·92	8·06	+1·55	17·49	0·4037	0·4159	0·91	+0·09	3·93	42·33	+38·40
315	76·1		3·82	55·66	+10·88	*Total Gain*	3·6006	1·9898	6·43	+0·84	18·74	294·65	+276·01
45	*10·8*	*75·8*	*0·54*	*7·95*	*+1·56*	*+270*	*0·5143*	*0·2842*	*0·92*	*+0·12*	*2·68*	*42·09*	*+39·43*
50	11·6	76·8	0·69	8·76	+1·89	17·49	0·4298	0·2679	1·01	+0·31	2·53	42·31	+39·78
—	—	—	—	9·21	+3·72		0·5386	—	1·01	+0·47	—	42·31	+42·31
88	21·8	75·0	1·31	9·31	+0·61		0·4461	0·5034	1·01	+0·06	4·75	41·53	+36·78
—	—	—	—	8·59	+2·18		0·5820	—	0·91	+0·33	—	39·98	+39·98
51	12·4	75·7	0·75	8·59	+1·29		0·5222	0·3289	0·91	+0·06	2·77	40·12	+37·35
61	14·9	75·6	0·89	8·59	+0·32		0·4816	0·3952	0·91	+0·03	3·32	40·12	+36·80
87	16·2	81·4	0·97	8·59	+1·00	17·49	0·3913	0·4296	0·91	+0·09	3·62	40·12	+36·50
337	76·9		4·61	61·64	+11·01	*Gain*	3·3916	1·9250	6·67	+1·35	16·99	306·49	+269·50
48	*10·9*	*77·2*	*0·66*	*8·80*	*+1·57*	*∓0*	*0·4845*	*0·2750*	*0·95*	*+0·19*	*2·42*	*43·78*	*+38·50*

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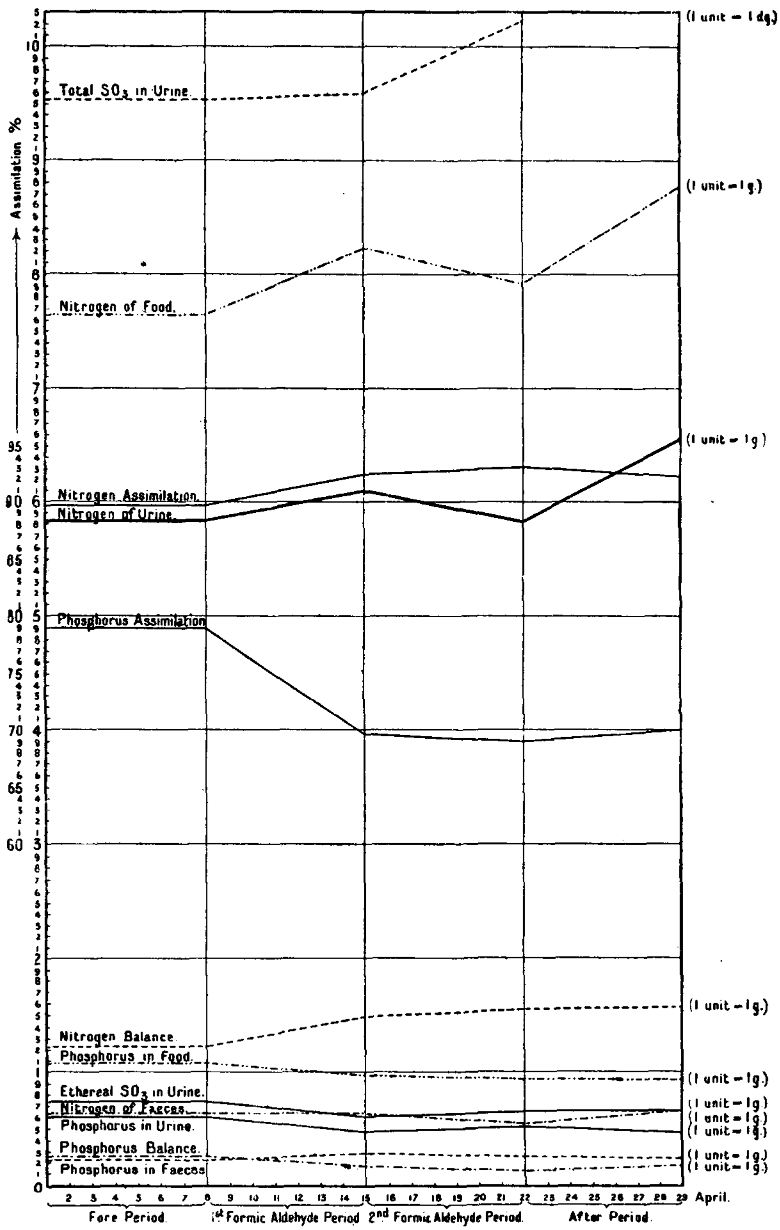
The results expressed in the above table are graphically represented in the following curves:

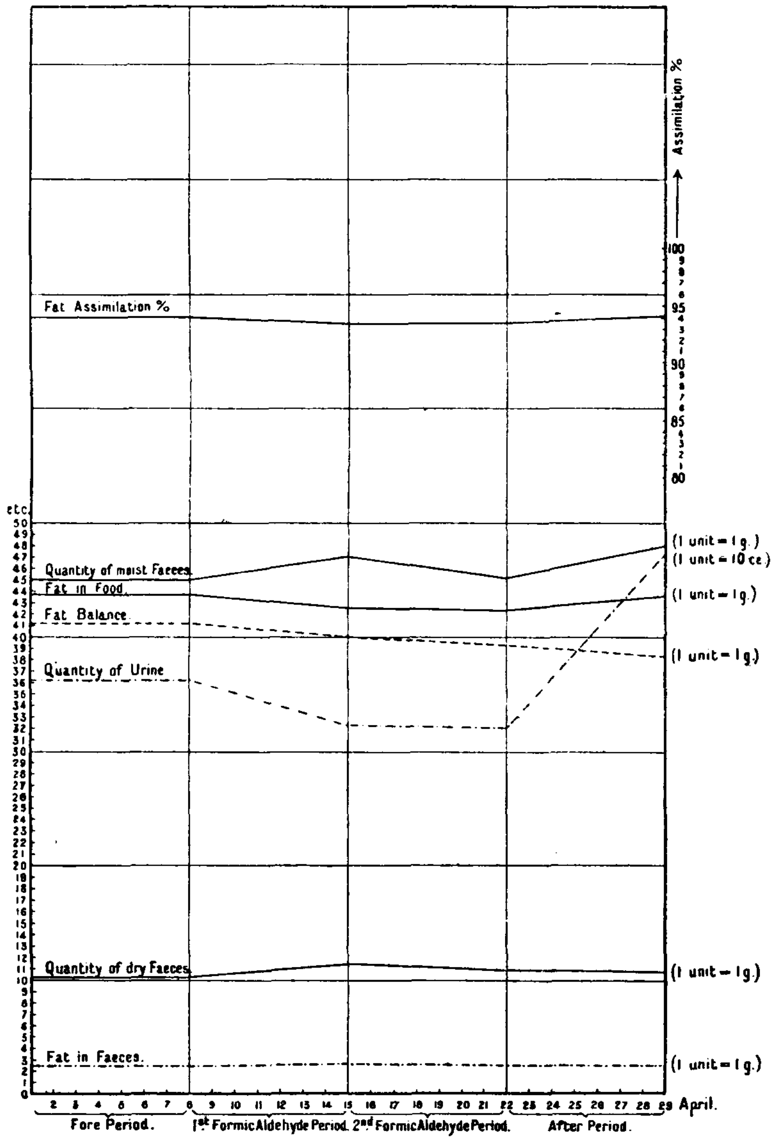
CURVE III.,

showing the influence of formic aldehyde upon nitrogen and phosphorus metabolism, etc.



Curve IV.,

showing the influence of formic aldehyde upon fat assimilation and the quantity of faeces and urine.



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Nitrogen Metabolism.

Adopting the same method of reasoning as in Observation I. we arrive at the following results with regard to the nitrogen balance and assimilation. These are best expressed in a tabular form.

—	Fore period	First F.A. period	Second F.A. period	After period
Nitrogen of Food	7·68	8·23	7·95	8·80
„ „ Urine	5·83 }	6·12 }	5·85 }	6·57 }
„ „ Faeces	0·62 }	0·62 }	0·54 }	0·66 }
Balance	+1·23	+1·49	+1·56	+1·57
Assimilation %	89·82	92·46	93·21	92·50
Nitrogen % in dry Faeces ...	6·0	5·4	5·0	6·0

From these results we can draw the conclusion that formic aldehyde in both periods seemed to have a slightly beneficial effect upon proteid assimilation. This is indicated by a rise in the percentage of nitrogenous food assimilated. The nitrogen percentage of the faeces shows a diminution. This result may find an explanation in a stimulating action of formic aldehyde upon the secretion of the digestive enzymes.

Phosphorus Metabolism.

The results in this connection expressed in a tabular form are as follows:

—	Fore period	First F.A. period	Second F.A. period	After period
Phosphorus of Food	1·09	0·97	0·92	0·95
„ „ Urine	0·6088 }	0·4859 }	0·5413 }	0·4845 }
„ „ Faeces	0·2286 }	0·2984 }	0·2842 }	0·2750 }
Balance	+0·26	+0·19	+0·12	+0·19
Assimilation %	79·03	69·23	69·11	71·05
Phosphorus in dry Faeces % ...	2·2	2·6	2·6	2·5

From the above table it will be seen that the absolute differences in the several periods are small. Nevertheless if any positive conclusion may be drawn, it is in this case that the formic aldehyde had a slightly depressing effect upon the assimilation of phosphorus as expressed by the slight increase of the phosphorus in the faeces. It must not be overlooked that the percentage figures in this case are a very large

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magnification of the absolute variations in amount. The formic aldehyde seemed to have no influence in stimulating the breaking down of the phosphorus-containing substances in the body itself; in fact there seems to be a suggestion, from the diminished amount of phosphorus in the urine, that it acted in the opposite direction.

Fat Assimilation.

As in the preceding cases we express these results for the sake of convenience in the following tables:

—	Fore period	First F.A. period	Second F.A. period	After period
Fat in Food	43·98	42·73	42·09	43·78
,, Faeces	2·62	2·72	2·68	2·42
Balance	+41·36	+40·01	+39·43	+38·50
Assimilation %	94·05	93·63	93·63	94·47
Fat in dry Faeces %	25·7	23·7	24·8	22·1

From these figures it will be seen that the remarks we made with regard to the effect of formic aldehyde upon fat assimilation in Observation I. hold good in this case, viz. that there is no influence.

In so far as concerns lecithin the following figures express our results:

—	Fore period	First F.A. period	Second F.A. period	After period
Lecithin in grammes of 100 g. fat	21·09	22·60	14·59	17·30

Formic aldehyde seems to have the same influence here as in Observation I.

With regard to the remaining factors of general metabolism in this case it will be seen from the chief table (Table III) that the *quantity of urine* as in Observation I. decreased in the first formic aldehyde period, but that the influence upon the quantity of faeces and their water content is less marked. In the second formic aldehyde period the quantity of urine continued to be less than that of the fore period, whilst the *quantity of faeces* and their water content remained practically constant. In the after period the quantity of urine increased to an amount exceeding that of the fore period. The quantity of faeces

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and their water content remained in this period also constant. It would seem therefore that, as in the former case, formic aldehyde had a tendency to cause a retention of water in the body. The reaction of the urine remained acid through the whole observation. The *uric acid* excretion diminished to some extent in the formic aldehyde period, while the total nitrogen and the total sulphuric acid remained practically unaffected. If the slightness of the changes do not preclude us from drawing any conclusions at all, we should infer that in this case formic aldehyde exerted a specific action upon either the formation or retention of uric acid. The result in this case is the more interesting in that this child seemed to belong to the uric acid type. Under the influence of formic aldehyde the *ethereal sulphates* of the urine underwent a slight diminution; this was more pronounced than in Observation I. There seemed, however, to be practically no action upon intestinal putrefaction. We are the more entitled to draw this conclusion as the indoxyl reaction was equally intense throughout the whole observation. The *body weight* as in the former observation went up in the formic aldehyde period and remained constant in the after period. The increase in the formic aldehyde periods must be ascribed rather to a retention of water than to actual growth. We may epitomise the above observations in tabular form as follows:

TABLE III A.

——	Nitrogen assimilation %	% N. of dry faeces	Phosphorus assimilation %	% P. of dry faeces	Fat assimilation %	% fat of dry faeces	$\frac{A}{B}$ *	$\frac{N}{SO_3}$ †
Fore period ...	91·42	6·1	81·00	2·0	93·99	27·1	16·7	6·1
First F.A. period	91·22	5·9	72·57	2·1	92·96	25·6	15·5	6·4
Second F.A. period	91·99	5·9	74·80	2·3	94·30	25·8	16·9	6·1
After period ...	92·38	5·8	73·24	2·3	92·90	28·7	15·5	6·1

* As in Table II A. † As in Table II A.

OBSERVATION III. CHILD C.

This child was a delicate girl, aged four years; she was convalescent from pneumonia and was, as compared with the other children, ill-nourished, and poorly developed. Her weight was 15 kilos. She consumed daily 200 g. of bread, 550 c.c. of milk, 20 g. of butter, 30 g. of meat, 50 g. of apple compote, 10 g. of sugar, 50 c.c. of water, 5 g. of toffee. The observation lasted for 21 days; seven days were used as fore period, seven days as formic aldehyde period and seven days as after period. The method of administering the formic aldehyde was the same as in the previous observations, but it was given in this case throughout in a concentration of

1 in 5,000 of milk, occasionally some of the formic aldehyde was given in the meat; the total food was formalised to the extent of 1 in 9,000. The total quantity given per diem was 0·1 g. The child's general health and behaviour did not seem to be affected in any way throughout the whole observation. The analytical results obtained throughout this observation are recorded in the table on pp. 354, 355.

Nitrogen Metabolism.

Following the same methods as before, the results in this connection are expressed in tabular form as follows:

——	Fore period	F.A. period	After period
Nitrogen in Food per diem ...	6·65	7·01	6·99
,, ,, Urine ,, ...	4·84	5·13	5·29
,, ,, Faeces ,, ...	0·54	0·77	0·68
Balance	+1·27	+1·11	+1·02
Assimilation %	91·86	89·01	90·27
Nitrogen % in dry Faeces ...	6·4	5·07	6·2

From these figures, speaking generally, we cannot say that the nitrogenous metabolism was to any extent affected. The quantity of nitrogen in the faeces however was certainly increased, and the effect seemed to be prolonged into the after period. The difference in absolute quantity as compared to the fore period is however very small (0·23 g. in the formic aldehyde period, and 0·14 g. in the after period). If one were to regard this result superficially one would be tempted to at once draw the conclusion that formic aldehyde in this proportion, viz. 1 in 5,000, had rendered the proteid constituents of the food less digestible. Upon closer inspection, however, it seems that this increase of nitrogen in the faeces is rather to be explained by formic aldehyde exerting a slight irritant action upon the intestine, involving an increased shedding of epithelial cells. We are brought to this conclusion by the fact that the total quantity of the faeces was increased, and that the effect was prolonged into the after period. In this connection, however, we must not overlook the possibility of formic aldehyde exerting an inhibitory action upon the *secretion* of the digestive enzymes. As we shall discuss this later in another connection we shall say nothing further about it here.

Table IV.

Showing the Influence of Formic Aldehyde upon

PERIOD	—	Date	Dose g	URINE Quantity c.c.	Reaction	Specific gravity	Total sulphuric acid g	Ethereal sulphuric acid g	Uric acid g	Nitrogen g
FORE PERIOD		18 IV.		265	Acid	1·0260	0·8326	0·0684	0·1187	4·62
		19 ,,		245	,,	1·0288	0·7618	0·0632	0·1097	4·76
		20 ,,		275	,,	1·0287	0·8640	0·0709	0·1232	4·86
		21 ,,		280	,,	1·0292	0·8798	0·0722	0·1253	4·72
		22 ,,		205	,,	1·0316	0·6441	0·0529	0·1918	4·20
		23 ,,		330	,,	1·0300	0·8038	0·0498	0·1795	5·83
		24 ,,		305	,,	1·0250	0·7430	0·0461	0·1659	4·86
	Total	7 days		1,905			5·5291	0·4235	1·0141	33·85
	Average	*1 day*		*258*		*1·0282*	*0·7898*	*0·0605*	*0·1306*	*4·84*
FORMIC ALDEHYDE PERIOD		25 IV.	0·1	360	Amphoteric	1·0270	0·8769	0·0544	0·1958	5·64
		26 ,,	0·1	250	Acid	1·0190	0·6090	0·0378	0·1360	3·21
		27 ,,	0·1	420	Amphoteric	1·0180	1·0208	0·0634	0·2285	5·33
		28 ,,	0·1	335	,,	1·0250	0·8348	0·0556	0·1715	5·84
		29 ,,	0·1	340	,,	1·0230	0·8473	0·0564	0·1740	5·13
		30 ,,	0·1	260	,,	1·0180	0·6479	0·0432	0·1331	2·89
		1 V.	0·1	415	Acid	1·0250	1·0340	0·0689	0·2124	7·88
	Total	7 days	0·7	2,380			5·8707	0·3797	1·2513	35·92
	Average	*1 day*	*0·1*	*340*		*1·0221*	*0·8386*	*0·0542*	*0·1787*	*5·13*
AFTER PERIOD		2 V.		300	Acid	1·0281	0·9141	0·0609	0·1008	5·24
		3 ,,		275	Amphoteric	1·0272	0·8379	0·0558	0·0924	4·92
		4 ,,		280	,,	1·0286	0·8532	0·0568	0·0940	5·68
		5 ,,		270	,,	1·0293	0·8227	0·0548	0·0907	5·01
		6 ,,		260	Acid	1·0293	0·7922	0·0528	0·0874	6·57
		7 ,,		210	Amphoteric	1·0276	0·7757	0·0379	0·0189	3·81
		8 ,,		255	,,	1·0318	0·9227	0·0450	0·0229	5·80
	Total	7 days		1,850			5·9185	0·3640	0·5071	37·03
	Average	*1 day*		*264*		*1·0288*	*0·8455*	*0·0520*	*0·0724*	*5·29*

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TABLE IV.

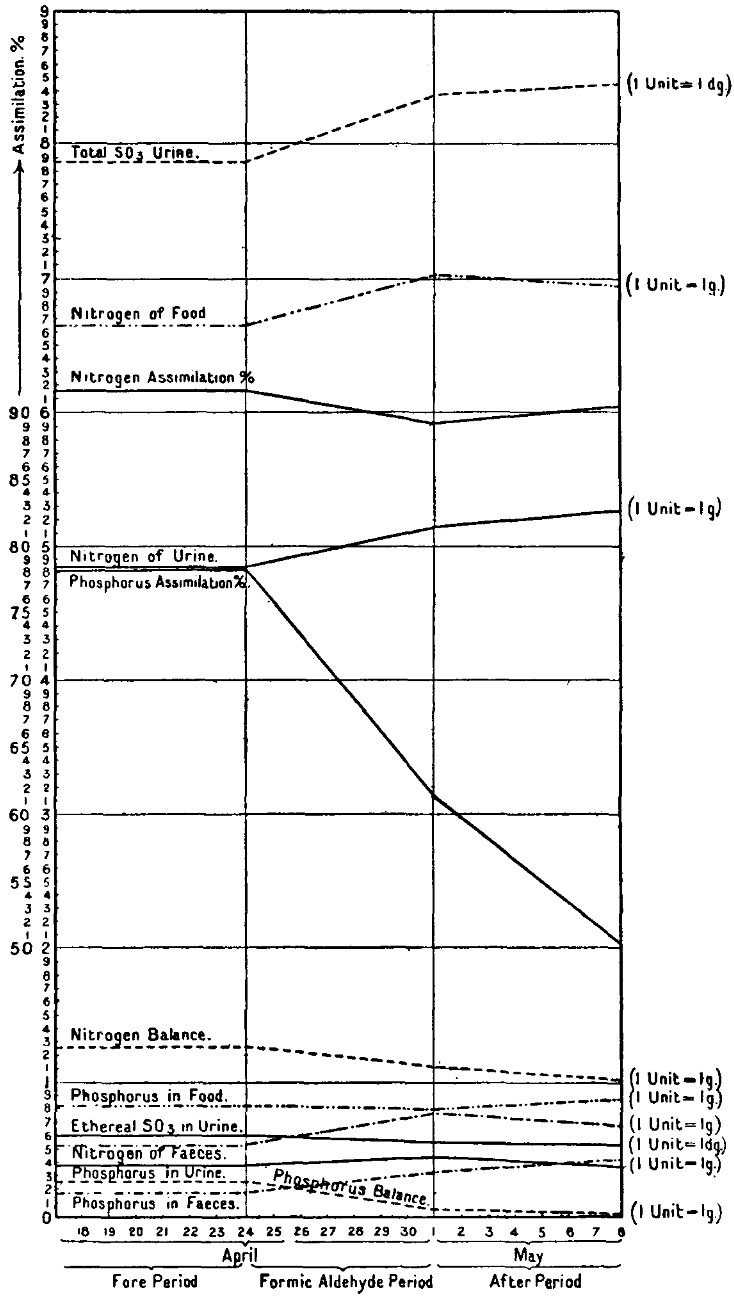
THE GENERAL METABOLISM OF THE INVALID CHILD C.

FAECES							PHOSPHORUS				FAT		
Moist g	Dry g	Water %	Nitrogen g	Nitrogen of food g	Balance g	Body weight kg	Urine g	Faeces g	Food g	Balance g	Faeces g	Food g	Balance g
97	14·0	85·6	0·89	6·35	+0·84	15·06	0·4123	0·2915	0·79	+0·09	2·94	38·90	+35·96
—	—	—	—	6·35	+1·59		0·3813	—	0·79	+0·41	—	38·90	+38·90
63	12·5	80·2	0·80	6·35	+0·69		0·4279	0·2602	0·79	+0·10	2·63	38·90	+36·27
—	—	—	—	6·35	+1·63		0·4357	—	0·79	+0·35	—	38·90	+38·90
100	20·0	80·0	1·27	6·44	+0·97		0·3189	0·4164	0·78	+0·04	4·20	39·04	+34·84
75	12·7	83·1	0·82	7·36	+0·71		0·3683	0·2644	0·86	+0·23	2·67	39·02	+36·35
—	—	—	—	7·36	+2·50	15·12	0·3402	—	0·86	+0·52	—	39·02	+39·02
335	59·2		3·78	46·56	+8·93	+*60 g.*	2·6846	1·2325	5·66	+1·74	12·44	272·68	+260·24
48	*8·4*	*82·3*	*0·54*	*6·65*	*+1·27*	*Gain*	*0·3835*	*0·1760*	*0·81*	*+0·25*	*1·77*	*38·95*	*+37·18*
54	15·7	72·8	0·84	7·45	+0·97	15·12	0·4016	0·3532	0·86	+0·11	3·57	38·31	+34·74
77	15·0	80·5	0·81	6·89	+2·87		0·2790	0·3375	0·78	+0·16	3·41	37·32	+33·91
69	11·6	83·2	0·63	6·89	+0·93		0·4687	0·2610	0·78	+0·05	2·63	37·46	+34·83
37	10·3	72·2	0·56	6·89	+0·49		0·4559	0·2317	0·78	+0·09	2·34	37·46	+35·12
136	21·9	83·9	1·32	6·89	+0·44		0·4637	0·4861	0·78	−0·17	4·98	37·46	+32·48
35	7·5	78·6	0·45	7·05	+3·71		0·3546	0·1664	0·78	+0·26	1·71	37·56	+35·85
74	13·5	81·8	0·81	7·05	−1·64	15·40	0·5660	0·2996	0·78	−0·09	3·07	37·56	+34·49
482	95·5		5·42	49·11	+7·77	+*280 g.*	2·9895	2·1355	5·54	+0·41	21·71	263·13	+241·42
69	*13·6*	*80·3*	*0·77*	*7·01*	*+1·11*	*Gain*	*0·4270*	*0·3050*	*0·79*	*+0·06*	*3·10*	*37·59*	*+34·49*
21	4·4	79·0	0·30	7·08	+1·54	15·40	0·4119	0·5114	0·78	−0·14	0·89	37·56	+36·67
113	22·0	80·5	1·49	7·08	+0·67		0·3774	0·1023	0·78	+0·30	3·16	37·56	+34·40
28	3·6	87·1	0·21	7·06	+1·17		0·3843	0·9736	0·84	−0·52	0·68	36·20	+35·52
105	18·1	82·7	1·07	6·92	+0·85		0·3705	0·4895	0·84	−0·02	3·43	45·78	+42·35
47	8·5	81·9	0·51	6·92	−0·16		0·3568	0·2299	0·84	+0·25	1·61	45·78	+44·17
87	13·9	84·0	0·83	6·92	+2·28		0·3533	0·3759	0·84	+0·11	2·63	45·78	+43·15
31	6·6	78·7	0·39	6·97	+0·78	15·62	0·4289	0·1785	0·84	+0·23	1·25	45·78	+44·53
432	77·1		4·80	48·95	+7·13	+*220 g.*	2·6831	2·8611	5·76	+0·22	13·65	294·44	+280·79
62	*11·0*	*81·9*	*0·68*	*6·99*	*+1·02*	*Gain*	*0·3833*	*0·4087*	*0·82*	*+0·03*	*1·95*	*42·06*	*+40·11*

The results expressed in the above table are graphically represented in the following curves:

CURVE V.,

showing the influence of Formic Aldehyde upon phosphorus and nitrogen metabolism.



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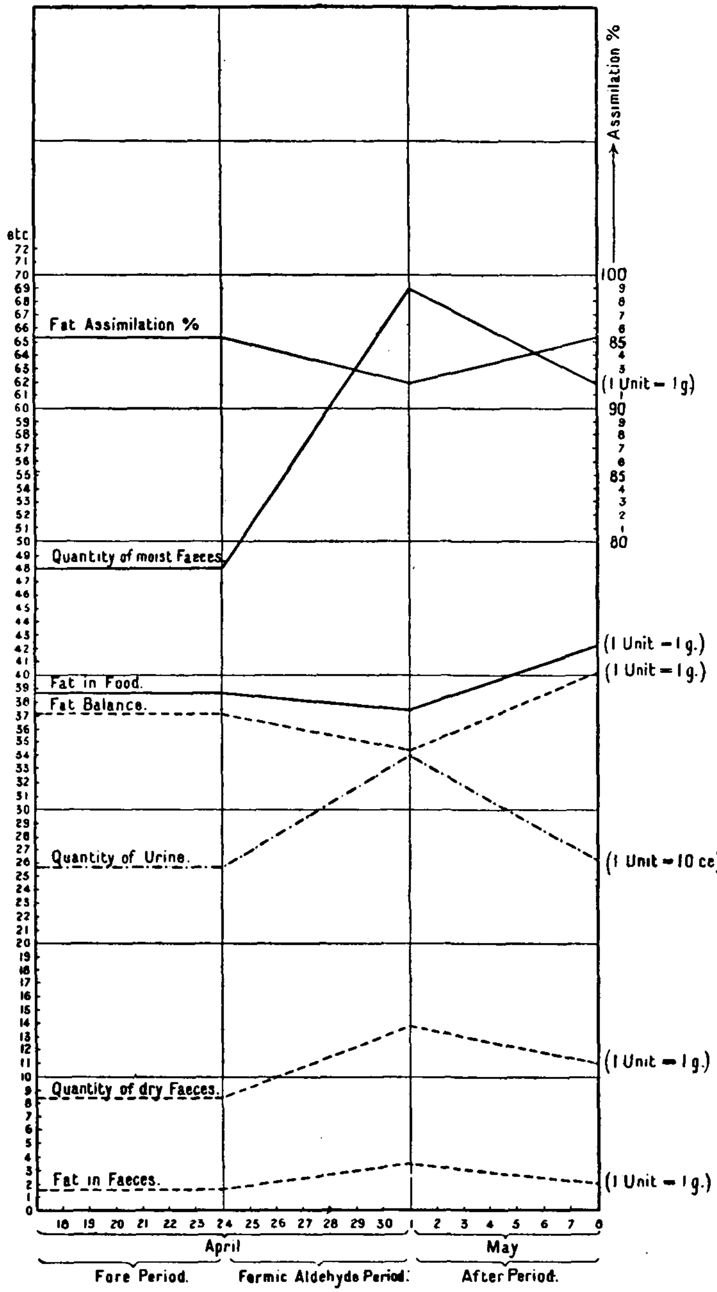
CURVE VI.,

showing the influence of Formic Aldehyde upon fat assimilation and upon the quantity of urine and faeces.



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Phosphorus Metabolism.

The results in this connection expressed in a tabular form are as follows:

—	Fore period	F.A. period	After period
Phosphorus of Food per diem ...	0·81	0·79	0·82
,, ,, Urine ,, ...	0·3835	0·4270	0·3833
,, ,, Faeces ,, ...	0·1760	0·3050	0·4087
Balance	+0·25	+0·06	+0·03
Assimilation %	78·28	61·39	50·16
Phosphorus % in dry Faeces ...	2·1	2·2	3·7

From these figures we come to the conclusion that the phosphorus balance, although approaching nearer to the equilibrium during the formic aldehyde and after period, never actually reached it, and hence cannot be considered to have been seriously affected. On the other hand, reasoning from the increased amount of phosphorus in the faeces, there can be no doubt that speaking generally the phosphorus of the food has not been assimilated during the formic aldehyde and after periods to the same extent as during the fore period. Further, taking into consideration the increased amount of phosphorus in the urine during the formic aldehyde period, along with the diminished assimilation and the fact that the phosphorus in the food remained constant, formic aldehyde seemed to exert a slight stimulating action upon the breaking down of the body proteids rich in phosphorus.

As this case affords the first example of tangible increase in the phosphorus of the faeces we examined it more carefully. Keeping in mind the results of the experiments *in vitro* a probable explanation appeared to be that the formalisation of the proteid constituents of the food had rendered them less susceptible to the action of the pancreatic secretion. It must be remembered however in this connection that the pancreatic juice acts upon the residue of gastric digestion, the phosphorus-containing compounds of which are chiefly nucleo-proteids, and nucleo-albumins. An indication of the extent to which pancreatic digestion was deranged would be given by an estimation of the nucleo-proteid and nucleo-albumin phosphorus in the faeces. This we proceeded to do, following generally the method described by Knöpfelmacher[1], modified by Müller[2]. It must be noted

[1] *Wiener klin. Wochenschr.*, 1898, No. 45.

[2] *Zeitschr. f. Biologie*, 1900, p. 451.

at once however that this method is not an absolute analytical one, but simply comparative[1].

Another possible explanation of the increased amount of phosphorus in the faeces would be an increased excretion of lecithin with them. Our attention was drawn to the possibility of this explanation by the fact, as will be seen later, that the substances soluble in ether in the faeces were actually increased during the formic aldehyde period. We proceeded therefore to estimate the phosphorus due to lecithin, and found it contrary to our expectation to have considerably decreased during the formic aldehyde period.

Having obtained the figures for phosphorus due to lecithin and due to nucleo-proteids, we were enabled by subtraction of their sum from the total phosphorus to obtain a phosphorus value representing in all probability inorganic phosphorus.

These results in a tabular form are as follows:

—	Total P.	Nucleo-proteid P.	Lecithin P.	Inorganic P.
Fore period	0·1760	0·0085	0·0226	0·1459
Formic Aldehyde period ...	0·3050	0·0178	0·0086	0·2786
After period	0·4087	0·0149	0·0264	0·3674

It will be seen from the above table that the nucleo-proteids of the faeces as measured by their phosphorus content are increased, and from this we are justified in concluding that formic aldehyde has exerted some influence upon their digestion. Since this effect is continued into the after period the conclusion seems justified that it is due rather to a specific action upon the secretion of the pancreatic enzymes than to a diminished digestibility of the food. Whatever explanation of the increase in nucleo-proteids we may adopt, this latter is not sufficient of itself to explain the actual increase in the total phosphorus; much less does the lecithin afford an explanation of this. We are forced therefore to assume that the increased phosphorus excretion is due mainly to an increased excretion of what we have termed inorganic phosphorus. A further confirmation of this conclusion would be found in an increased excretion by the faeces of those bases with which

[1] The faeces (about 5 g.) freed from fat were ground up with 200 c.c. of dilute HCl containing some tannic acid, to fix the nucleo-proteid phosphorus. After 24 hours' standing the mixture was filtered, and washed with the tannic acid HCl solution till 100 c.c. of the washings contained no trace of phosphoric acid. Phosphorus was then estimated in the residue by Neumann's method described under general methods.

phosphoric acid is usually combined in an insoluble form, viz., Calcium and Magnesium. A quantitative analysis of the faeces in this respect showed an actual increase, proportional to that of the inorganic phosphorus, in these bases during the formic aldehyde and after periods. The results are expressed in the following table:

——	% Ash of Faeces	Absolute Amount		% CaO of Ash	% MgO of Ash
		CaO per diem	MgO per diem		
Fore period	22·11	0·6654	0·0674	3·58	0·36
Formic Aldehyde period ...	32·51	1·2139	0·1162	3·96	0·38
After period	20·77	0·8688	0·0829	3·84	0·36

Taking all these results into consideration, we should be inclined to conclude that the increase of phosphorus in the faeces depends upon an increase in inorganic phosphorus due to the co-operation of two causes. Firstly to a stimulating action exerted by formic aldehyde, or more probably formic acid, upon the intestinal secretion, and secondly to a less extent to an increased splitting up of lecithin and the transformation of the glycero-phosphoric acid produced, into insoluble phosphates[1].

Fat Assimilation.

The results are as in former cases represented in tabular form:

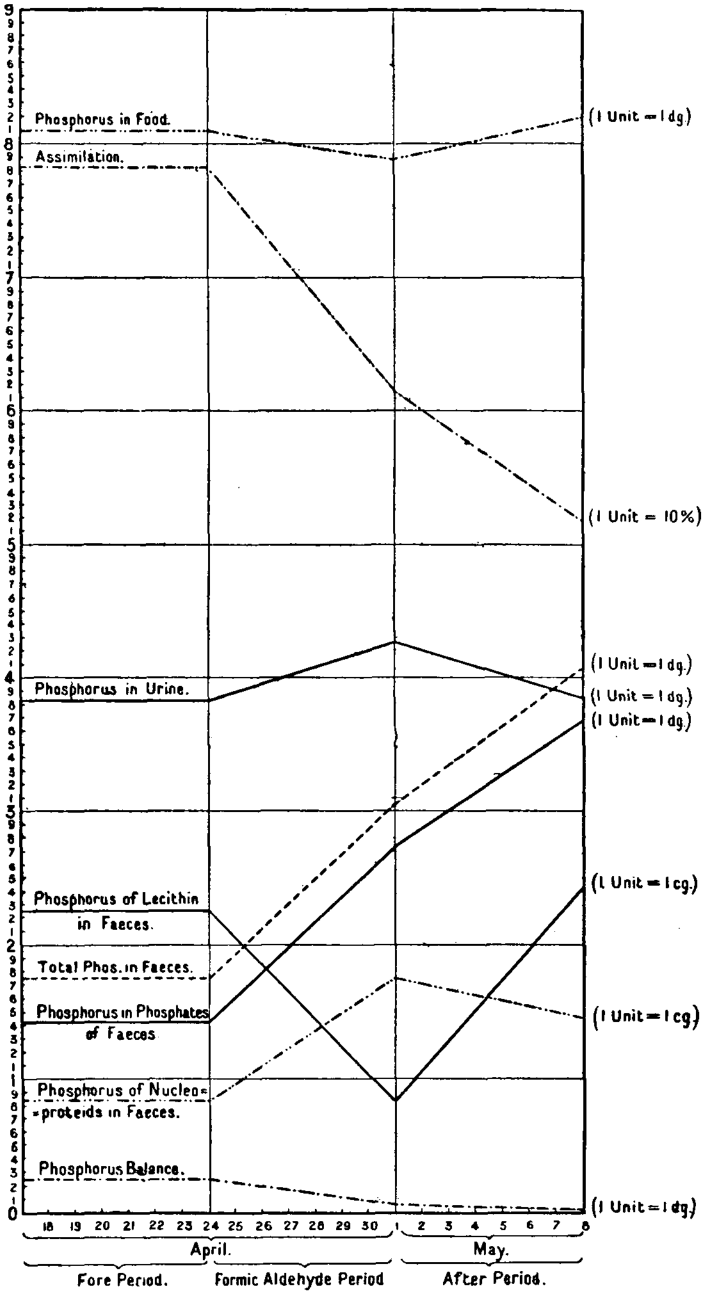
——	Fore period	F.A. period	After period
Fat in Food	38·95	37·59	42·06
„ Faeces	1·77	3·10	1·95
Balance	+37·18	+34·49	+40·11
Assimilation %	95·46	91·75	95·37
Fat in dry Faeces %	21·1	22·9	17·7

It will be seen from these figures that formic aldehyde interfered in this case with the assimilation of the fat of the food. The interference did not extend into the after period. From this latter fact we may conclude that in this case formic aldehyde exerted a specific action upon the fat-splitting enzyme of the pancreas.

[1] Noël Paton (*Journ. of Phys.*, 1900) found that the calcium salt of glycero-phosphoric acid administered to a goat was excreted in the faeces as inorganic phosphate.

Curve VII.,

representing graphically the phosphorus metabolism under Formic Aldehyde in a delicate child.



With regard to lecithin, we have already given the phosphorus corresponding to the lecithin, but following our previous procedure we now give the percentage of lecithin in the total fat.

—	Fore period	F.A. period	After period
Lecithin in grammes of 100 g. fat	21·15	7·25	24·77

In this case the effect on the lecithin excretion is most marked: we are inclined to ascribe this decrease and that which took place in the other cases to formic aldehyde having exerted a stimulating effect upon the lecithin-splitting ferment of the pancreas, which according to Bokai[1] splits up lecithin into glycero-phosphoric acid, free fatty acids and cholin. That the diminished excretion of lecithin is not due to a retention of lecithin in the body by a direct absorption of it as such, may be concluded from the phosphorus balance.

On referring to the chief table, we see that the *quantity of urine* in this case was increased in the formic aldehyde period, an exactly opposite effect to that observed elsewhere. The specific gravity of the urine fell during this period. With regard to the excretion of *uric acid*, also an opposite effect was produced, viz., an increase. As in the after period the average uric acid figure fell below the fore period level, we infer that either a dissolving out of uric acid from the tissues took place under formic aldehyde, or a stimulated production of it. The *total sulphuric acid* excretion was somewhat increased both during the formic aldehyde and the after periods; this together with a slightly increased total nitrogen excretion suggest an effect upon general proteid katabolism in the inverse sense to that observed in Child A. The decrease in *ethereal sulphuric* acid is too small to enable us to draw any conclusions other than negative ones from it. The indoxyl test remained constant throughout the whole observation. During the formic aldehyde and the after period the *body weight* increased, and this cannot be explained in this case as in the preceding ones by a retention of water in the body. This latter occurrence together with the fact that the general health of the child remained unaffected during the formic aldehyde period must tend to minimise any adverse deductions which may be made from the above results.

[1] *Zeitschr. f. physiol. Chem.*, 1877, I. p. 162.

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These observations may be summarised in tabular form as follows:

TABLE IV A.

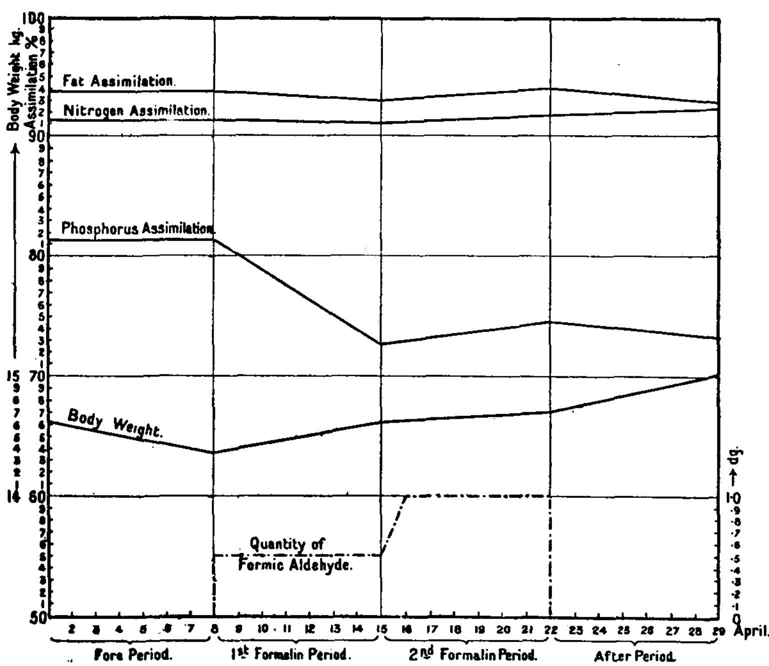
—	Nitrogen assimilation %	% N. of dry faeces	Phosphorus assimilation %	% P. of dry faeces	Fat assimilation %	% fat of dry faeces	A/B *	N/SO_3 †
Fore period ...	91·88	6·4	78·28	2·1	95·46	21·1	12·0	6·1
Formic Aldehyde period	89·01	5·7	61·39	2·2	91·75	22·9	14·5	6·1
After period ...	90·27	6·2	50·16	3·7	95·37	17·7	15·8	6·1

* As in Table II A. † As in Table II A.

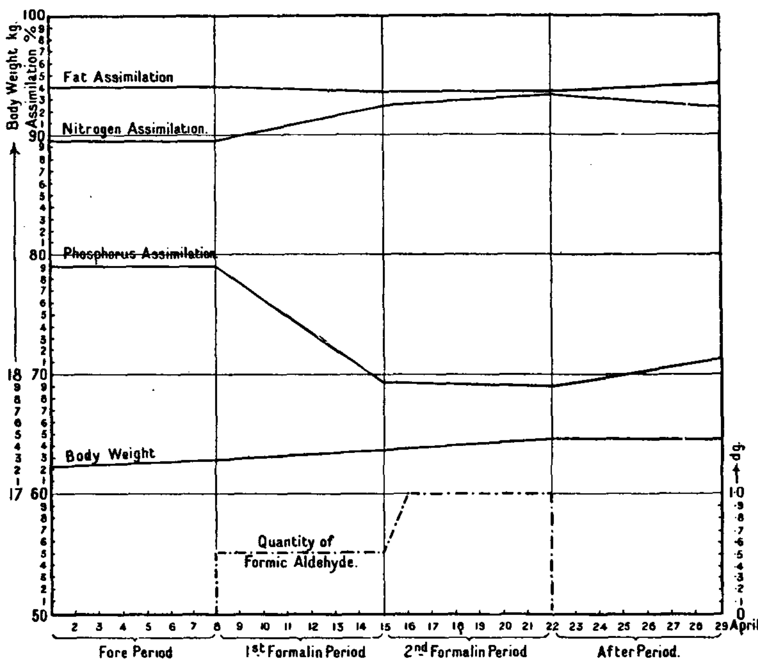
CURVE VIII.,

showing the influence of Formic Aldehyde upon the body weight and upon the nitrogen, phosphorus and fat assimilation of three children.

CHILD A.



CHILD B.



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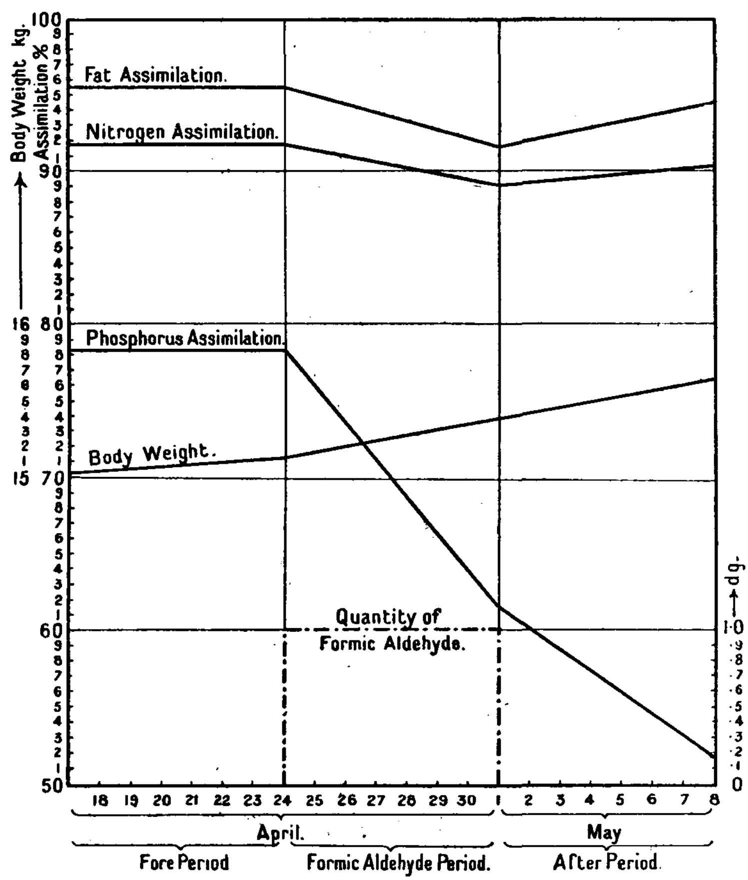
Child C.



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General Conclusions.

(1) In healthy children formic aldehyde administered with the food in doses up to 1 : 5000 in milk or 1 : 9000 in total food and drink exerted no appreciable effect on the nitrogen or phosphorus metabolism or fat assimilation.

The analytical figures suggest, however, that formic aldehyde has a tendency to diminish phosphorus and fat assimilation, and hence it may be inferred that in larger doses, or if continued for a longer period, it would act in this direction. This effect is referable to an influence upon pancreatic digestion.

(2) In healthy children formic aldehyde in the above doses produces a retention of water in the body.

(3) In a delicate child formic aldehyde in the above maximum dose had a chemically measurable deleterious effect upon the nitrogen, phosphorus, and fat assimilation, again referable to an action upon the pancreatic digestion, combined with a slight intestinal irritant action. There was a slight tendency to stimulate the katabolism of proteid material.

(4) In a delicate child formic aldehyde increased the volume of urine and the weight of faeces.

(5) In all cases the excretion of lecithin in the faeces was diminished under the influence of formic aldehyde. This effect is probably referable to a stimulating action of formic aldehyde on the lecithin-splitting ferment of the pancreas.

(6) In no instance did formic aldehyde exert any appreciable intestinal antiseptic action.

(7) In no instance was there any influence on the general health or well-being of the children.

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January 1901.