Dann and Handler[9] and Snell and Quarles[10] have given evidence for the occurrence of a marked increase in the nicotinic acid content of the incubating egg and have suggested, therefore, that the hatched chick does not require a dietary source of this vitamin. From our experiments we may conclude that if such synthesis of nicotinic acid does exist in the growing chick there is not sufficient formation to supply enough of the vitamin for optimal growth and for the prevention of chick "blacktongue." The question of the synthesis of nicotinic acid by the chick can only be answered by further experimentation.

Summary. The growing chick requires a dietary source of nicotinic acid for optimal growth, and for the prevention of chick "blacktongue" as shown by the use of highly purified rations. The minimal level of this vitamin needed is approximately 1.8 mg per 100 g of ration.

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13827

Effect of Liver Damage on Urinary Morphine Excretion.

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Gross, Plant and Thompson[1] reported that liver damage by chloroform caused an increased urinary excretion of morphine in both tolerant and non-tolerant dogs. At the time of this report the presence of conjugated morphine was not recognized. Gross and Thompson[2] demonstrated that dogs excreted morphine in a combined form, and Oberst[3] in the same year showed that man also excreted a combined form of morphine. The excretion of combined morphine has shown that morphine undergoes far less destruction in the animal body than formerly supposed. While the nature of the combined morphine excretion product is still unknown, Oberst[4] believes that the morphine is conjugated with glucuronic acid. He has further demonstrated that the conjugation occurs with the hydroxyl groups and that both the phenolic and alcoholic hydroxyls may be conjugated.

Thompson and Gross[5] studying the combined morphine excretion compound in dog urine found that in this animal the combined morphine is excreted in two forms, namely a fraction which is easily hydrolyzed and the other which hydrolyzes only with more drastic procedure.

With the information that liver damage caused an increase in the excretion of free morphine in dogs, a study of the effect of liver damage on the combined morphine was undertaken in both tolerant and non-tolerant dogs.

Five non-tolerant and 3 tolerant animals were used in these experiments. The dogs were maintained on a constant diet and water intake. Morphine determinations were made before and after liver damage on a constant dose of morphine. As an indication of hepatic damage bromsulphalein dye determinations were also made before and after the liver damage. Five mg per kg of the dye were injected intravenously and the dye in 1 cc of clear serum determined at 3, 8 and 15 min after the injection. Carbon tetra-

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TABLE I.
Non-tolerant Female. Weight 5 kg.

Days	Mg morphine inj. daily	Urine vol. 24 hr	Mg morphine recovered				Bromsulphalein in serum Min after injection		
			Total	Free	Easily Hydrolyzed	Difficultly Hydrolyzed	3	8	15
1	100	172	68	11.2	3.2	53.6			
2	100	209	73	12.6	5.1	55.3			
3	100	250	76	11.9	4.9	59.2			
4	100	190	78	12.1	4.8	60.6	.036	.015	.00
Avg			73.7	11.9	4.5	57.2			
(5-12)	None								
13	100	350	82	15.9	2.6	63.5			*
14	100	165	69.5	23.2	1.3	54.5	.036	.02	.006*
15	100	385	87	34.4	0.0	52.6			
16	100	180	86.3	32.0	1.5	52.8	.038	.025	.012
17	100	168	79.1	27.0	1.2	50.9			
Avg			80.8	26.5	1.32	54.8			

*15 cc CCl_4 in 200 cc H_2O.

TABLE II.
Tolerant Female. Weight 5.5 kg.

Days	Mg morphine inj. daily	Urine vol. 24 hr	Mg morphine recovered				Bromsulphalein in serum Min after injection		
			Total	Free	Easily Hydrolyzed	Difficultly Hydrolyzed	3	8	15
1	110	325	39.9	8.3	9.0	22.6	Control period		
2	110	375	46.6	12.4	10.6	23.6			
3	110	250	46.0	10.3	8.0	27.7			
4	110	200	42.8	11.8	8.9	22.1	.032	.01	.00
Avg			43.8	10.7	9.1	24.0			
5	110	275	48	11.5	7.1	29.4			*
6	110	330	56	15.0	2.0	39.0	.036	.02	.004*
7	110	365	42.5	15.8	3.3	23.4			
8	110	240	42.8	27.0	4.0	11.8			†
9	110	400	46.2	13.2	2.0	30.7			
10	110	200	45.7	26	.00	29.7	.05	.04	.025
11	110	220	48.2	23.0	.00	25.2			
12	110	190	43.6	20.9	.00	22.7			
13	110	280	40	17.3	.00	23.7	.05	.036	.034
14	110	230	36	15.5	1.7	18.8			
15	110	210	48.5	17.3	1.5	29.7			
Avg			45.2	18.4	1.9	25.8			

*11 cc CCl_4 in 100 cc water.
†27.5 cc CCl_4 in 200 cc water.

chloride was used as the liver damaging agent. The agent was administered orally in doses of 2-5 cc per kg body weight after fasting the animal for 24 hr. The carbon tetrachloride was given in repeated or single doses. The urine was analyzed for total, free and easily hydrolyzable morphine according to the procedure of Thompson and Gross.[5] The difficultly hydrolyzable morphine fraction is obtained by difference.

Results of such studies on a non-tolerant and a tolerant dog are given in Tables I and II.

From the results in Tables I and II, the delayed disappearance of the dye indicates some hepatic damage after the administration of carbon tetrachloride. Our earlier observation[1] that liver damage by chloroform

produced an increase in free morphine excretion, also holds true when carbon tetrachloride was used as the damaging agent. In addition to the marked increase in the free morphine there is a decrease in the excretion of the easily hydrolyzable fraction of the combined morphine. As the total recoverable morphine is not materially altered and the difficultly hydrolyzable portion remains fairly constant, the easily hydrolyzed compound appears as free morphine.

One might interpret from these experiments that the easily hydrolyzed form is the only form of conjugation that takes place in the liver, and the formation of the difficultly hydrolyzable fraction occurs at other sites. However, until the conjugation products are identified and their metabolism studied, it is impossible to make any definite statements as to the site of the morphine conjugation. However, liver damage does inhibit the conjugation of morphine to a certain extent as shown by the fact that the free morphine found in the urine is increased without increasing the total morphine excreted.

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Relation of Pancreatic Secretion to Fatty Changes in the Liver.*

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The question whether following ligation of all pancreatic ducts infiltration of the liver can be prevented by pancreatic juice or by an internal secretion of the pancreas is still controversial.

Dragstedt and collaborators did not observe fatty livers following ligation of all pancreatic ducts, nor following complete loss of all external secretion of the pancreas, and they could not prevent or cure fatty livers by administration of large amounts of pancreatic juice.[1,2] This has been in part confirmed by Boyce and McFetridge,[3] but the results of a number of investigators have been opposed to their findings.[4-10] The latter group found fatty livers following ligation of all pancreatic ducts and Montgomery and collaborators were able to prevent these changes by the feeding of pancreatic juice.[9,10] Our observations in long term experiments on dogs may contribute to decide this controversy.

Results. Two animals, with all pancreatic ducts ligated and cut in an aseptic operation and with omentum interposed between duodenum and pancreas were kept for about one year. Both dogs had a good appetite and were kept on a ratio of bread, vegetables, meat and a yeast-bonemeal-salt mixture, with weekly feedings of cod liver oil and dried ox blood. One of the animals lost weight

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