It had been hoped that the E.E.G. record would give objective evidence of the onset of the transitional phase between sleep and wakefulness; that the rhythm would revert to normal before the patient awoke. This did not occur. Clinical observation gave as early information as did the E.E.G.

Two patients admitted to hospital in barbiturate coma were given bemegride, and their course was followed by intermittent E.E.G. recordings. Each patient returned to consciousness while on treatment with bemegride, but the E.E.G. records gave no indication of the depth of coma, and indeed evidence of barbiturate activity on the E.E.G. persisted for many hours after the patient wakened. This confirms the findings of Peacock (1956).

The E.E.G. evidence might suggest that bemegride is not a specific barbiturate antagonist, but the site of action of sodium amylobarbitone may be principally in the hypothalamus, as may also be that of bemegride. The E.E.G. records only electrical potential changes in the cerebral cortex.

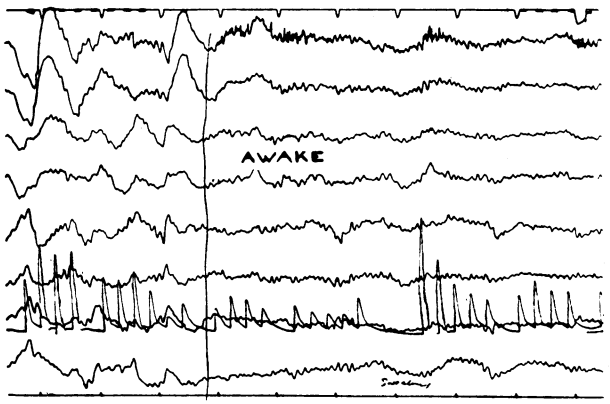

FIG. 1.—E.E.G. record showing change in pattern coinciding with clinical arousal.

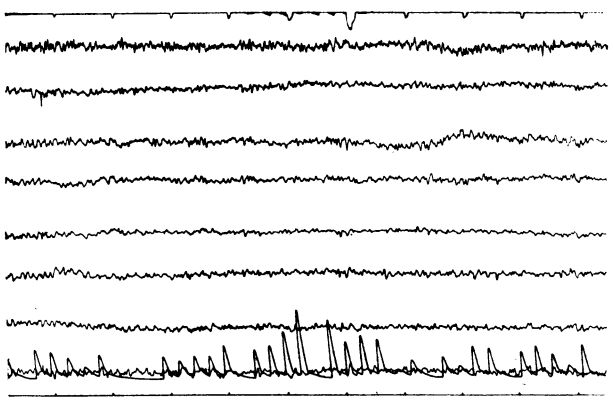

FIG. 2.—Persistence of barbiturate activity in Case 7 after wakening.

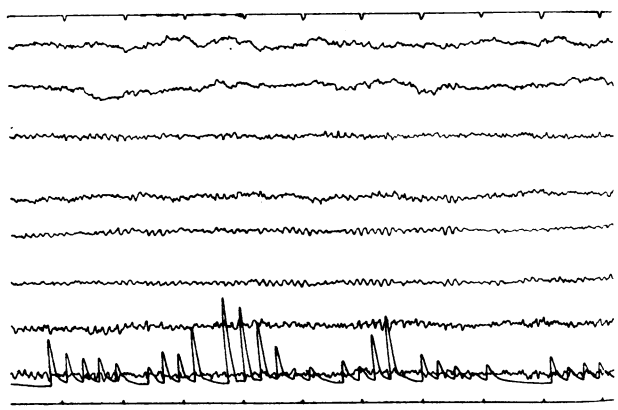

FIG. 3.—Normal resting E.E.G. record for Case 7.

Summary

The effects of bemegride and saline in terminating thiopentone anaesthesia in 20 women were compared, using the "double-blind" technique. There was no significant difference in the "wakening times" after either substance. The fallacies of using such a method to evaluate the action of bemegride are stressed.

Continuous E.E.G. records were taken in eight volunteers who were roused with bemegride from sleep induced by sodium amylobarbitone. The E.E.G. pattern of deep sleep did not alter until the subjects wakened. In three patients who showed barbiturate activity on the E.E.G. this was not dispelled by bemegride.

The significance of these findings is briefly discussed.

I thank Dr. D. McKay Hart for permission to study the gynaecological patients; Dr. O. Watt, who administered the anaesthetics; and Dr. S. Renfrew, Mrs. I. S. Haggar, and Miss M. Watson, of the E.E.G. department of the Glasgow Royal Infirmary, for their co-operation and guidance. My thanks are also due to the volunteers.

REFERENCES

Bentel, H., Barlow, M. B., and Ginsberg, H. (1956). *Med. Proc.*, 2, 198.
Canbäck, T., Diding, N., Ohlsson, W. T. L., and Werkö, L. (1955). *Svenska Läk.-Tidn.*, 52, 2356.
Clemmesen, C. (1956). *Lancet*, 2, 966.
Dotevall, G., and Herner, B. (1957). *Brit. med. J.*, 2, 451.
Harris, T. A. B. (1955). *Lancet*, 1, 181.
Peacock, J. M. (1956). *Electroenceph. clin. Neurophysiol.*, 8, 289.
Rowell, N. R. (1957). *Lancet*, 1, 407.
Shaw, F. H., Simon, S. E., Cass, N. M., Shulman, A., Anstee, J. R., and Nelson, E. R. (1954). *Nature (Lond.)*, 174, 402.
Shulman, A., Shaw, F. H., Cass, N. M., and Whyte, H. M. (1955). *Brit. med. J.*, 1, 1238.

A COMPARISON OF MATERNAL AND FOETAL FOLIC ACID AND VITAMIN B_{12} AT PARTURITION

BY

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In a previous study comparing folic acid (P.G.A.) and vitamin B_{12} during normal pregnancy (Baker *et al.*, 1957) it was reported that maternal vitamin B_{12} blood levels were low and P.G.A. levels high. Recent studies on the vitamin B_{12} serum levels in mothers and infants at delivery show that maternal levels decline through pregnancy and infant levels are approximately twice that of the mother (Okuda *et al.*, 1956; Boger *et al.*, 1957; Dumont, 1957). Since both P.G.A. and vitamin B_{12} play significant parts in pregnancy and foetal development (O'Dell *et al.*, 1951; Nelson *et al.*, 1956; Nelson and Evans, 1956), a comparison of vitamin B_{12} and P.G.A. serum levels in mothers and infants at parturition was carried out.

Methods.—Vitamin B_{12} assays on maternal and infant serum were carried out in parallel with *Euglena gracilis* and *Ochromonas malhamensis* by methods previously described (Hutner *et al.*, 1956; Baker *et al.*, 1956). The P.G.A. levels were assayed with a thermophilic bacillus (Baker *et al.*, 1955, 1957). Maternal blood was collected from an antecubital vein at the time of delivery. Infant blood was obtained from the cord. Samples were collected from 113 patients admitted to the obstetrical service of the Mount Sinai Hospital.

Results

The results are given in Table I. The median value of 190 μμg. of vitamin B_{12} per ml. in the maternal serum is lower than that of 390 μμg./ml. in infant serum. The same relationship is shown for P.G.A. levels; the median

TABLE I.—*Vitamin B_{12} and P.G.A. Content of Maternal and Infant Blood*

Quartile	Vitamin B_{12} (μμg./ml.)		P.G.A. (mμg./ml.)	
	Maternal	Infant	Maternal	Infant
1st	25–120	35–250	1–4	1–9
2nd	120–190	200–390	4–7·5	9–40
3rd	190–270	390–600	7·5–22·5	40–90
4th	>270	>600	>22·5	>90
Median	190	390	7·5	40
No. of patients ..	104	70	67	38

in maternal serum is 7.5 mμg./ml., and in infant serum 40 mμg./ml. A total of 104 specimens of maternal blood and 70 samples of cord blood were assayed for vitamin B_{12}; 67 maternal and 38 infant samples were assayed for P.G.A. Only 14% of the infant blood showed vitamin B_{12} values below the median of the mothers. Likewise, 26% of the infant blood fell into the P.G.A. 0–10 mμg./ml. range, which comprises 66% of the maternal samples.

In Table II a total of 22 paired mother and infant vitamin B_{12} and P.G.A. levels are listed. Except for two cases (Nos. 17 and 22) the vitamin B_{12} and P.G.A. levels in infant blood are higher than in the corresponding maternal serum.

TABLE II.—*Paired Mother and Infant P.G.A. and Vitamin B_{12} Serum Values**

Patient No.	Mother		Infant	
	Vitamin B_{12}	P.G.A.	Vitamin B_{12}	P.G.A.
1	53	3	115	4
2	80	2·5	310	3·5
3	90	1	330	3·5
4	100	5	270	11
5	121	5·5	225	51
6	125	2	325	5
7	128	7	246	41
8	135	5	250	50
9	165	2	650	5·5
10	170	2	1,150	5·5
11	180	5	300	100
12	200	2·5	334	12
13	200	100	450	120
14	200	100	770	250
15	217	5	437	41
16	233	9	265	9·5
17	250	50	150	200
18	250	33	250	100
19	250	100	600	150
20	300	3	390	100
21	350	27	700	60
22	550	11	120	3·5

* Vitamin B_{12} values given μμg./ml., P.G.A. in mμg./ml.

Discussion

Vitamin-B_{12} levels in the serum decrease throughout pregnancy (Boger *et al.*, 1956). The higher infant blood levels (Table I) suggest that during this state the foetus draws upon maternal vitamin-B_{12} stores, causing a temporary vitamin-B_{12} depletion in the mother. This is in agreement with reported results (Karlin and Dumont, 1955; Okuda *et al.*, 1956). Vitamin B_{12} is essential for proper metabolic functions in man and animals (Jukes and Williams, 1954); the part it plays in foetal growth and tissue nucleic acid synthesis is of primary significance. Animals deficient in vitamin B_{12} give birth to hydrocephalic young (O'Dell *et al.*, 1951) with a high incidence of skeletal abnormalities (Grainger *et al.*, 1954). The nucleic acid content of the tissues also becomes altered (Bruemmer *et al.*, 1955). The interrelationship between vitamin B_{12} and P.G.A. in nucleic acid synthesis (Mueller and Will, 1955) explains the foetal needs for these two vitamins. As in the case of vitamin B_{12}, the foetus draws P.G.A. from the maternal circulation, lowering the amount of circulating P.G.A. (Tables I and II).

Another role of P.G.A. lies in its effect on hormonal responses (Baker *et al.*, 1957). P.G.A. antagonists inhibit progesterone activity and cause foetal death. These actions are overcome by P.G.A. (Thiersch and Philips, 1950; King and Velardo, 1951). At parturition the elevated progesterone level noted during pregnancy falls (Pearlman, 1954); at this time the P.G.A. levels also fall (Baker *et al.*, 1957) (Table I). These observations suggest an interrelated action between progesterone and P.G.A. during pregnancy; at term this action ceases. The ability of P.G.A. to overcome the adverse effects of P.G.A. antimetabolites on progesterone activity, and its action in catalysis of varied essential synthetic processes, make P.G.A. important for normal pregnancy and foetal viability.

The paired samples of mother and infant serum (Table II) illustrate the differentials in vitamin B_{12} and P.G.A. at delivery. In some cases the infant vitamin-B_{12} and P.G.A. levels are over four times as high as those of the mother. The high infant P.G.A. and vitamin-B_{12} serum levels explain the stress imposed by pregnancy on maternal metabolism and indicate the avidity of rapidly growing foetal tissues for these vitamins.

Summary

A comparison of vitamin B_{12} and P.G.A. serum levels of mothers and infants at parturition was carried out. Vitamin-B_{12} and P.G.A. levels are lower in the mothers. The role of P.G.A. and vitamin B_{12} in pregnancy is discussed.

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REFERENCES

Baker, H., Erdberg, R., Pasher, I., and Sobotka, H. (1957). *Proc. Soc. exp. Biol. (N.Y.)*, **94**, 513.
—— Hutner, S. H., and Sobotka, H. (1955). Ibid., **89**, 210.
—— Sobotka, H., Pasher, I., and Hutner, S. H. (1956). Ibid., **91**, 636.
Boger, W. P., Bayne, G. M., Wright, L. D., and Beck, G. D. (1957). *New Engl. J. Med.*, **256**, 1085.
—— Wright, L. D., Beck, G. D., and Bayne, G. M. (1956). *Proc. Soc. exp. Biol. (N.Y.)*, **92**, 140.
Bruemmer, J. H., O'Dell, B. L., and Hogan, A. G. (1955). Ibid., **88**, 463.
Dumont, M. (1957). *Presse méd.*, **65**, 601.
Grainger, R. B., O'Dell, B. L., and Hogan, A. G. (1954). *J. Nutr.*, **54**, 33.
Hutner, S. H., Bach, M. K., and Ross, G. I. M. (1956). *J. Protozool.*, **3**, 101.
Jukes, J. H., and Williams, W. L. (1954). In *The Vitamins*, edited by W. H. Sebrell, jun., and R. S. Harris, **1**, 421. Academic Press, New York.
Karlin, R., and Dumont, M. (1955). *C.R. Soc. Biol. (Paris)*, **149**, 1986.
King, C. T. G., and Velardo, J. T. (1951). *Fed. Proc.*, **10**, 208.
Mueller, J. F., and Will, J. J. (1955). *Amer. J. clin. Nutr.*, **3**, 30.
Nelson, M. M., and Evans, H. M. (1956). *Proc. Soc. exp. Biol. (N.Y.)*, **91**, 614.
—— Wright, H. V., Baird, C. D. C., and Evans, H. M. (1956). Ibid., **92**, 554.
O'Dell, B. L., Whitley, J. R., and Hogan, A. G. (1951). Ibid., **76**, 349.
Okuda, K., Helliger, A. E., and Chow, B. F. (1956). *Amer. J. clin. Nutr.*, **4**, 440.
Pearlman, W. H. (1954). *Acta Endocr. (Kbh.)*, **17**, 321.
Thiersch, J. B., and Philips, F. S. (1950). *Proc. Soc. exp. Biol. (N.Y.)*, **74**, 204.

The National Society for Clean Air has recently issued a new edition of the *Clean Air Year Book*. It contains information about the Clean Air Act and related matters, together with general and technical information on the problem of air pollution, and lists of recent papers, publications, and interested organizations. The *Year Book* also includes the Society's annual report for 1957 and information about its organization and activities. The report, discussing the Clean Air Act, is optimistic. "The central government," it says, "has done much to ensure that the Act is in no way neglected," and adds, "How industry as a whole will meet the challenge of the Act remains to be seen." Local authorities, the report continues, are giving considerable attention to their responsibilities under the Act, although the number and size of the smoke control areas so far projected is comparatively small when measured against the annual target proposed by the Beaver Committee. The *Year Book* may be obtained from the Society, Palace Chambers, Bridge Street, London, S.W.1, price 2s. (or 2s. 4d. by post).