CHAPTER IX

DEXAMETHASONE INDUCED ALTERATIONS IN GLUCOSE TOLERANCE AND, INSULIN, GLUCAGON AND ADRENALINE RESPONSES DURING THE FIRST MONTH OF POST-HATCHED DEVELOPMENT OF WHITE LEGHORN BREED OF CHICKS

The immediate post-hatched phase of chick development is marked by changes in metabolic attributes (Rajeha et al., 1971a). A shift in emphasis from gluconeogenic lipid utilization in the embryonic phase to glycolytic carbohydrate utilization in the post-hatched phase is characterized by changes in tissue metabolite contents and enzyme activities (Raheja et al., 1971a; Hazelwood, 1986). The post-hatched phase of development can be considered as a phase of metabolic modulations leading to adaptive physiological maturation and adult homeostatic pattern. This phase of development is also an intricate one involving changes in secretory dynamics of various endocrine glands and alterations in target sensitivity to various hormones, ultimately producing a functional interrelationship and target sensitivity of the adult types. In this behest, it is presumable that any single endocrine disfunctioning can have profound effects on the physiology of the organism in this sensitive phase as the progressively balancing dynamics of interaction between the various hormonal principles get disrupted. Adrenocortical hormones being permissive hormones for the actions of other hormones, any alteration in their circulating titre during post-natal development of chicks could have profound effects. This is corroborated by the earlier observations of alterations in carbohydrate, protein and lipid metabolism by the functional manipulation of adrenal cortex (Chapters III, IV and V). It is presumbale that the response of the

chicks to various other hormones under altered functional status of the adrenal cortex would be altered. The present chapter in this context addresses to this contention and has evaluated glucose tolerance and, insulin, glucagon and adrenaline responses in terms of glycemic levels in DXM treated chicks in a state of functional hypocorticalism.

MATERIAL AND METHODS

As outlined in Chapter I.

RESULTS

The glycemic level after glucose loading and insulin, glucagon and adrenaline injections and the percentage alterations are represented in tables and figures 1 - 4 and 1a -4a. For the sake of convenience and ease of discussion, the per minute glucose elevation rate and subsequent per minute glucose clearance rate after glucose, glucagon and adrenaline administration and the per minute glucose clearance rate and subsequent glucose normalization rate after insulin administration have been calculated. These rates together with the respective elevation to clearance or clearance to normalization rates are given in table 5.

Glucose tolerance test (GTT)

One day old chicks

Maximum hyperglycemic condition due to glucose loading in one day

old chicks was obtained by 30 minutes (17.4%). Subsequently the blood glucose level dropped steadily and attained fasting levels by 120 min which further got reduced to a hypoglycemic condition by 150 min. Thereafter normoglycemia was attained by 180 min.

10 day old chicks

The basal glucose level was significantly low ($P < 0.01$) in dexamethasonised chicks prior to glucose loading throughout the present study. Maximum glycemic condition (only 15.4%) was attained by 120 min in dexamethasonised chicks while in the case of control it was recorded by 90 min (28.2%). Fasting level was attained in the control by 150 min, while in the treated chicks the glucose levels decreased beyond the fasting levels (-15.7%) by 180 min and continued to remain so even at 240 min.

20 day old chicks

After glucose loading, the maximum hyperglycemic condition (17.4%) was attained by 30 min in control and 60 min in dexamethasonised chicks (6.8%). On a percentage basis, the glucose elevation was significantly less in DXM treated chicks compared to that of controls. The recovery was faster in the case of DXM treated chicks (90 min) as compared to controls (120 min).

30 day old chicks

In control chicks, maximum hyperglycemia of 17.6% occurred at 60 min after glucose loading and normoglycemia was established by 120 min. Thereafter there was increasing hypoglycemia at 210 min. In contrast, DXM treated chicks showed a very attenuated hyperglycemic condition

Table 1 Chronological alterations in glycemic levels after glucose loading in normal (C) and dexamethasonised (DXM) chicks during the first month of post-hatched development. Values are expressed in mg/100ml blood and represented as Mean ±SE.

Days post-hatch		Time in minutes 0	30	60	90	120	150	180	210	240
One day	C	228.98 ± 6.71	268.86^{c} ±13.25	250.35^{d} ± 8.06	248.10^{d} ± 6.82	229.60 ± 4.53	201.18^{b} ± 6.47	224.60 ± 6.24		
10 days	C	230.60 ± 6.66	250.97 ±11.00	287.41^{a} ± 6.83	295.80^{a} ±11.42	258.60^{c} ±10.04	250.26 ± 7.26	244.77 ± 7.00		
	DXM	195.63** ± 9.20	183.30 ±12.02	198.71 ±9.65	195.50 ±19.43	225.88^{d} ±13.80	208.88^{d} ±10.37	164.75^{c} ± 8.20	158.60^{b} ± 9.39	157.00^{c} ±11.15
20 days	C	223.00 ± 4.03	261.97^{a} ± 8.38	253.58^{a} ± 9.05	241.52^{b} ± 5.89	220.25 ± 3.86	271.81 ± 5.05	210.80 ± 8.08	205.10^{d} ± 7.48	
	DXM	205.80** ± 4.40	216.60 ± 6.60	220.00 ±14.60	206.60 ± 4.20	205.14 ± 7.00	200.60 ± 9.10	200.00 ±13.99		
30 days	C	232.83 ± 5.82	257.82 ± 9.72	274.02 ±15.34	266.62 ±10.31	242.55 ±13.82	240.25 ±11.31	224.51 ± 8.42	201.55^{a} ± 6.86	
	DXM	206.62** ± 6.73	212.56 ± 8.58	183.68 ±13.13	167.85 ±10.63	159.96 ±14.36	154.02 ±13.37	145.63 ±11.24		

a : $P<0.001$; b : $P<0.01$; c : $P<0.02$; d : $P<0.05$ significant with zero minute.

** $P<0.01$ significant with corresponding normal values.

Table 1a Chrnological percentage alterations in glycemic level after glucose loading in normal (C) and dexamethasonised (DXM) chicks during the first month of post-hatched development. Values represent Mean ±SE.

Days post-hatch		Time in minutes							
		30	60	90	120	150	180	210	240
One day	C	17.40 ± 0.85	9.30 ± 0.29	8.30 ± 0.22	0.270 ± 0.004	-12.10 ± 0.38	- 1.90 ± 0.05		
10 days	C	8.80 ± 0.38	24.60 ± 0.58	28.20 ± 1.08	12.10 ± 0.46	8.50 ± 0.24	6.10 ± 0.17		
	DXM	- 6.30[a] ± 0.41	1.50[a] ± 0.07	- 0.060[a] ± 0.005	15.40 ± 0.94	6.70 ± 0.95	-15.70[a] ± 0.78	-18.90[a] ± 1.11	-19.70[a] ± 1.39
20 days	C	17.40 ± 0.55	13.60 ± 0.48	8.30 ± 0.20	- 1.29 ± 0.02	- 5.00 ± 0.11	- 5.40 ± 0.20	- 8.00 ± 0.29	
	DXM	5.20[a] ± 0.15	6.80[a] ± 0.45	- 0.36[a] ± 0.07	- 0.32 ± 0.01	- 2.50[a] ± 0.11	- 2.80[a] ± 0.19		
30 days	C	10.70 ± 0.40	17.60 ± 0.98	14.50 ± 0.56	4.10 ± 0.23	3.10 ± 0.14	- 3.50 ± 0.13	-13.40 ± 0.45	
	DXM	2.80[a] ± 0.11	-11.10[a] ± 0.79	-18.70[a] ± 1.18	-22.50[a] ± 2.01	-25.40[a] ± 2.20	-29.50[a] ± 2.27		

a : $P < 0.001$ significant with the corresponding normal values.

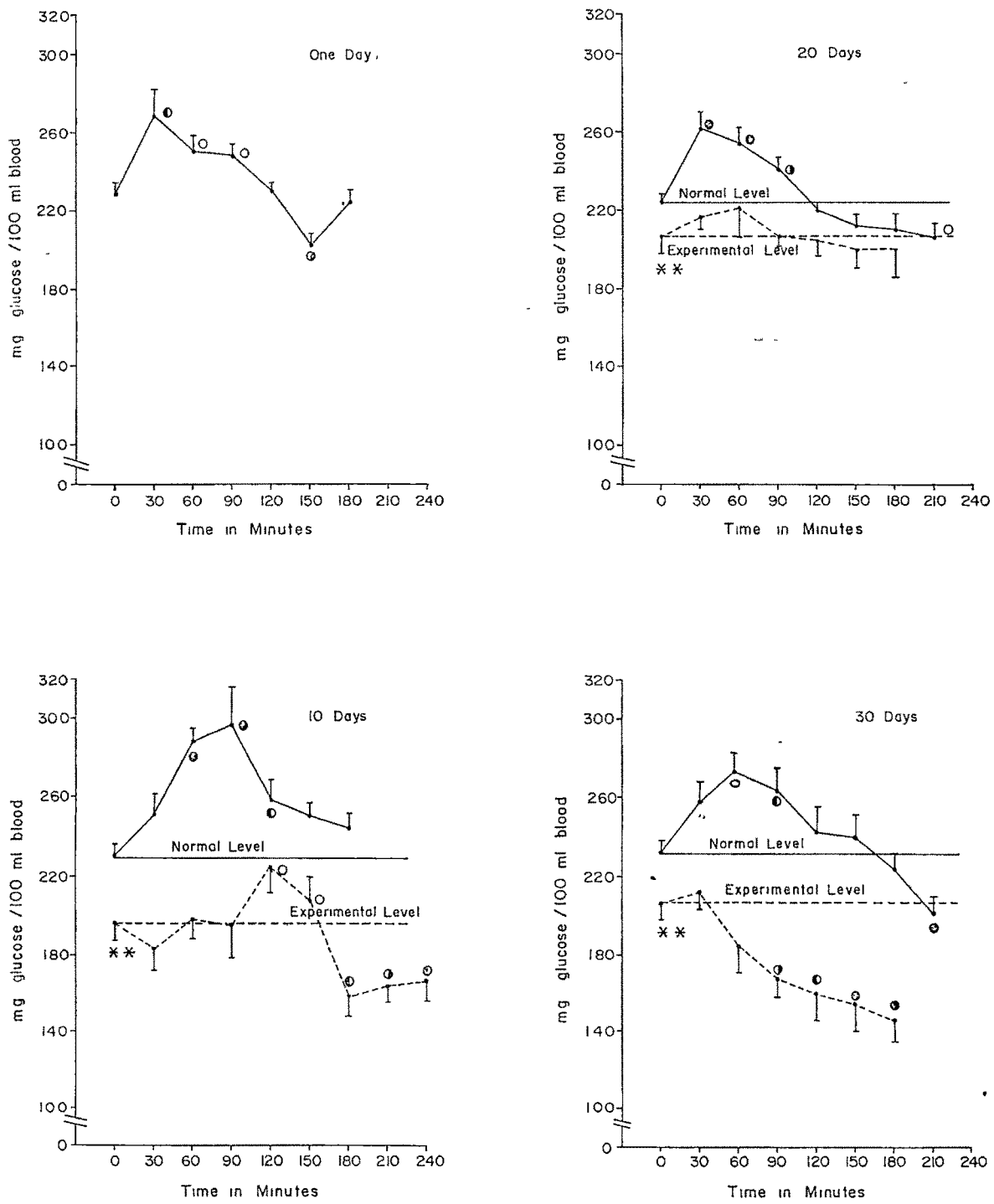

Fig 1 Chronological alterations in glucose tolerance curve in normal (⟷) and dexamethasonised (⟷) chicks during the first month of post-hatched development. Values represent mean ± SE. ⊙ $P < 0.001$, ⊙ $P < 0.01$, ⊙ $P < 0.02$, ⊙ $P < 0.05$ with the corresponding zero level; ** $P < 0.01$ with normal

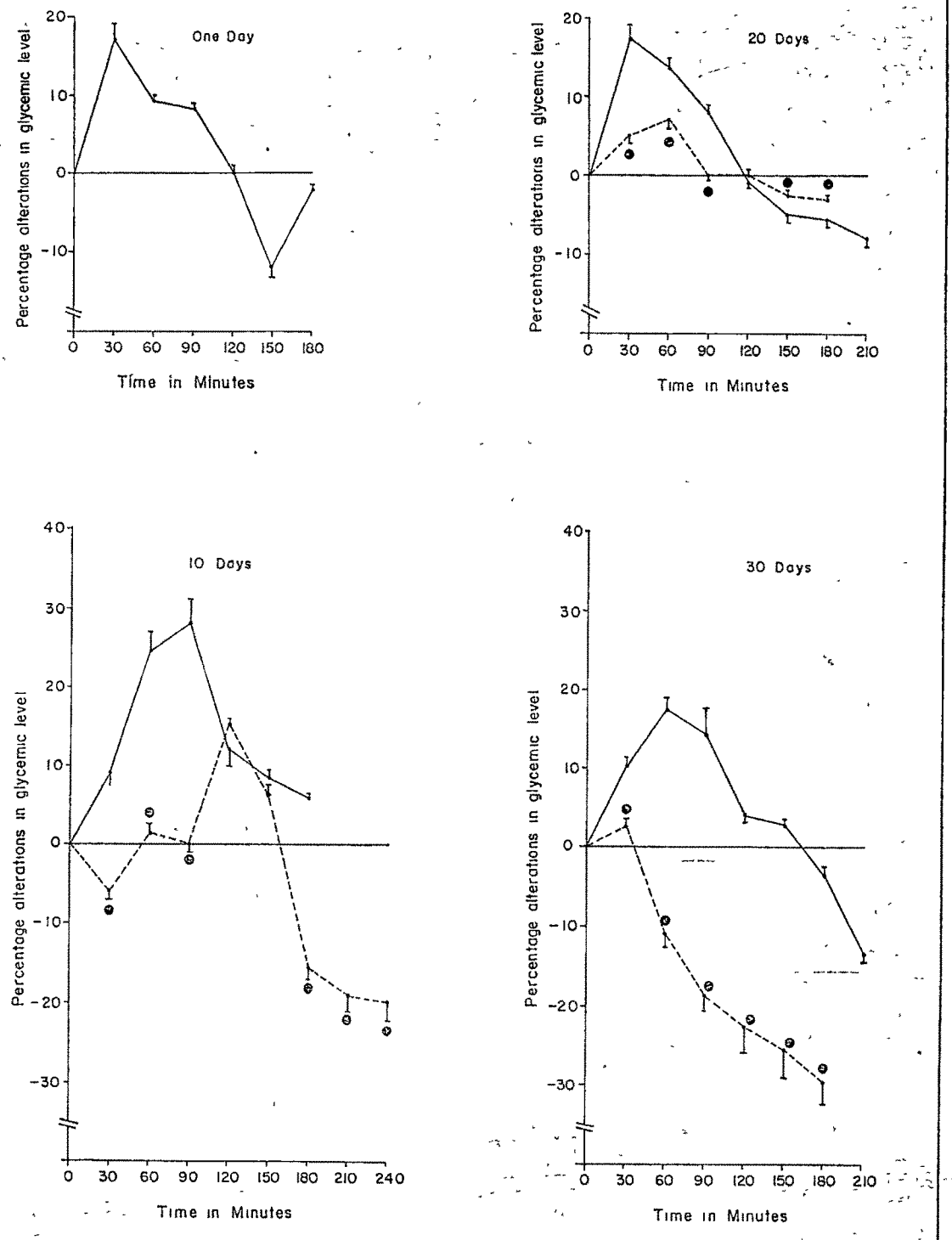

Fig. 1a Chronological percentage alterations in glycemic level after glucose loading in normal (——) and dexamethasonised (- - -) chicks in the first month of post-hatched development. Values represent mean ± S.E.
• P< 0.001 with the corresponding control.

(2.8%) at 30 min, whereafter there was a progressively increasing hypoglycemic condition from 60 to 180 min.

Insulin response test (IRT)

One day old chicks

The glucose level after insulin injection dropped by 42.6% within half an hour which further got accentuated to 75.5% by 210 min without any trace of recovery.

10 day old chicks

The basal glucose level was significantly low ($P < 0.02$) in DXM treated chicks. Insulin induced hypoglycemia was maximal at 90 min in both control (61.2%) and experimental (85.8%) groups of birds, after which the levels started increasing gradually though normoglycemia was not attained even by 240 min.

20 day old chicks

The basal glucose level was significantly low ($P < 0.01$) in DXM treated chicks. Insulin induced hypoglycemia was maximal at 90 min in control (51.1%) and at 120 min in experimentals (85.5%). Recovery to normoglycemic level was more gradual and slow in dexamethasonised chicks. Even by 4 hrs DXM treated chicks did not reach normal glycemic levels.

30 day old chicks

The basal glucose level was significantly low ($P < 0.01$) in dexamethasonised chicks. Maximal hypoglycemic condition subsequent to insulin injection was attained at 90 min in both groups of chicks with a relatively more pronounced decrease (75%) in DXM treated chicks

Table 2 Chronological alterations in glycemic level after insulin injection in normal (C) and dexamethasonised (DXM) chicks during the first month of post-hatched development. Values are expressed in mg/100ml blood and represented as Mean ±SE.

Days post-hatch		Time in minutes								
		0	30	60	90	120	150	180	210	240
One day	C	233.30 ± 9.50	133.91[a] ± 8.67	133.30[a] ±10.90	110.46[a] ± 8.57	92.54[a] ±11.12	87.38[a] ±10.26	66.60[a] ± 5.10	56.98[a] ± 7.81	
10 days	C	219.81 ± 6.22	135.40[a] ± 8.05	93.70[a] ± 6.83	85.13[a] ± 8.23	102.37[a] ± 5.10	112.77[a] ± 5.65	119.36[a] ±11.70	126.20[a] ±12.19	134.35[a] ± 6.74
	DXM	195.63[*] ± 7.20	118.42[a] ± 4.47	49.90[a] ± 9.83	27.70[a] ± 7.00	40.20[a] ±16.30	52.10[a] ±12.20	37.40[a] ±10.90	54.25[a] ±12.50	86.10[a] ±10.30
20 days	C	224.35 ± 4.01	145.96[a] ± 5.81	134.97[a] ± 8.62	109.58[a] ±10.19	116.85[a] ±10.84	162.41[a] ±10.81	187.21[a] ± 2.16		
	DXM	195.63[**] ± 6.22	117.50[a] ±11.60	83.00[a] ±15.29	55.00[a] ±12.41	28.30[a] ± 6.00	68.33[a] ±16.91	66.66[a] ± 8.30	80.00[a] ±10.40	95.00[a] ± 7.60
30 days	C	212.95 ± 3.82	105.80[a] ± 5.53	91.91[a] ±12.08	80.78[a] ± 5.92	89.46[a] ± 6.86	96.58[a] ± 6.40	132.56[a] ± 9.74	143.71[a] ±10.37	149.96[a] ±11.10
	DXM	186.70[**] ± 4.43	94.40[a] ± 8.23	77.36[a] ±11.58	46.60[a] ± 9.91	50.34[a] ± 9.03	69.20[a] ±15.60	72.18[a] ±14.70	89.30[a] ± 7.97	94.13[a] ± 4.40

a : $P < 0.001$ significant with zero minute.

** $P < 0.01$; * $P < 0.02$ significant with corresponding normal values.

Table 2a Chronological percentage alterations in glycemic level after insulin injection in normal (C) and dexamethasonised (DXM) chicks during the first month of post-hatched development. Values represent Mean ±SE.

Days post-hatch		Time in minutes							
		30	60	90	120	150	180	210	240
One day	C	-42.60 ± 2.75	-42.80 ± 3.49	-52.60 ± 4.08	-60.90 ± 7.31	-62.50 ± 7.33	-71.40 ± 5.46	-75.50 ±10.34	
10 days	C	-38.40 ± 2.28	-57.30 ± 4.17	-61.20 ± 5.91	-53.40 ± 2.66	-48.60 ± 2.43	-45.60 ± 4.46	-42.50 ± 4.10	-38.80 ± 1.94
	DXM	-39.40 ± 1.48	-74.40[a] ±14.65	-85.80[a] ±26.90	-79.40[a] ±28.00	-73.30[a] ±17.16	-80.80[a] ±23.54	-72.20[a] ±16.63	-55.90[a] ± 6.68
20 days	C	-34.90 ± 1.38	-39.80 ± 2.54	-51.15 ± 4.75	-47.90 ± 4.44	-27.60 ± 1.83	-16.50 ± 0.19		
	DXM	-39.90 ± 3.93	-57.50[a] ±10.59	-71.80[a] ±16.20	-85.50[a] ±18.12	-65.00[a] ±16.08	-65.90[a] ± 8.20	-59.10 ± 7.68	-51.40 ± 4.11
30 days	C	-50.30 ± 2.62	-56.80 ± 7.46	-62.66 ± 4.59	-57.90 ± 4.45	-54.60 ± 3.61	-37.70 ± 2.77	-32.50 ± 2.34	-29.50 ± 2.18
	DXM	-49.40 ± 4.30	-58.50 ± 8.75	-75.00[a] ±16.15	-73.80[a] ±13.23	-62.90[a] ±14.17	-61.30[a] ±12.48	-52.10[a] ± 4.64	-49.50[a] ± 2.31

a : $P < 0.001$ significant with the corresponding normal values.

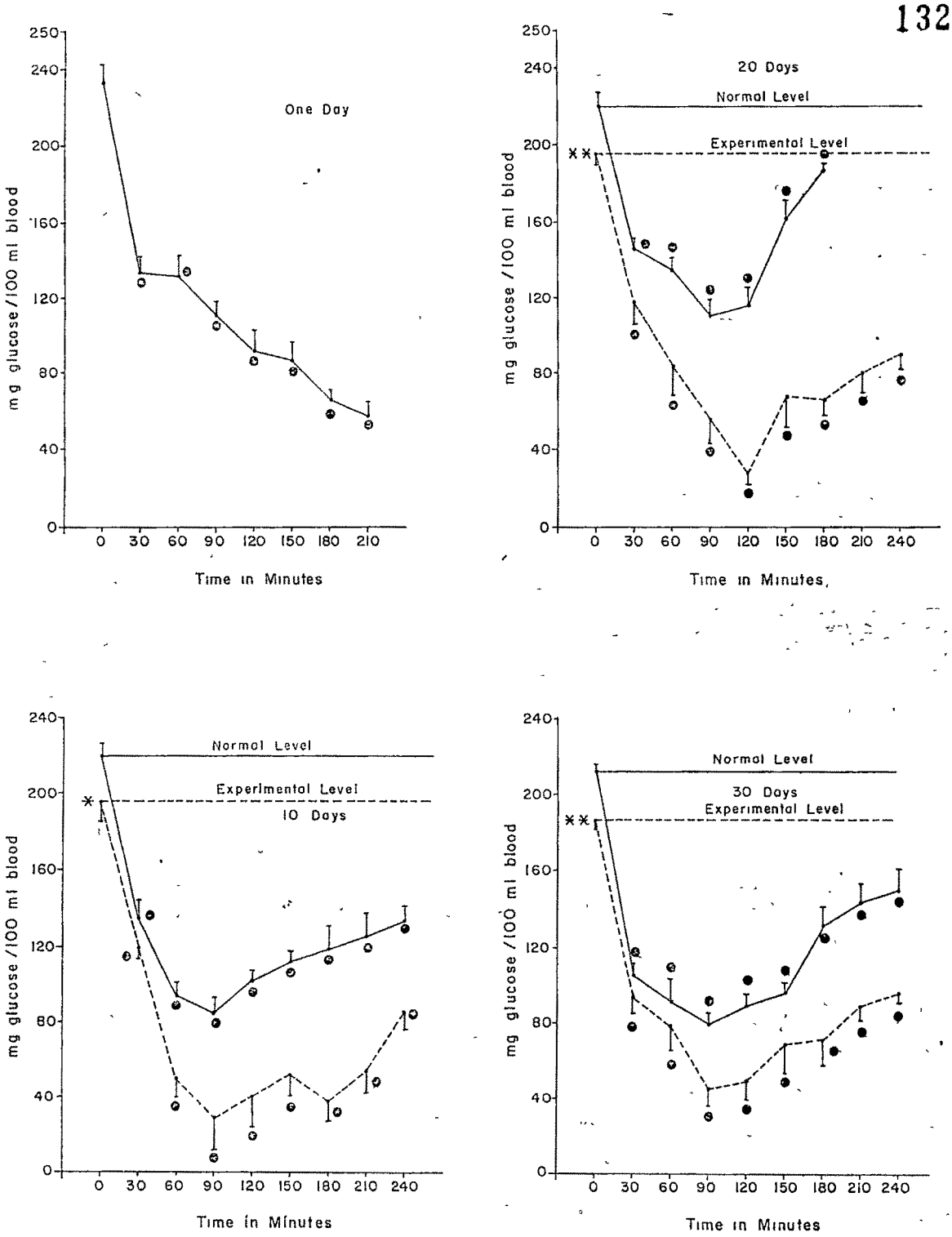

Fig. 2 Chronological alterations in insulin resistance curve in normal (⟵) and dexamethasonised (⟵) chicks during the first month of post-hatched development. Values represent mean ± S E. ● $P<0.001$, ◉ $P<0.01$, ◉ $P<0.02$, ○ $P<0.05$ with the corresponding zero level. ** $P<0.01$; * $P<0.02$ with normal.

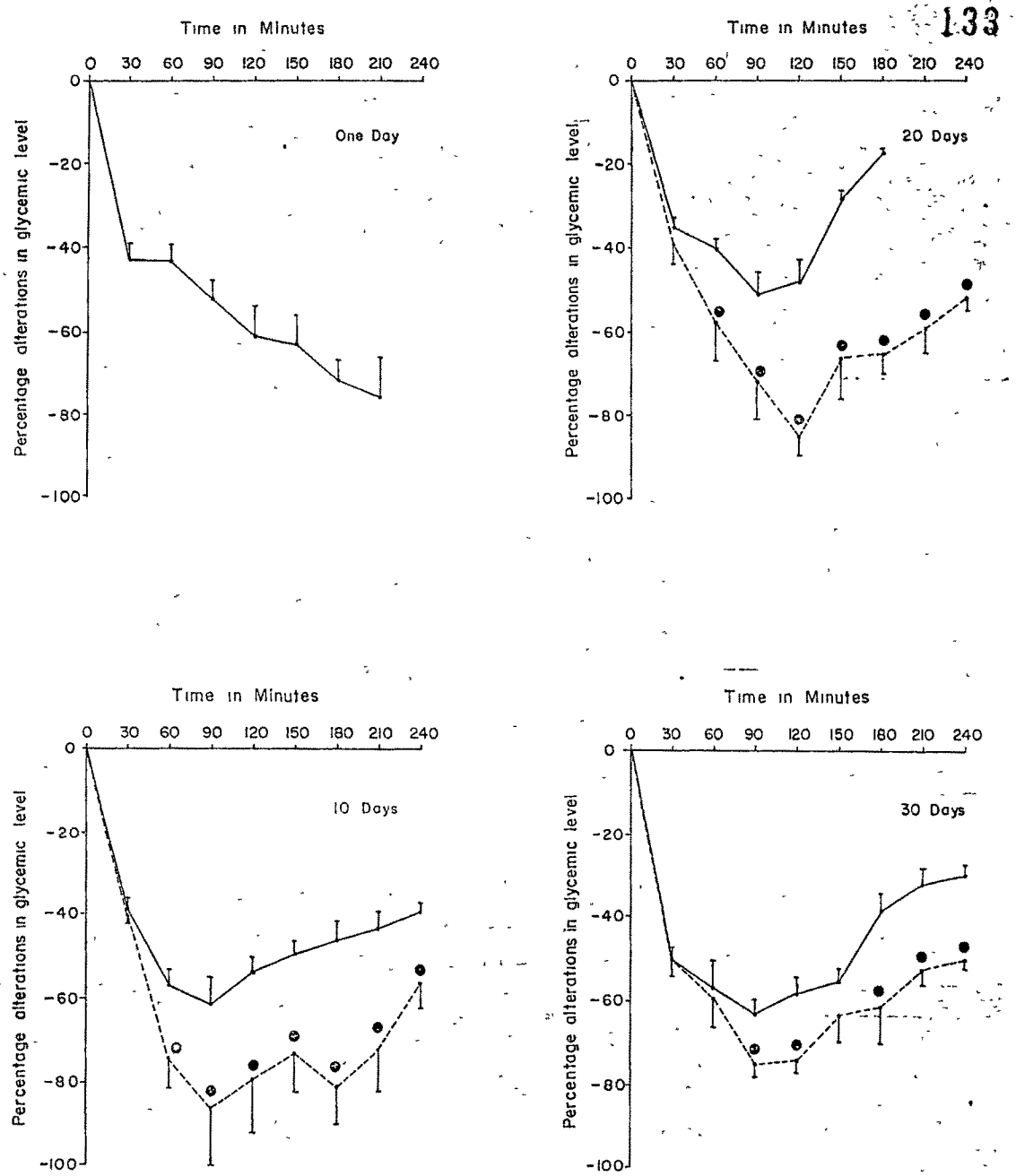

Fig. 2a Chronological percentage alterations in glycemic leval after insulin injection in normal (—) and dexamethasonised (---) chicks in the first month of post-hatched development. Values represent mean ± SE. • $P < 0.001$ with the corresponding control.

compared to controls (62.6%). Though normoglycemia was not established even after 240 min in both DXM treated and control chicks, the recovery to normoglycemia was more slow and gradual in dexamethasonised chicks.

Adrenaline response test (ART)

One day old chicks

The blood glucose level after adrenaline injection showed maximum hyperglycemia (28.2%) by 90 min. However, second peak of hyperglycemia was observed at 180 min after lowered levels at 120 and 150 min. By 210 min, normoglycemic condition was established.

10 day old chicks

Maximum hyperglycemic condition (20.7%) was reached by 30 min in DXM treated chicks while maximum percentage elevation (32.8%) in the control was observable at 90 min. In both groups apparent normoglycemia was attained immediately (at 120 min in controls and 90 min in experimentals).

20 day old chicks

Maximum hyperglycemia in response to adrenaline administration was attained at 60 min in experimentals (54.2%) and 90 min in the controls (26.2%). Thereafter the blood glucose level declined in both groups and reached normoglycemia by 180 min.

30 day old chicks

The maximum hyperglycemia in control chicks in response to adrenaline occurred at 120 min which was 34.9% on a percentage basis. On the other hand, in DXM treated chicks a maximum elevation of only 15.1%

Table 3 Chronological alterations in glycemic levels after adrenaline injections in normal (C) and dexamethasonised (DXM) chicks during the first month of post-hatched development. Values are expressed in mg/100ml blood and represented as Mean ±SE.

Days post-hatch		Time in minutes								
		0	30	60	90	120	150	180	210	240
One day	C	233.30 ± 9.50	250.60 ±13.40	274.20^{b} ±10.90	299.20^{a} ±15.10	259.60 ±14.60	258.80 ±18.10	276.90^{a} ± 9.90	233.30 ± 7.30	251.30 ±10.40
10 days	C	211.70 ± 7.20	213.30 ±12.50	253.40^{c} ±12.10	281.22^{b} ±20.59	241.60 ±14.60	249.10 ±22.10	235.40 ±11.90	234.10 ±12.50	215.80 ±15.60
	DXM	187.60* ± 5.31	227.60^{c} ±14.23	226.50^{c} ±13.80	204.80 ±17.60	182.16 ±20.19	169.50 ±15.30	191.06 ±17.16	192.52 ± 8.01	161.35 ±15.95
20 days	C	202.95 ± 4.69	223.75^{b} ± 5.10	233.28^{d} ±13.70	256.20^{a} ±16.50	244.96^{a} ± 7.40	234.12^{c} ±16.83	222.30^{c} ±14.77	214.12^{d} ±12.52	213.30 ±15.35
	DXM	179.88** ± 6.36	201.16 ± 7.44	277.50^{a} ± 7.89	253.33^{a} ± 9.98	251.86^{a} ±12.50	257.00^{a} ± 7.26	195.00 ±10.12	177.00 ± 9.65	191.19 ±10.12
30 days	C	218.18 ± 3.62	262.17^{b} ±14.99	263.12^{c} ±17.18	293.16^{a} ±12.95	294.39^{a} ±14.43	274.00^{a} ± 7.10	262.90^{a} ± 8.77	247.50^{d} ±14.50	245.98^{c} ±10.01
	DXM	202.62** ± 3.73	233.30^{c} ± 9.86	223.30^{d} ± 6.24	218.30^{d} ± 8.50	181.20^{d} ± 7.83	160.80^{a} ± 6.30	154.00^{a} ± 9.40	158.90^{a} ± 8.20	162.40 ±11.00

a : $P < 0.001$; b : $P < 0.01$; c : $P < 0.02$; d : $P < 0.05$ significant with zero minute.

** $P < 0.01$ * $P < 0.02$ significant with corresponding normal values.

Table 3a Chronological percentage alterations in glycemic level after adrenaline injection in normal (C) and dexamethasonised (DXM) chicks during the first month of post-hatched development. Values represent Mean ±SE.

Days post-hatch		Time in minutes							
		30	60	90	120	150	180	210	240
One day	C	7.40 ± 0.39	17.53 ± 0.69	28.20 ± 1.42	11.20 ± 0.62	10.90 ± 0.76	18.60 ± 0.66	0	7.70 ± 0.31
10 days	C	0.75 ± 0.04	19.60 ± 0.93	32.80 ± 2.40	14.10 ± 0.85	17.60 ± 1.56	11.10 ± 0.56	10.50 ± 0.56	1.90 ± 0.13
	DXM	21.30[a] ± 1.33	20.70 ± 1.26	9.10[a] ± 0.78	- 2.80[a] ± 0.31	- 9.60[a] ± 0.86	1.84[a] ± 0.16	2.60[a] ± 0.10	-13.90[a] ± 1.37
20 days	C	10.20 ± 0.23	14.90 ± 0.87	26.20 ± 1.68	20.60 ± 0.69	15.30 ± 1.41	9.50 ± 1.42	5.50 ± 0.81	5.09 ± 0.98
	DXM	11.70 ± 0.43	54.20[a] ± 1.54	40.80[a] ± 1.60	40.00[a] ± 1.98	42.80[a] ± 1.20	8.40 ± 0.43	- 1.60[a] ± 0.08	6.20 ± 0.32
30 days	C	20.10 ± 1.14	20.50 ± 1.33	34.30 ± 1.51	34.90 ± 1.71	25.50 ± 0.66	20.40 ± 0.68	13.40 ± 0.78	12.74 ± 1.51
	DXM	15.10 ± 0.63	10.20[a] ± 0.36	7.73[a] ± 0.57	-10.50[a] ± 0.59	-20.60[a] ± 0.80	-23.90[a] ± 1.45	-21.50[a] ± 1.10	19.80[a] ± 1.34

a : $P < 0.001$ significant with the corresponding normal values.

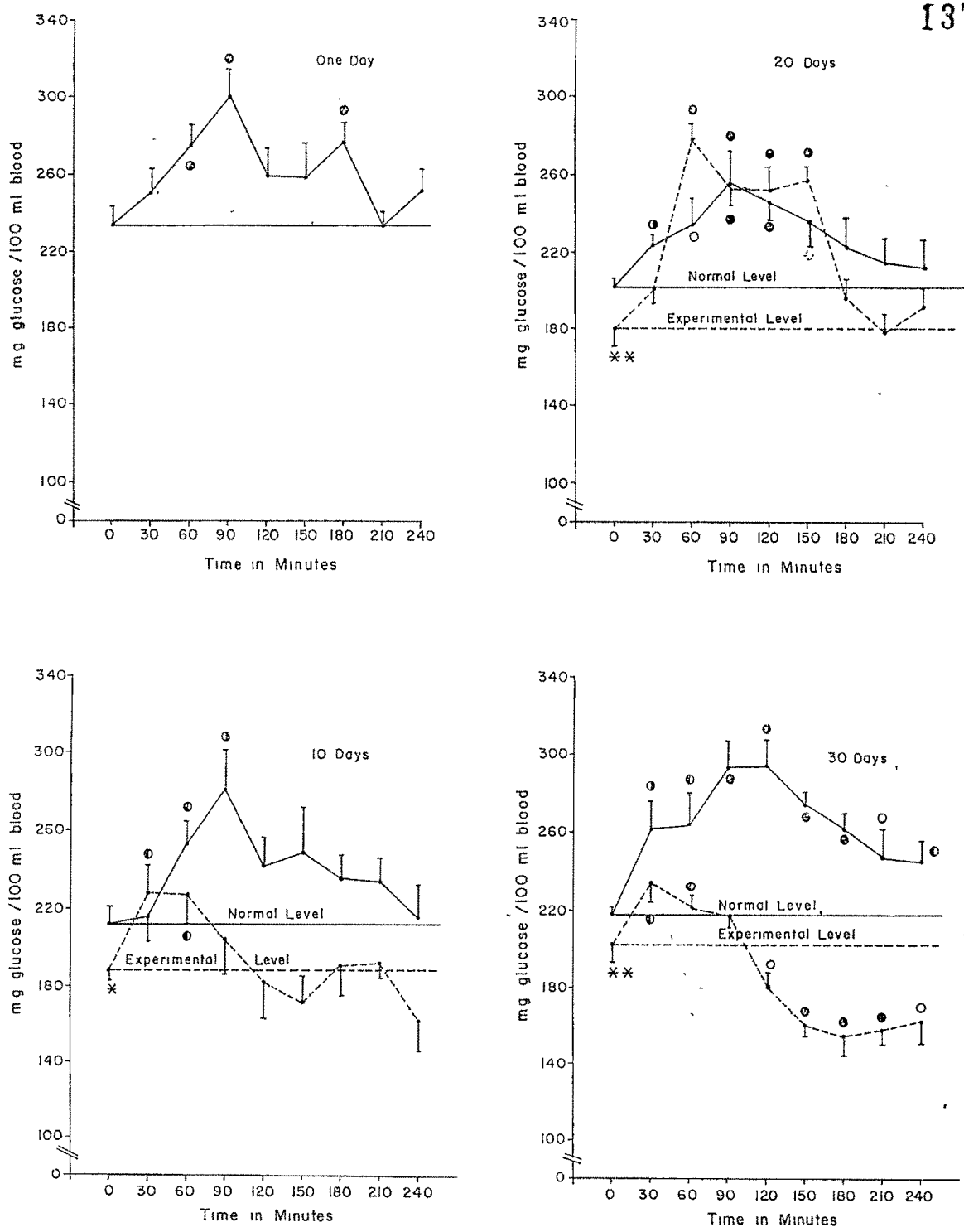

Fig. 3 Chronological alterations in adrenaline response curve in normal (⟶) and dexamethasonised (---) chicks during the first month of post-hatched development. Values represent mean ± S E. ○ $P<0.001$, ◉ $P<0.01$, ◉ $P<0.02$, ○ $P<0.05$ with the corresponding zero level. ** $P<0.01$; * $P<0.02$ with normal.

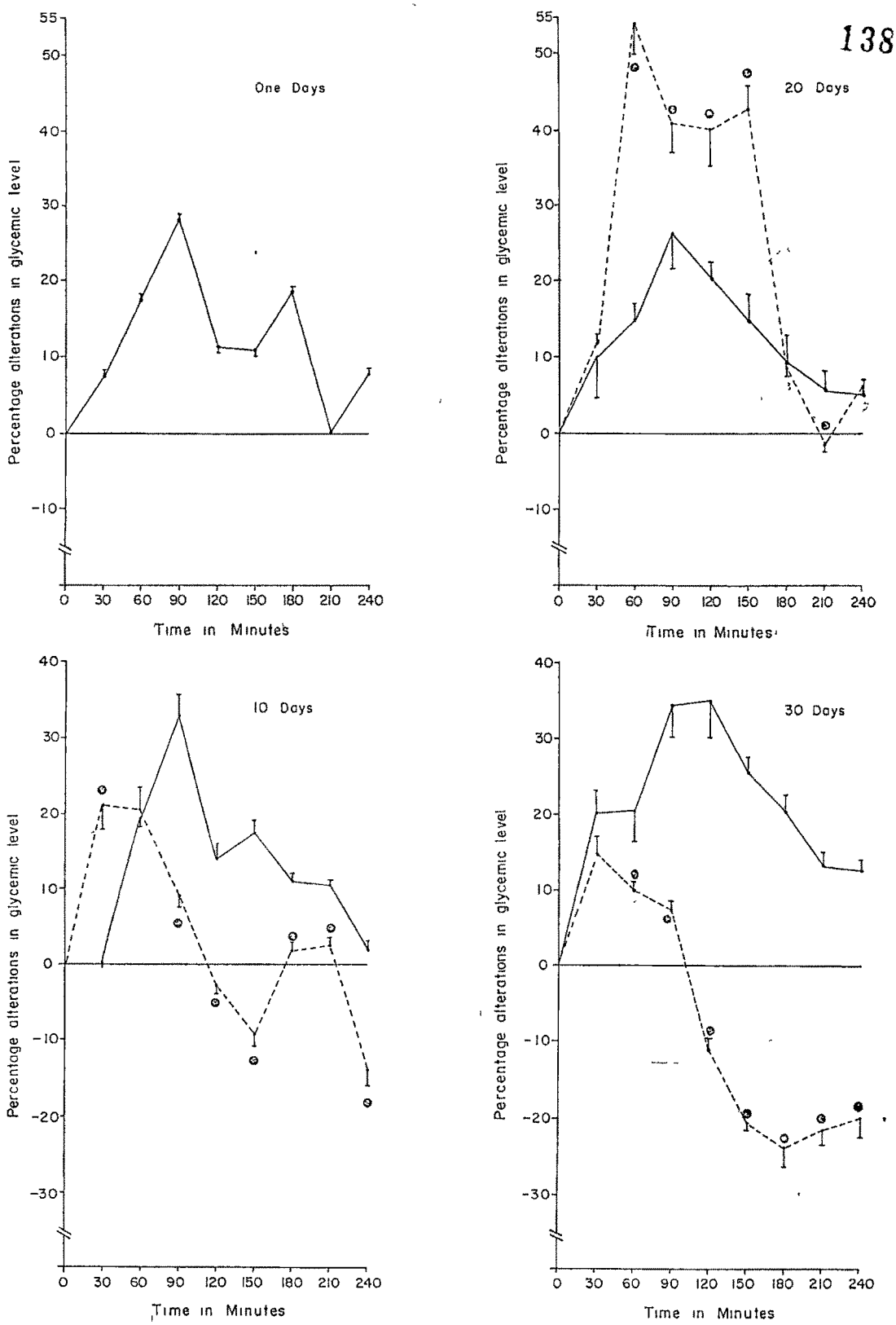

Fig. 3a Chronological percentage alterations in glycemic level after adrenaline injection in normal (——) and dexamethasonised (----) chicks in the first month of post-hatched development. Values represent mean ± SE.
o P<0.001 with the corresponding control.

occurred by 30 min. The subsequent fall in the glucose level was very gradual in the case of controls with the result that normoglycemia was not attained even at the end of 240 min while it was very steep in the case of experimentals resulting in significant hypoglycemia by 120 min. This hypoglycemic condition reached its maximum by 180 min, whereafter, there was very gradual increase in glycemic level though not reaching normoglycemia even at 240 min.

Glucagon response test (GRT)

One day old chicks

Glucagon induced maximum hyperglycemia was attained by 90 min which was only 10.6% and reached normal level by 180 min which further got reduced to hypoglycemic condition at 210 min before recovery again by 240 min.

10 day old chicks

Though there was a significant decrease ($P < 0.02$) in basal glucose level in dexamethasonised chicks, the glucagon induced hyperglycemic condition was significantly higher in relation to the controls. Maximum hyperglycemic condition was reached at 120 min in DXM treated chicks (97.4%) as compared to the 21.5% in controls at 90 min. While in the experimentals there was a steep fall in glycemic level ultimately reaching a significant hypoglycemic condition by 180 min which started recovering to normoglycemia thereafter; the controls attained normoglycemia by 150 min itself.

20 day old chicks

The maximum elevation in blood glucose in response to glucagon was attained at 60 min in both the control and experimental chicks.

Table 4 Chronological alterations in glycemic levels after glucagon injections in normal (C) and dexamethasonised (DXM) chicks during the first month of post-hatched development. Values are expressed in mg/100ml blood and represented as Mean ±SE.

Days post-hatch		Time in minutes 0	30	60	90	120	150	180	210	240
One day	C	228.98 ± 6.71	234.23 ±10.95	246.37 ±13.17	253.46 ±14.44	248.29 ± 8.80	239.40 ±10.42	219.16 ±14.00	208.62^{d} ± 7.28	215.45 ±13.67
10 days	C	199.90 ± 9.00	205.00 ± 7.33	222.90 ±11.10	242.20 ±15.20	209.90 ± 7.70	200.30 ± 4.60	195.60 ± 5.40	187.30 ± 6.82	177.10 ± 8.20
	DXM	168.80^{*} ± 8.40	249.70^{a} ±13.70	279.00^{a} ±15.80	311.00^{a} ±22.20	333.30^{a} ±46.20	266.60^{a} ± 6.40	135.10^{b} ± 8.00	146.23 ±11.26	
20 days	C	223.00 ± 4.03	296.11^{b} ±25.80	379.60^{a} ±29.53	246.26 ±18.53	211.08 ±12.38	199.98^{a} ±13.32	189.67^{a} ± 7.27	180.90^{a} ± 7.39	179.82^{a} ± 3.87
	DXM	169.59^{***} ± 8.10	182.65 ± 4.94	185.13 ± 8.01	167.83 ± 6.80	175.23 ± 3.12	157.35 ± 3.54	124.02 ±14.70	134.22 ± 8.04	135.52 ± 4.15
30 days	C	218.03 ± 5.69	312.43^{a} ±14.46	396.71^{a} ±26.90	412.91^{a} ±29.34	310.02^{a} ±28.80	268.46^{b} ±18.05	263.65^{c} ±17.05	257.36^{c} ±14.33	236.88^{d} ± 8.27
	DXM	196.62^{*} ± 5.73	214.02 ± 9.41	236.98^{d} ±16.55	240.68 ±28.69	183.64 ±11.81	165.88^{d} ±14.17	202.90 ±22.04	173.10 ±19.09	181.30 ±27.08

a : $P < 0.001$; b : $P < 0.01$; c : $P < 0.02$; d : $P < 0.05$ significant with zero minute.

*** $P < 0.001$ * $P < 0.02$ significant with corresponding normal values.

Table 4a Chronological percentage alterations in glycemic level after glucagon injection in normal (C) and dexamethasonised (DXM) chicks during the first month of post-hatched development. Values represent Mean ±SE.

Days post-hatch		Time in minutes							
		30	60	90	120	150	180	210	240
One day	C	2.20 ± 0.10	7.50 ± 0.40	10.60 ± 0.60	8.40 ± 0.29	4.50 ± 0.19	- 4.20 ± 0.26	- 8.80 ± 0.30	- 5.90 ± 0.37
10 days	C	2.50 ± 0.08	11.50 ± 0.57	21.50 ± 1.33	5.10 ± 0.18	0.20 ± 0.004	- 2.15 ± 0.05	- 6.30 ± 0.22	-11.40 ± 0.52
	DXM	47.90[a] ± 2.62	65.20[a] ± 3.69	84.20[a] ± 6.01	97.40[a] ±13.50	57.90[a] ± 1.38	-19.90[a] ± 1.17	-13.30[a] ± 1.02	
20 days	C	33.60 ± 2.90	70.20 ± 5.46	10.90 ± 0.82	- 5.30 ± 0.31	-10.30 ± 0.17	-14.90 ± 0.57	-18.80 ± 0.76	-19.30 ± 0.41
	DXM	7.70[a] ± 0.20	9.10[a] ± 0.39	- 1.03[a] ± 0.04	3.30[a] ± 0.05	- 7.20 ± 0.16	-26.80[a] ± 3.17	-20.80 ± 1.24	-20.08 ± 0.61
30 days	C	43.20 ± 1.99	81.90 ± 5.55	89.30 ± 6.34	42.10 ± 3.91	23.10 ± 1.55	20.90 ± 1.16	18.03 ± 1.16	8.60 ± 0.30
	DXM	8.80[a] ± 0.38	20.50[a] ± 1.43	22.40[a] ± 2.67	- 6.60[a] ± 0.42	-15.60[a] ± 1.33	3.10[a] ± 0.33	-11.90[a] ± 1.31	- 7.70[a] ± 1.15

a : $P < 0.001$ significant with the corresponding normal values.

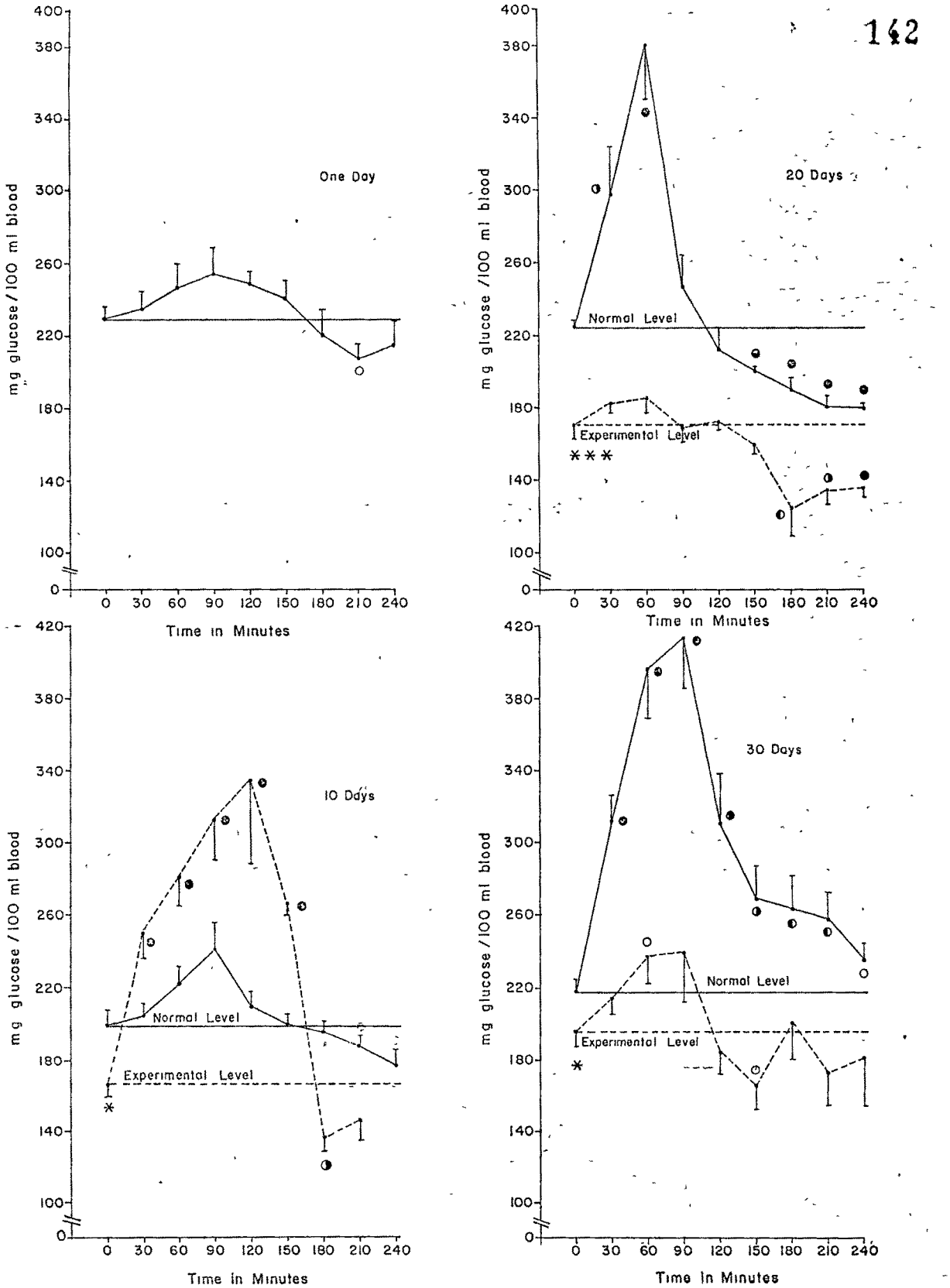

Fig. 4 Chronological alterations in glucagon response curve in normal (⟶) and dexamethasonised (- - -) chicks during the first month of post-hatched development. Values represent mean ± S E. • P< 0 001, ◑ P< 0·01, ◦ P< 0·02, ○ P< 0·05 with the corresponding zero level. *** P< 0·001, * P< 0·02 with normal

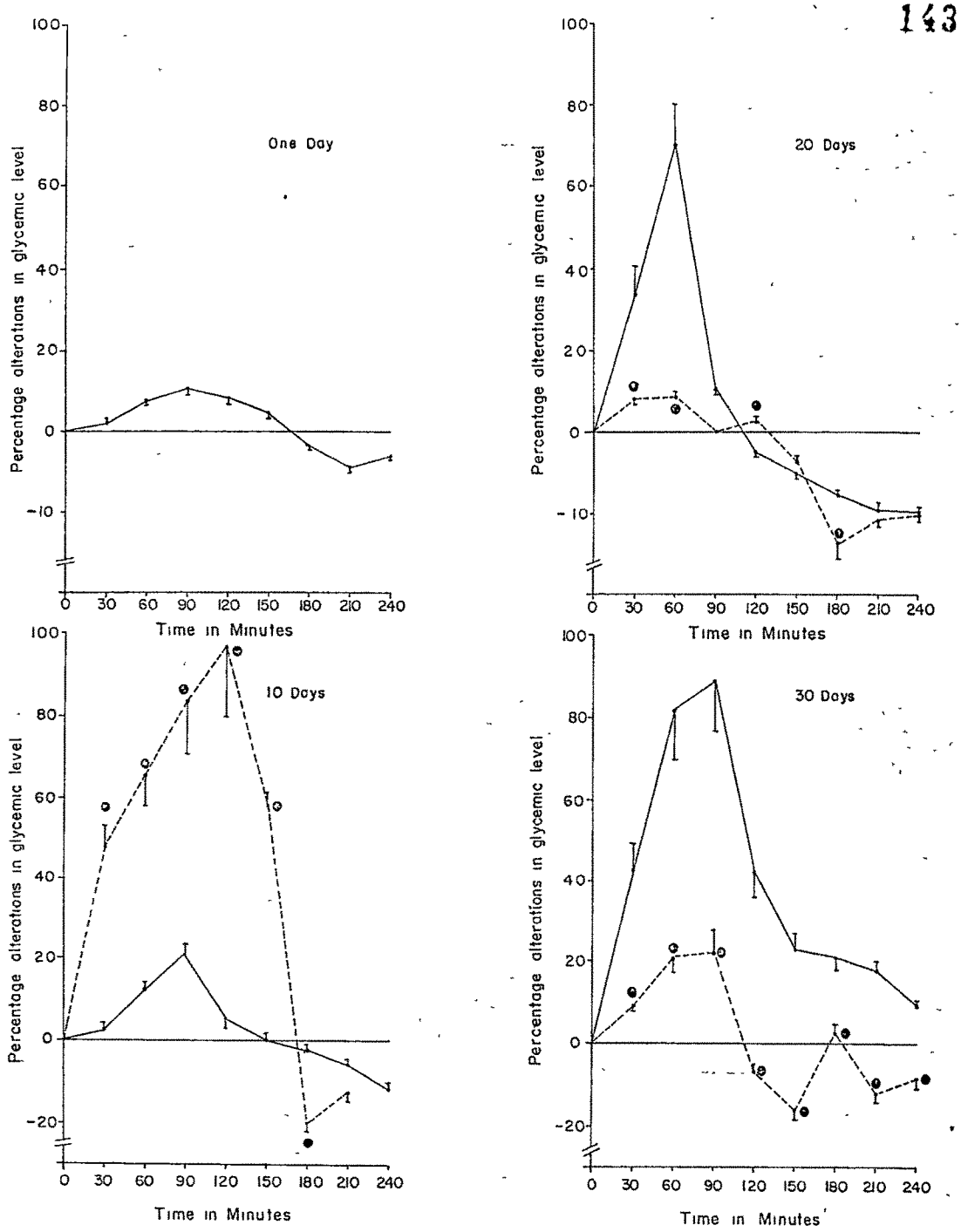

Fig. 4a Chronological percentage alterations in glycemic level after glucagon injection in normal (——) and dexamethasonised (- - -) chicks in the first of post-hatched development. Values represent mean ± SE.

• $P < 0.001$ with the corresponding control

Table 5 Alterations in GTT, ART and GRT induced glucose elevation and clearance rate and IRT-induced glucose clearance and normalization rates.

		CONTROL Age of chicks				DEXAMETHASONISED Age of chicks		
		ONE DAY	10 DAYS	20 DAYS	30 DAYS	10 DAYS	20 DAYS	30 DAYS
Glucose	E	1.320	0.724	1.290	0.686	0.252	0.236	0.198
	K	0.432	0.567	0.463	0.524	0.574	0.646	0.962
	E/K	3.020	1.270	2.780	1.300	0.439	0.365	0.205
Insulin	Ki	0.839	1.490	1.270	1.460	1.860	1.390	1.550
	Ni	0.466	0.380	0.862	0.575	0.271	0.555	0.284
	Ki/Ni	1.800	3.920	1.470	2.530	6.860	2.500	5.450
Glucagon	Eg	0.272	0.470	2.610	2.160	1.370	0.259	0.489
	Kg	0.381	0.776	2.800	1.650	3.300	0.576	1.900
	Eg/Kg	0.713	0.605	0.932	1.300	0.421	0.449	0.257
Adrenaline	Ea	0.732	0.772	0.591	0.629	1.330	1.620	1.020
	Ka	0.549	0.436	0.376	0.403	0.504	0.670	0.434
	Ea/Ka	1.330	1.770	1.560	1.560	2.630	2.410	2.340

E : Glucose elevation rate
K : Glucose clearance rate
Ki : Insulin induced glucose clearance rate
Ni : Insulin induced glucose normalization rate
Ea : Adrenaline induced glucose elevation rate
Ka : Adrenaline induced glucose clearance rate
Eg : Glucagon induced glucose elevation rate
Kg : Glucagon induced glucose clearance rate

However, the percentage elevation in the case of dexamethasonised chicks was significantly low (9.1% as compared to 70.2% in controls). Both groups of chicks attained significant hypoglycemia thereafter (150 min in control and 180 min in experimental) and continued to remain so even at 240 min.

30 day old chicks

The glucagon induced maximum hyperglycemia occurred by 90 min in both DXM treated and control chicks. The percentage elevation was significantly higher in controls (89.3%) as compared to the experimentals (22.4%). Thereafter, whereas the controls recorded gradual decrease in glycemic level though not reaching normoglycemia by 240 min, the experimentals reached normoglycemia by 180 min through a hypoglycemic state at 150 min.

DISCUSSION

Coordinated functioning of pancreatic hormones in birds is necessary for meeting the various adaptive physiological requirements in keeping with the diverse activities characteristic of this class of vertebrates. Appropriate mixture of insulin, glucagon, somatostatin and even avian pancreatic polypeptide is considered necessary for birds to adjust their nutrient availability and disposal (Hazelwood, 1984). Avian carbohydrate homeostasis is ultimately due to the fine tuned interdigitated functioning of the pancreatic hormones. Of the two major pancreatic hormones, insulin and glucagon, the latter is considered to be the principal

director of avian carbohydrate metabolism in adult birds (Hazelwood, 1986). However, the right proportion of pancreatic hormones necessary for avian carbohydrate homeostasis will have to be essentially established during the post-natal phase of development. Changing levels of insulin and glucagon reported to occur during various days of post-natal development in chicks (see Sinsigalli et al., 1987) are corroborative of this contention, though, a clear elucidation of this is yet to come. During this purported crucial phase of establishment of appropriate adult type hormonal milieu, a disturbance affecting any of the permissive hormonal components could have profound effects on carbohydrate metabolism. Corticosterone being one of the permissive hormones influencing the actions of pancreatic hormones (Mialhe, 1958, 1969), either hypo- or hypercorticalism is likely to affect the role of pancreatic hormones in carbohydrate homeostasis. As such dishomeostasis in carbohydrate metabolism has been recorded under chronic hypo- and hypercorticalism in one month old chicks (Chapter III). The glucose tolerance test provides a clue to the functional status of pancreas, specifically the β cells. Decreased glucose tolerance is indicative of reduced functional ability of β cells, while increased glucose tolerance is indicative of greater functional ability. This study conducted as a follow-up on the basis of previous findings on altered carbohydrate metabolism in DXM induced hypocorticalism (Chapter III), has revealed altered glucose tolerance and insulin resistance. Similarly, altered response to glucagon and adrenaline have also been recorded in dexamethasonised chicks.

It is also interesting to note that even the control chicks showed differential glucose tolerance and insulin, glucagon and adrenaline responses on a chronological basis. Moreover, during the first 30 days of post-natal development, the chicks appear to be relatively more insulin sensitive than glucagon. This is borne out by the the observed pronounced percentage fall in blood glucose level after insulin administration and relatively poor percentage increment after glucagon administration especially on the day of hatching and the 10th day. Presumably, glucagon induced glucose elevation is relatively less as compared to insulin induced glucose clearance except for 20th and 30th days when glucagon induced glucose elevation is greater. The progressively increasing glucagon sensitivity is denoted by the increasing hyperglycemia and glucose elevation rate from 1-30 days. Insulin release in response to increased glucose elevation by glucagon is also indicated by the correspondingly increasing clearance rate. However, the increasing Eg/Kg values from 10-30 days indicate increasing glucagon responsiveness and decreasing insulin sensitivity. In this context it is well established that glucagon is a powerful stimulus to insulin release in chickens (Hazelwood, 1986). Some fluctuation in the circulating level of insulin in its sensitive phase during the first month of post-natal development is also suggested. This is assumable by the decreased glucose elevation on 10th and 30th days relative to the 1st and 20th days subsequent to glucose loading though the clearance rate is much the same. Accordingly the E/K values are higher on 1st and 20th days and lower on 10th and 30th days of development. Hence it is likely that relatively more insulin release occurs during the second and fourth

week. Adrenaline has been known as a potent glycogenolytic hormone in chicken (Golden and Long, 1942; Langslow et al., 1970; Cramb et al., 1982; Picardo and Dickson, 1982). Glucagon has been considered to be the more potent glycogenolytic agent than adrenaline in birds (Hazelwood, 1986). In the present study though this has been found to hold true for 20 and 30 days old chicks, adrenaline was found to be more potent than glucagon on 1st and 10th days as revealed by the greater glucose elevation rates with adrenaline on 1st and 10th days and with glucagon on 20th and 30th days. Obviously, in neonatal chicks, adrenaline may function as the more potent glycogenolytic agent during the first fortnight after hatch, a period corresponding to low glucagon responsiveness as inferred above.

Dexamethasone induced hypocorticalism seems to increase insulin sensitivity as well as decrease glucagon responsiveness. Evidences available in this context from this study are, attenuated hyperglycemia on glucose loading and better glucose tolerance, and pronounced hypoglycemia in response to insulin injection as compared to the control chicks. Decreased glucose elevation rate on glucose loading with resultant low E/K values, greater clearance rate subsequent to glucagon induced glucose elevation with corresponding low Eg/Kg values and greater glucose clearance in response to insulin followed by slower normalization rate with resultant higher Ki/Ni values are collateral corroborative evidences strengthening this contention. All these observations taken together indicate stimulated insulin sensitivity together with attenuated glucagon responsiveness in chicks with hypocorticalism

during the first 30 days of post-natal development. The purported role of corticosterone in potentiating the action of glucagon and checking that of insulin, as is being inferred from this study, finds adequate support from the observations of Mialhe (1958, 1969) of the corrective influence of corticosterone on insulin hypersensitiveness and markedly impaired hyperglycemic effect of glucagon in hypophysectomized ducks. The observations of significantly increased hepatic glycogen content and hypoglycemia occurring in response to DXM treatment in chicks (Chapter III) lend further evidence to the concept of a permissive role of corticosteroids in establishing and maintaining carbohydrate homeostasis by way of their modulatory actions on pancreatic hormones.

Another interesting inference that could be drawn from the present observations is the potentiated glycogenolytic response to adrenaline due to hypocorticalism during the first month of post-natal development in chicks. This is well evidenced by the adrenaline induced markedly higher glucose elevation rate and double the Ea/Ka values obtained in DXM treated chicks relative to the controls. The more or less identical glucose clearance rate recorded in both control and DXM treated chicks subsequent to adrenaline induced hyperglycemia also suggests the immunity of post-natal chicks to the antagonistic effect of adrenaline on insulin action observed in adult mammals and birds (Ensinck and Williams, 1981; Patel and Ramachandran, 1989). The present study on the whole suggests a definite modulatory role for corticosteroids in the chronological set of events leading to the establishment of adult pattern of functional interrelationship between pancreatic hormones *vis a vis* carbohydrate homeostasis during the post-natal phase of chick development.