Treatment of Diabetic Coma with Low-Dose Hourly Intramuscular Insulin

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SUMMARY

Ten diabetics with severe hyperglycaemia were treated with hourly low-dose intramuscular insulin injections. Five patients were keto-acidotic with a mean initial plasma glucose of 842 mg/100 ml and 5 were non-ketotic with a mean initial plasma glucose of 1223 mg/100 ml. In every case there was an approximately linear and predictable lowering of plasma glucose, the average rate being 79 mg/100 ml/h in the ketotic group and 132 mg/100 ml/h in the non-ketotic group. Results closely paralleled those reported with continuous low-dose infusion techniques and this study supports the view of Alberti et al. that hourly intramuscular insulin therapy is a simple and reliable alternative to infusion therapy where necessary equipment is unavailable.


The use of small doses of insulin in the treatment of diabetic 'coma' is currently arousing interest, as it appears to be a considerable advance in this notoriously difficult area of therapeutics. Although first reported as early as 1927 by Faber and Holst and later in 1946 and 1970, this form of therapy has not until recently gained clinical recognition. In June 1974 papers from three separate centres reported the successful experience with low-dose constant infusion of insulin, and highlighted the advantages of constant infusion. In 1973, Alberti et al. drew attention to the effectiveness of small hourly doses of intramuscular insulin in the treatment of diabetic coma.

This presentation reflects the results of treatment of keto-acidotic and non-ketotic coma and precoma with small hourly doses of intramuscular insulin, and it is suggested that in the absence of infusion apparatus, this method of treatment is a satisfactory and practical alternative.

PATIENTS AND METHODS

Ten diabetics with hyperglycaemic coma or precoma were treated with hourly intramuscular injection of small doses of soluble insulin; 5 patients were keto-acidotic and 5 were non-ketotic.

Clinical and biochemical details on admission are shown in Table I. Seven patients were female and 3 male, with a mean age of 54 years (range 30 - 72). Three patients were known diabetics on oral antidiabetic agents and 7 were previously unknown. All patients manifested states of impaired consciousness, 4 being confused, 2 in precoma and 4 in coma. All patients were dehydrated, 5 severely so, 2 were hypotensive and 3 hypothermic. Clinical and laboratory evidence of acute infection was present in 2 patients, involving the urinary tract in one, and broncho-pneumonia and ischiorectal abscess in the other. One patient had pulmonary tuberculosis of 1 year's duration. One patient had chemical peritonitis following perforation of a stomal ulcer.

Initial investigations included plasma glucose (measured by the copper reduction method), urea, electrolytes and ketones (Ketostix; Ames), blood count, urinary glucose (Clinitest; Ames) and ketones. Repeat estimations of plasma glucose, serum urea and electrolytes were made at 1 hour, 2 hours and thereafter at hourly or 2-hourly intervals. Plasma ketones were estimated every second hour and urine glucose and output hourly. Arterial blood gases were measured at the start of treatment in 4 ketogenic patients.

In the keto-acidotic group mean plasma glucose was 842 mg/100 ml (range 585 - 1116) and in the non-ketotic group 1223 mg/100 ml (range 810 - 1700). Serum potassium on admission ranged from 2.7 to 6.2 mEq/litre (mean 4.6), serum sodium from 123 to 146 mEq/litre (mean 134), serum chloride from 79 to 107 mEq/litre (mean 96) and serum urea from 30 to 160 mg/100 ml (mean 88). Plasma Ketostix was strongly positive (3+) in all ketogenic patients.

Treatment

At the time of diagnosis, treatment with soluble insulin by deep intramuscular injection was initiated. The starting dose was 10 units in 7 cases and 5 units in 3 cases, and thereafter 5 units hourly. Hourly insulin therapy was stopped when: (a) urine glucose fell below 4+; (b) ketones had disappeared from plasma; or (c) plasma glucose levels of less than 250 mg/100 ml had been recorded.

Thereafter further insulin was given subcutaneously at 6-hourly intervals on the basis of a sliding scale determined by urinary glucose levels as assessed by Clinitest. Intravenous fluid and electrolyte replacement was initiated with 0.9% sodium chloride and this was continued at varying rates dependent upon the needs of the particular patient until: (a) a serum sodium level of 155 mEq/litre or more was recorded, in which case 0.45% sodium chloride was substituted; or (b) the criteria for discontinuing hourly insulin were obtained, as mentioned, when 5% dextrose water solution was started.
TABLE I. CLINICAL AND BIOCHEMICAL DETAILS ON ADMISSION

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age (yrs)</th>
<th>Duration of diabetes (yrs)</th>
<th>Previous therapy</th>
<th>Precipitating factor</th>
<th>Blood pressure (mmHg)</th>
<th>Rectal temp. (°C)</th>
<th>Pulse (min)</th>
<th>Respiration (rate/min)</th>
<th>Dehydration</th>
<th>Conscious state*</th>
<th>Initial blood or plasma values</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>50</td>
<td>10</td>
<td>Chlorpropamide</td>
<td>Urinary infection</td>
<td>145/80</td>
<td>34.8</td>
<td>96</td>
<td>48</td>
<td>Severe</td>
<td>Precoma*</td>
<td>Plasma glucose (mg/100ml)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Chlorpropamide, phentoin</td>
<td>None found</td>
<td>160/100</td>
<td>37.2</td>
<td>120</td>
<td>30</td>
<td>Mild</td>
<td>Confusion</td>
<td>Serum potassium (mg/100ml)</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>30</td>
<td>1</td>
<td>None found</td>
<td>None found</td>
<td>150/115</td>
<td>36.8</td>
<td>100</td>
<td>32</td>
<td>Moderate</td>
<td>Confusion</td>
<td>Serum sodium (mmol/L)</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>54</td>
<td>Prev. undiagnosed</td>
<td>None</td>
<td>Bronchopneumonia, ischiorectal abscess</td>
<td>110/70</td>
<td>35.2</td>
<td>124</td>
<td>46</td>
<td>Severe</td>
<td>Precoma</td>
<td>Serum chloride (mmol/L)</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>39</td>
<td>Prev. undiagnosed</td>
<td>None</td>
<td>None found</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Serum calcium (mg/100ml)</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>61</td>
<td>14</td>
<td>Chlorpropamide</td>
<td>Not taking therapy</td>
<td>120/70</td>
<td>37.1</td>
<td>100</td>
<td>35</td>
<td>Moderate</td>
<td>Confusion</td>
<td>Serum uric acid (mg/100ml)</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>72</td>
<td>Prev. undiagnosed</td>
<td>None</td>
<td>None found</td>
<td>140/95</td>
<td>37.3</td>
<td>96</td>
<td>18</td>
<td>Moderate</td>
<td>Confusion</td>
<td>Albumin (g/L)</td>
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<tr>
<td>7</td>
<td>F</td>
<td>58</td>
<td>1</td>
<td>None</td>
<td>Perforated ulcer, peritonitis surgery</td>
<td>90/60</td>
<td>37.3</td>
<td>140</td>
<td>26</td>
<td>Moderate</td>
<td>Postoperative prolonged coma</td>
<td>Urea (mmol/L)</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>65</td>
<td>Prev. undiagnosed</td>
<td>None</td>
<td>None found (probable infection)</td>
<td>170/90</td>
<td>38.6</td>
<td>130</td>
<td>24</td>
<td>Severe</td>
<td>Coma</td>
<td>Creatinine (umol/L)</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>40</td>
<td>Prev. undiagnosed</td>
<td>None</td>
<td>None found</td>
<td>85/50</td>
<td>35.3</td>
<td>88</td>
<td>22</td>
<td>Severe</td>
<td>Coma</td>
<td>Urea (umol/L)</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>60</td>
<td>Prev. undiagnosed</td>
<td>None</td>
<td>None found</td>
<td>146/86</td>
<td>37.0</td>
<td>96</td>
<td>22</td>
<td>Severe</td>
<td>Coma</td>
<td>Creatinine (umol/L)</td>
</tr>
</tbody>
</table>

* Precoma is defined as responsiveness to pain or loud noise only.

** Potassium chloride was added to these solutions when required.

Plasma glucose mg 100ml

Fig. 1. Individual plasma glucose responses.

Plasma glucose mg 100ml

Fig. 1.

Details of treatment and response are shown in Table I.

RESULTS

Potassium chloride was added to these solutions when required. Sustained urine output was observed and serum levels of 4.5 mmol/L were monitored with or without continuous replacement when necessary. The patient was placed on a continuous saline infusion as the need for potassium and as a guide to the rate of supplementation.
the first hour and which has been clearly shown to cause a substantial decrease in glucose levels prior to the institution of insulin therapy and in excess of that attributable to the dilution factor alone.\textsuperscript{1,4,7}

It has been previously observed that in those patients with infections, the rate of decline of plasma glucose was significantly slower than in those without.\textsuperscript{1,4} This was found to be the case in this group of patients where in the 2 with proven acute bacterial infections (cases 1 and 4) the percentage fall at 3 hours was 25\% and 17\% respectively, while in those without infection it was 1\% to 3 times this rate (see Table II). This order of difference was present at all points in the time response curves.

In case 8 the response was similar to that of the infected patients, the fall being approximately 15\% in 3 hours. Despite the absence of demonstrable infection, a fever and neutrophilia suggested underlying infection. The response of the patient with pulmonary tuberculosis was similar to that of the non-infected group, but the tuberculosis had been treated for 1 year and was inactive.

The rate of glucose response has been reported to be unaffected by the presence or severity of ketosis.\textsuperscript{4,5,7} In these patients, however, there was a significantly greater decline in the non-ketotic group ($P<0.005$). It was not possible to assess adequately the effects of degree of acidosis on response, but in the non-infected cases the response in the most severely acidic (pH 7.1) was not significantly different from that in the less acidic cases (pH 7.22 and 7.27).

Effects of previous insulin therapy on response could not be assessed as these patients had not previously received insulin, with the exception of 2 patients who had received insulin for a short time in the past.

Renal plasma thresholds for glucose, normally considered to be between 180 - 240 mg/100 ml (plasma glucose), have been found to be very variable in the absence of renal disease. Thus 2 patients had no urine glucose in a freshly voided specimen when plasma glucose levels were over 500 mg/100 ml and 1 case gave a 4+ positive reaction for glucose in the urine with a plasma glucose level of 130 mg/100 ml. These variations were presumably the result of altered renal haemodynamics associated with the metabolic derangement. Irregularities of this nature will naturally produce difficulties in control based on urine glucose levels, and frequent plasma glucose estimations are necessary.

**Ketones**

After 7 hours of therapy ketones had disappeared from undiluted plasma in 4 of the 5 ketotic patients, while in the fifth a trace was present at 9 hours.

**Fluid Therapy**

A mean of 1,9 litres of fluid was administered in the first 2 hours (range 1 - 3), a mean of 4,3 litres in the first 6 hours (range 2 - 6) and a mean of 6,8 litres in the first 12 hours (range 3,5 - 10). In 3 patients (cases 4, 6 and 8) 0,45\% sodium chloride solution was infused when
serum sodium levels of 155 mEq/litre or more were recorded. There was no significant difference in the fluid requirements between the ketotic and non-ketotic patients.

**Potassium**

One of the most striking aspects of low-dose insulin techniques of management of diabetic coma is the relative constancy of serum potassium levels throughout therapy. This was previously observed and was a feature of these patients in whom hourly potassium flux was by and large minimal (Table II). Three patients had hypokalaemia on admission, 2 of these requiring heavy replacement for persistent hypokalaemia (case 4, 215 mEq in first 16 hours, and case 8, 221 mEq in first 14 hours). Four patients required small amounts of potassium and 4 required none at all. The fastest rate of potassium administration was 26 mEq/h. Three of the 4 patients who became hypokalaemic were non-ketotic.

**Insulin Therapy**

The mean dose of insulin administered between admission and metabolic 'control' was 50 units. In 2 ketotic cases 35 units were sufficient and in a third ketotic patient 30 units, while in 2 non-ketotic cases 30 units, and in a third non-ketotic patient 40 units were adequate.

Duration of hourly insulin administration was 10 hours or less in 7 cases (7 hours or less in 6 cases) and would have been within the time in an eighth case (case 7) but for the inadvertent stoppage of insulin for 3 hours. In 2 patients (cases 4 and 8) hourly insulin was continued beyond 10 hours.

In case 8 (initial plasma glucose 1700 mg/100 ml) 10 units of insulin were injected between the 9th and 12th hours in an effort to accelerate the rate of fall of glucose. The rate was in fact accelerated from 82 mg/100 ml/h to 150 mg/100 ml/h.

In case 4, after initial fall of 706 mg/100 ml in 9 hours, urine sugar diminished and hourly intramuscular insulin was accordingly stopped. However, on discovery that plasma glucose levels at that time were above 400 mg/100 ml, hourly insulin was restarted at the same dose. Despite 6 hours' additional insulin totalling 30 units, plasma glucose remained fairly static at above 400 mg/100 ml and then fell sharply over the next 2 hours to hypoglycaemic levels. This was the only instance of unpredictable response experienced in this study, and might have been related in some way to the severe infection which was present in two sites in this patient.

In case 7, insulin was inadvertently omitted for 3 hours, producing a temporary relapse in plasma glucose response, with return to approximately the same response curve on reinstitution of hourly insulin.

**Mortality**

One patient died (case 4). He was a 39-year-old man, not previously known to be diabetic, who presented to us with severe keto-acidosis, extensive bilateral bronchopneumonia and an ischiorectal abscess, severe dehydration and hypothermia. His hyperglycaemia and keto-acidosis responded to treatment, and at 5 hours his plasma glucose had fallen by 35% of its initial value of 1116 mg/100 ml, and at 9 hours by 65%, at which time plasma ketones gave a trace positive reaction. An erratic response was then encountered as mentioned above, but glucose levels were eventually controlled. He died 48 hours after admission, the probable cause of death being pneumonia rather than metabolic reasons.

**DISCUSSION**

Hourly administration of small doses of insulin by deep intramuscular injection is clearly highly effective in the treatment of both keto-acidotic and non-keto-acidotic diabetic coma, conditions which are difficult to treat and associated with a high mortality rate even in the best centres. The Black patient often presents very late in the course of disease. This is particularly so in diabetic coma, yet satisfactory response was observed in a number of cases with the most extreme stages of metabolic derangement. Furthermore, the effectiveness of this means of therapy does not appear to be altered significantly by severe dehydration and hypothermia, which might be expected to impair tissue blood flow, producing irregular absorption.

The advantages of low doses of insulin lie in the avoidance of many of the special hazards with which the treatment of diabetic coma has hitherto been associated. Some of these pitfalls in the treatment of diabetic coma are mentioned below.

1. A rapid decline in plasma glucose, resulting in hypoglycaemia.
2. A rapid decline in plasma glucose, usually associated with high doses of insulin, leading to rapid and large potassium fluxes and resultant dysrhythmias which are frequently fatal. In this respect it is of significance that the cardiac effects of potassium depend upon the gradient between the intra- and extracellular potassium concentration, and dysrhythmias can therefore occur in the presence of a normal serum potassium, where rapid alterations in this gradient have occurred.
3. The development of 'resistance' to insulin used in hitherto conventional doses producing little or no fall in plasma glucose levels and in some cases a continuing rise.
4. A rapid decline in plasma glucose which may result in the plasma becoming temporarily hypotonic with regard to intracellular fluid, where the glucose decline lags behind. This may result in fluid shifts into the cells, and, in the brain, may produce cerebral oedema. This rare complication of diabetic coma has been observed in cases where the plasma glucose was lowered rapidly to near normal levels. However, Clements et al. have suggested that it may be the result of neuronal polyol accumulation as a result of insulin-deprived neuronal metabolism.

These problems are largely avoided by the gradual lowering of plasma glucose. Hypoglycaemia can be avoided by anticipation based on the decline curve of plasma glucose.
Two other recently challenged 'cornerstones' of the therapy of diabetic coma may contribute to some of the above hazards. These are:

**Sodium bicarbonate.** The highly acidic ketone bodies acetooacetate and β-hydroxybutyrate are rapidly disposed of in the presence of insulin. Acidosis may therefore be readily reversed in the absence of bicarbonate administration. Infusion of bicarbonate in amounts sufficient to restore only 50% of the base deficit often results in mild metabolic alkalosis. Besides accelerating the already facilitated potassium decline and favouring the development of dysrhythmias, there are other theoretical objections to routine use of bicarbonate. Felig suggests that bicarbonate should be restricted to those cases with arterial pH of 7.1 or less.

**Hypotonic fluids.** The rapid infusion of hypotonic saline is under some question at present. Isotonic saline is a highly satisfactory fluid for rehydration in the majority of cases. Hypotonic saline is advisable if serum sodium rises above 155 mEq/litre, or, if the metabolic status warrants it, 5% dextrose water may be used.

**Insulin ‘Resistance’**

Recent developments in the treatment of diabetic coma have strongly challenged the validity of insulin resistance as an entity. Large bolus doses of insulin result in very high serum insulin levels, but these are short-lived because of rapid hepatic and renal clearance of insulin before the onset of action. Lavis and Williams have shown that large amounts of insulin may 'block' the metabolic activity obtained with smaller doses. Thus, while adrenaline-induced lipolysis in rat fat cells was inhibited by insulin at a concentration of 50 μU/ml, it was not inhibited by 1000 μU/ml. This exciting work awaits further elucidation, but in the meantime it serves to emphasise one potential problem with large doses of insulin which is seemingly avoided with low-dose regimens. Slightly higher doses have been suggested in infected and severely ill patients, but this order of 'resistance' is well below the degree of resistance which may be encountered with larger dosage schemes.

The advantages of low-dose infusion of insulin over other methods of low-dose therapy have been emphasised and the superiority over subcutaneous insulin is unquestionable. Nevertheless, intramuscular insulin produces results closely paralleling infusion techniques. Thus, while insulin guarantees a steady delivery of insulin, intramuscular insulin, even in the presence of dehydration, hypothermia, acidosis and some degree of shock, seems to provide a fairly steady 'infusion'.

The danger of hypoglycaemia with intramuscular insulin is greater because intramuscular insulin has a longer half-life than the 3-4-minute half-life of intravenously infused insulin. This complication can, however, be anticipated in most cases and prevented by administering dextrose earlier rather than later in the recovery, as indicated previously. Ewing preferably on the side of slight hyperglycaemia rather than aiming for normoglycaemia. Nor is the slight delay in the onset of action of intramuscular insulin important since intravenous fluid therapy will initiate the fall in plasma glucose. Outweighing these apparently largely theoretical risks are the advantages of simplicity and practicality, and the non-dependence on specialised apparatus, which at the present time is unavailable in many hospitals.

**Practical Aspects**

1. It is important to ensure that administration is by deep intramuscular insulin as subcutaneous injections produce irregular absorption and uncontrolled responses.
2. Since small doses of insulin are used, it is essential to use a mini syringe and low concentration insulin (40 units/ml). Doses will otherwise be inaccurate.
3. Progress of cases is according to routine principles. It is obviously vital to have frequent measurements of all parameters and particularly so in the first 3-4 hours, when a 'response curve' is being established. Once established, fall of blood glucose was found to be regular along that particular curve, thus facilitating subsequent management. Since plasma acetone and acetooacetate may initially rise with insulin therapy despite a simultaneous and greater fall in β-hydroxybutyrate, plasma ketones are less reliable as an index of insulin requirements. Nevertheless, disappearance of ketones from plasma was found to correlate well with an acceptable point of metabolic recovery and termination of hourly therapy. Urine ketones, which may persist for up to 24 hours after ketoacidemia, are obviously of little value in monitoring the patient.
4. Although in these patients low doses were found to be adequate. Semple et al. have suggested that higher doses be used in infected and severely ill cases.

It appears likely that overactive therapy of diabetic ketoacidosis and non-ketotic hyperglycaemia may well have been partly responsible for the poor results experienced in the treatment of these conditions. As long as plasma glucose levels are decreasing steadily at an acceptable rate (> 50 mg/100 ml/h) a policy of minimal interference would seem to be the safest one. Potassium should naturally be added as indicated by serum levels and ECG, but this therapy should likewise not be over-enthusiastic. Hourly intramuscular administration of insulin matches the control of insulin techniques very closely, even in states of compromised tissue perfusion. Its use in frank clinical shock, however, has not been evaluated and might be hazardous.

Alberti et al. observed that infusion techniques would not be possible in most hospitals. Infusion therapy is, however, not complicated and quite feasible in many centres. Nevertheless, it seems likely that in the foreseeable future at least, there will always be peripheral hospitals and outlying centres where this is not possible.

This study supports the view of Alberti et al. that this intramuscular scheme of therapy is a reliable substitute for infusion, and in the light of current work, may be the treatment of choice wherever infusion cannot be carried out. It is equally applicable to ketogenic and non-ketotic patients.
ADDENDUM

Since the preparation of this report a further 27 patients (17 ketotic) with diabetic coma have been managed in this way. The responses to treatment were similar in all cases. Of the 27 patients, 3 died, 1 within the period of acute management (first 12 hours) and the others on the 3rd and 4th days, after initial satisfactory response to therapy. In 1 of these delayed deaths, despite metabolic recovery, a severe neurological deficit suggested a cerebral thrombosis during the period of coma.

REFERENCES


Bradycardia During Human Diving

P. G. LANDSBERG

SUMMARY

The bradycardial response to the diving reflex, which occurs in man and in diving animals, is thought to be a physiologically protective oxygen-conserving mechanism whereby the animal is kept alive during submergence. The physiology and nervous pathways are not yet fully understood, but several investigators have pointed out the potentially fatal outcome of an accentuated diving reflex.

The CO₂ content of the peripheral venous blood has been proved variable and unpredictable during the hyperventilation-breath-hold dive cycle in man. A group of 8 male divers (average age 34 years) was investigated during breath-hold dives to 3.3 m in a swimming pool. Heart rates were recorded and compared at various stages during breath-hold and SCUBA (self-contained underwater breathing apparatus) dives, viz. when resting on the surface, breath-holding, hyperventilating and swimming underwater. Two divers performed extreme breath-hold endurance tests lasting 135 seconds underwater. All divers had a tachycardia after hyperventilation and a bradycardia after breath-hold diving, lasting 80 - 100 seconds. Extrasystoles were recorded during some of the breath-hold dives. Prolonged submergence caused extreme bradycardia (24/min) with central cyanosis. Bradycardia during diving may be a physiological O₂-conserving reflex or the start of a pathophysiological asphyxial response.


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Several physiological mechanisms can potentially cause unconsciousness underwater during breath-hold and SCUBA diving, viz. hypoxia (shallow water blackout); hypercapnia (CO₂ narcosis); bradycardia; cardiac arrhythmias; and ventricular fibrillation. The bradycardial response is found in human divers under widely differing environmental conditions, such as breath-holding in a hyperbaric chamber (simulated diving conditions); breath-holding on the surface; facial immersion in cold water; and during total body immersion in water. It has recently been postulated that the 'hyperbaric cardiovascular syndrome', i.e. bradycardia in divers in hyperbaric chambers, may be reversed by breathing helium-oxygen mixtures under pressure.

Wolf has postulated the mechanism of sudden death during submergence as follows: stimulus is the anticipation or fear that diving or forced immersion will cause extrasystoles; response is the O₂-conserving 'diving reflex' consisting of bradycardia initiated by parasympathetic vagal activity; blood pressure will drop, but peripheral vasoconstriction, brought about by sympathetic activity, will maintain blood pressure; skin, muscle and visceral blood flow will decrease, with lactic acid and CO₂ accumulation, causing metabolic acidosis, with low pH, high K and hypoxia; all these combined will cause extreme bradycardia, extrasystoles, arrhythmias, ventricular fibrillation and cardiac arrest. Recently Anderson and Blix confirmed this mechanism in ducks with alpha and neuronal adrenergic blockade experiments. They demonstrated the pharmacological components in the autonomic control of the diving reflex.

SUBJECTS AND METHODS

A group of 8 well-trained, adult male divers was investigated. Ages ranged from 24 to 60, with a mean of 34 years.