was not determined and for present purposes uniform distribution was assumed.

It is shown in Fig. 1 that the concentration of DNP corresponding to the maximum value of the stimulation ratio is nearly the same at 25°C and 37.5°C (0.4 mg % and 0.6 mg % respectively). However, the optimum concentration of DNP for stimulation of respiration in excised rat cerebral cortex at 37.5°C is much lower than the optimum concentration reported by Tainter[2] for stimulation of oxygen consumption in the intact rat (*ca* 6 mg %). This indicates either that the cerebral cortex is an atypical organ in this respect or that the experimental conditions were so different that direct comparison of the two findings cannot be made. Studies are in progress on other organs to clarify this point.

It is also shown in Fig. 1 that the maximum value of the stimulation ratio and the minimum inhibitory concentration of DNP are both considerably greater at 25°C than at 37.5°C. This is in concordance with our earlier observation[4] that the stimulation ratio corresponding to a single stimulating concentration of DNP (0.75 mg %) varies with temperature and increases with diminution in temperature over a wide range. It is also in accord with the findings of Hall, Crismon and Chamberlin[6] on the intact anesthetized cat.

Conclusions. The optimum concentration of DNP for the stimulation of oxygen consumption in excised rat cerebral cortex is approximately the same at 37.5°C and 25°C. However, the maximum value of the stimulation ratio and the minimum inhibitory concentration of DNP are considerably greater at 25° than at 37.5°C.

13610

Oxygen Uptake of Blood Serum.*

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In connection with experiments in which solutions containing normal human blood serum were used, it was found that at pH values slightly below 7.0 the serum consumed O_2. This report is concerned with results obtained from experiments performed in an attempt to obtain further information concerning this phenomenon.

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The serum was obtained from freshly drawn blood† in the usual manner and either used immediately or stored at 0°C for from 3 to 48 hours. The reaction was studied in Warburg manometers at 25°C. Buffers used were 0.5 M phosphate for pH values from 6.2 to 7.5 and Palitzsch's borax-boric acid mixtures for pH values from 7.5 to 8.5. One cc portions of serum from the same sample of blood showed almost identical values for O_2 consumption when buffered to the same pH (7.5) with either phosphate or borate. Each manometer cup contained either 1.0 cc or 2.0 cc of serum or dialysate, 0.2 cc of buffer, 0.1 cc of 10% KOH in the centerwell, and enough sterile 0.9% NaCl to make the total fluid volume 3.1 cc. Only serum or dialysate was omitted in the thermobarometer. When buffer was added from the side bulb of the flasks after temperature equilibration, measurable amounts of CO_2 were released, below pH 7.0, for at least 15 minutes after the pH was lowered. Therefore, buffer was added just before the flasks were attached to the manometers, and the first reading was taken 20 minutes later to allow time both for temperature equilibration and the evolution of CO_2. For this reason, the O_2 uptake measured below pH 7.0 was probably slightly smaller than the actual amount consumed.

The upper curve of Fig. 1 illustrates the time course of the O_2 uptake exhibited by 1.0 cc of serum at pH 6.5. The O_2 consumption is rapid during the first hour and is almost complete at the end of 90 minutes.

When serum is dialyzed in a cellophane tube against a large volume of 0.9% NaCl which is replaced several times during 24 hours, the serum then shows no O_2 uptake. However, if a given amount of serum is dialyzed against an equal volume of 0.9% NaCl, the dialysate and the serum each show an O_2 uptake which is just half that exhibited by an equal volume of undialyzed serum obtained from the same individual. The lower curve of Fig. 1 illustrates the rate of O_2 consumption of 1.0 cc of dialysate at pH 6.5. Dialysate heated for 15 minutes at 100°C (Table I) or boiled vigorously for 7 minutes shows the same O_2 uptake as the unheated control.

All samples of normal blood serum or dialysate showed an O_2 uptake when the pH was lowered; Table I summarizes the results obtained. The values at each pH range are averages of several determinations. At pH 6.2 to 6.6 the range of values for samples of serum from different individuals was from 30 to 70 mm^3 O_2 per cc of undialyzed serum and from 15 to 40 mm^3 O_2 per cc of dialysate. The

† The blood used in all the experiments was made available by Dr. J. A. Greene of the University of Iowa Hospital.

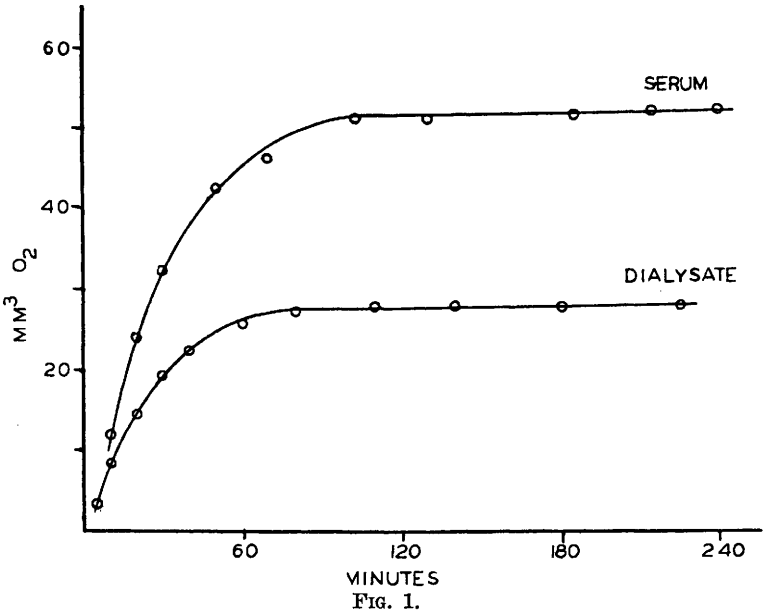

FIG. 1.

TABLE I.
Oxygen Uptake per cc of Serum or Dialysate.

	pH 6.2-6.6		pH 7.0		pH 7.5-7.8		pH 8.1-8.5		Unbuffered pH 8.4	
	No. of Exp.	Mm^3O_2	No. of Exp.	Mm^3O_2	No. of Exp.	Mm^3O_2	No. of Exp.	Mm^3O_2	No. of Exp.	Mm^3O_2
Serum	19	49.7							3	1.3
Dialysate	18	23.3	2	13.4	4	2.8	4	0.9	2	0.0
Heated	6	15.2								
Control	4	15.1								
Boiled	1	21.3								
Control	1	23.1								

figures in the column at the extreme right were obtained from experiments in which either 1.0 cc or 3.0 cc samples of unbuffered serum or dialysate were used. The serum from 2 individuals with a moderate hypertension yielded values of 36.8 and 38.4 mm^3 O_2 per cc and one sample of serum from a hyperthyroid patient gave a value of 33.7 mm^3 O_2 per cc.

Ramsey and Warren[1] found that at physiological pH normal rabbit plasma consumed O_2 at a steady rate of 1.7 mm^3 per cc per hour and that a temporary increase or "burst" occurred when hemolyzed cells were added. They state that both the steady oxidation and the

[1] Ramsey, Robert, and Warren, Charles O., Jr., *Quart. Exp. Physiol.*, 1934, **24**, 153.

"burst" are heat stable and only slightly cyanide sensitive, and suggest that the O_2 consumption is due to autoxidation of lipoids and proteins and may be catalyzed by the addition of pigments of the lysed cells. Canzanelli, *et al.*,[2] reported that horse serum consumed O_2 in small amounts at pH 10.5 and at a rate of about 50 mm^3 per cc per hour at pH 11.5 but none below that range.

Other workers have observed an O_2 uptake by plasma or serum but only under special conditions. Douglas[3] found that in the determination of the O_2 capacity of rabbit blood an absorption of O_2 occurred in alkaline plasma or serum when ferricyanide was added. More recently Litarczek[4] and Parsons and Parsons[5] have described a large O_2 uptake by alkaline rabbit plasma in the presence of ferricyanide but found no oxidation in its absence. They concluded that the O_2 uptake was due to oxidation of lipoids. Wright and Arthur[6] have made a further study of the reactions involved in such alkaline plasmas and their results indicate that unsaturated fatty acids may be largely responsible for the oxidation in the presence of ferricyanide. They showed, further, that, after dialysis of serum in a collodion sac, only about one-third of the original O_2 uptake was accounted for by dialyzable substances. Harris[7] showed that plasma irradiated with ultraviolet light consumed O_2 and Smetana[8] described a photo-oxidation of serum and serum proteins in the presence of hematoporphyrin as a sensitizer.

The small total O_2 consumption observed in slightly alkaline serum dialysate (Table I) seems somewhat comparable to the small rate of oxidation which Ramsey and Warren[1] found in rabbit plasma. They state, however, that this oxidation continued for several hours at nearly the same rate. The O_2 consumption of human serum and serum dialysate in acid solution and in the absence of oxidizing agents is of considerably smaller magnitude than that observed by Canzanelli, *et al.*,[2] for strongly alkaline horse serum and by several workers for alkaline rabbit plasma containing ferricyanide. Whether these facts mean (a) that the materials being oxidized under the various conditions are different, or (b) that the addition of an oxidizing agent enhances, in slightly alkaline solution, an oxidation that may

2 Canzanelli, Attilio, Greenblatt, Milton, Rogers, Gertrude A., and Rapport, David, *Am. J. Physiol.*, 1939, **127**, 290.

3 Douglas, C. G., *J. Physiol.*, 1910, **39**, 453.

4 Litarczek, G., *J. Physiol.*, 1928, **65**, 1.

5 Parsons, T. R., and Parsons, W., *Biochem. J.*, 1927, **21**, 1194.

6 Wright, G. P., and Arthur, B., *J. Biol. Chem.*, 1931, **90**, 757.

7 Harris, D. T., *Biochem. J.*, 1926, **20**, 271.

8 Smetana, Hans, *J. Biol. Chem.*, 1938, **124**, 667.

take place spontaneously in acid or very strongly alkaline solution, the present series of experiments does not indicate. If fatty acids undergo oxidation in human serum at acid reaction, as it seems likely that they do in alkaline rabbit serum in the presence of ferricyanide (Wright and Arthur[6]), they must be dialyzable.

Summary. An O_2 uptake is observed when the pH of normal human blood serum or its dialysate is lowered. Heated dialysate shows the same O_2 uptake as unheated dialysate. All of the material oxidized at acid reaction is dialyzable.

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Survival Time of Pregnant and Nonpregnant Rats after Bilateral Nephrectomy.*

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With total anuria, the duration of life is dependent upon the rate of development of a toxic factor which, in animals otherwise normal, has been shown by Hoff, Smith and Winkler[1] to be potassium. The cause of death after bilateral nephrectomy is not the same as the cause of death in uremia of nephritic origin, for in the latter state, in the absence of total anuria, the terminal potassium ion concentration does not reach fatal levels.

Bergman and Drury,[2] studying the survival time of normal fasting rats after bilateral nephrectomy state: "The low variability in the survival time of the standard nephrectomized rat under any well defined set of conditions makes it easy to determine whether any given factor or procedure is harmful or beneficial in renal insufficiency." They show that the survival time is shortened by such extraneous procedures as the administration of water or protein. In such experiments death is due to the accumulation of potassium, and the toxicity of meat was shown to be due to its high potassium content.[1, 2, 3]

Any factor which increases the rate of accumulation of potassium or causes the production of some other more toxic product which

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1 Hoff, Hebbel E., Smith, Paul K., and Winkler, Alexander W., *J. Clin. Invest.*, 1941, **20**, 607.

2 Bergman, Hyman C., and Drury, D. R., *J. Clin. Invest.*, 1939, **18**, 777.

3 Addis, T., and Lew, W., *J. Clin. Invest.*, 1939, **18**, 773.