exclusion of those transferred successfully to oral therapy leads to a reduction of the ultimate overall success rate from 42% to 37%, and even this value may be too high, since there may have been others controllable, but untried, with tablets. On the other hand, it should be observed that with I.Z.S., even after continuous administration for more than five years, a large number of patients still maintained good control. This was observed particularly in those with maturity onset (51%), those requiring less than 40 units of insulin (54%), and those who gave a history of former obesity (55%).

From the results presented it is apparent that more and more patients lapse from I.Z.S. control the longer it is continued. It might be thought that this was due simply to the diabetic state becoming more difficult to control. Good control can, however, be regained in some cases by a change from I.Z.S. to another insulin, whereas it cannot be achieved by increasing the dose of I.Z.S. itself. We suggest that part at least of the explanation of failing control with I.Z.S. is attributable to failure of its crystalline component to exert its desired effect, since its other component, I.Z.S. amorphous, often continues to be of great value.

Summary

A review was made of 211 non-obese diabetic patients who began taking insulin zinc suspension ("lente" insulin) between 1953 and 1957. Control was better in patients who received I.Z.S. as the first insulin than in those who were transferred from other insulin regimes. It was most readily maintained in

patients with maturity-onset diabetes, in those requiring less than 40 units of insulin daily, and in those who gave a history of previous obesity. A sulphonylurea drug was substituted for I.Z.S. in 39 cases, and patients who had been overweight in the prediabetic years showed a strikingly better response than those who had never been obese.

Initially 67% of all cases were well controlled by I.Z.S. but there was a decrease year by year in the proportion of those who maintained good control. This seemed to be related to the duration of treatment, and after five years only 42% of cases were satisfactory.

Attempts to obtain better control by other regimes were often successful in those who had failed on I.Z.S., and eventually 70.6% of all patients achieved good control. The most successful of these methods was two daily doses of insulin. For this purpose I.Z.S. amorphous ("semilente") often proved useful, and it is accordingly suggested that the poor results with I.Z.S. might be attributable to failure of the I.Z.S. crystalline ("ultralente") component.

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Treatment of Severe Decompression Sickness in Aviators

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Decompression sickness in aviators is normally relieved by descent to ground-level. In rare cases, however, especially after the onset of severe respiratory or neurological symptoms at altitude, signs and symptoms may persist or recur in spite of immediate recompression to ground-level, leading to the development of post-decompression collapse from circulatory failure (Adler, 1950). Treatment of post-decompression collapse in aviators has formerly been merely supportive (Malette, Fitzgerald, and Cockett, 1962). Conservative treatment, however, while involving prolonged care in hospital, has not prevented persistent sequelae in some cases (Berry, 1961 ; Berry and Smith, 1962), and of 35 cases reviewed by Malette *et al.* (1962) 16 had a fatal outcome, despite energetic therapy.

The four cases described in this paper developed decompression sickness while undergoing the Royal Naval "high-altitude selection test," which all Fleet Air Arm aircrew are required to do four-yearly. The test consists of exposure to a simulated altitude of 37,000 ft. (11,277 m.) (162 mm./Hg) in a decompression chamber for three one hour periods on alternate days in one week: 100% oxygen is breathed throughout. According to the results of this test, aircrew are categorized into three groups. In the majority of cases (category A) there are either

no symptoms or these are only minor—for example, pruritus, rash, or fleeting joint pains, not necessitating descent. The second largest group (category B) develop limb pain (the "bends") during the test, and this pain is severe enough to make descent to ground-level necessary. A small percentage (category C) show signs of severe decompression sickness, developing pulmonary symptoms ("chokes"), signs of central nervous involvement, or syncope. If these severe symptoms persist after descent to ground-level, institution of the most effective method of treatment available is immediately imperative.

Whereas the standard treatment for decompression sickness in divers has always been recompression, and the possible value of compression to greater than one atmosphere absolute in the treatment of aviators' decompression sickness has been suggested on theoretical grounds by Behnke (1955) and others, the first case treated in this way was not reported until some years later (Donnell and Norton, 1960). Since that time a further case has been treated elsewhere by this method (Berry and Smith, 1962), but, in general, conservative treatment has still been regarded as the method of choice.

Since the successful use of compression in the case reported by Donnell and Norton, four further cases of severe decompression sickness in aviators have been treated at the Royal Naval Air Medical School by compression to a pressure greater than one atmosphere. In all four the relief of signs and symptoms was so dramatic that this small series is reported

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here, since it is felt that the evidence is sufficient to advocate the further use of this method in cases of this type.

Case 1

A 47-year-old pilot who on the results of a high-altitude selection test 10 years previously had been placed in category A was found on initial examination to have a long-standing smoker's cough but to be otherwise completely fit. His height was 70 in. (178 cm.), and he weighed 173 lb. (78 kg.). Skinfold thicknesses measured with Harpenden callipers (Edwards, Hammond, Healey, Tanner, and Whitehouse, 1955) were subscapular 21 mm., triceps 18 mm., and suprailiac 20.5 mm.; and his endomorphic index (average=4), calculated from these figures, was $4\frac{1}{2}$ (Parnell, 1958). Resting blood-pressure was 140/70 and pulse 72/min.; a recent chest x-ray picture was normal. His first two runs of one hour at 37,000 ft. (11,277 m.) were completed uneventfully. On his third run, after 52 minutes at 37,000 ft. he was noticed to be having some difficulty in turning the pages of the book he was reading. On questioning he stated that he felt perfectly fit, and he was therefore allowed to complete the hour at altitude. Immediately after descent to ground-level he found he was unable to move his left leg, which felt as though it had "gone to sleep."

On examination his B.P. was 140/90 and pulse 120/min. No active movements of the knee, ankle, or foot on the left side were present, but the left hip flexed normally. Right leg movements were normal. Ankle and knee reflexes were present and equal in both legs, but plantar responses were equivocal. Skin sensation to light touch and pinprick was normal. Both legs were equally warm on palpation and the peripheral pulses were present and equal. The remainder of the general examination showed nothing abnormal.

Forty-five minutes later the patient was conscious of some return of power to the left leg. B.P. was 110/70 and pulse 100/min. Active ankle and knee movements were present but toe movements were absent on the left. Power of the left anterior and posterior tibial muscle groups was diminished. The left ankle reflex and the left plantar response were absent. All other reflexes were present and the right plantar reflex was flexor. Sensation and peripheral pulses were normal in both legs.

Seventy-five minutes after his descent the patient insisted that he felt completely recovered, but on trying to walk showed a pronounced left foot-drop. B.P. supine 110/70, sitting 70/50, pulse 120/min. All pulses were present and equal in both legs, but the left ankle and foot were palpably cooler than the right. Power of the left anterior and posterior tibial muscles was still diminished. The left ankle reflex was absent and the left plantar response was extensor. All other reflexes were normal.

After this examination the patient complained of feeling faint and then vomited. He was pale and was perspiring profusely. Systolic pressure was 50 mm. Hg and the diastolic pressure could not be determined. His pulse was weak, fluctuating between 100 and 120/min. At this juncture he was transferred to a recompression chamber five miles (8 km.) away.

Two hours after descent from altitude he was compressed to a pressure depth of 66 ft. (20 m.) of water (3 atmospheres absolute) in 60 seconds. At this depth there was a marked subjective improvement. B.P. had risen to 110/60, pulse was 100/min. Power of the anterior and posterior tibial muscle groups was still diminished. The left knee reflex was present but the ankle reflex was absent and the plantar response equivocal. The right leg reflexes were normal. Peripheral pulses were present and equal in both legs, although the left leg was colder than the right below the mid-shin region. Skin sensation to touch and pinprick was normal over both legs. The fundi appeared normal.

After five minutes at depth the power of the posterior tibial muscles on the left had improved, but the anterior tibial muscles were still weak and toe movements were only just apparent; B.P. 120/70, pulse 100/min.

Twenty-five minutes after compression was started B.P. was 120/80, and pulse 95/min. Toe movements were present on the left side and the anterior tibial muscles were stronger. Knee reflexes in both legs and the right ankle reflex were present. Both plantar responses were flexor but the left ankle reflex remained absent.

Decompression was begun after 30 minutes at depth, the pressure being reduced to an equivalent of 20 ft. (6 m.) of water over a period of 60 seconds. The patient's condition was unchanged at

this depth, and the left ankle reflex was still unobtainable. After a stop of six minutes at 20 ft., pressure was reduced to an equivalent of 10 ft. (3 m.) of water, again in 60 seconds. At this pressure depth the toe movements on the left deteriorated and the left plantar reflex became equivocal. B.P. 100/70, pulse 96/min. After 25 minutes at 10 ft. the chamber was surfaced and the patient removed. B.P. 100/70. The left plantar response was now extensor. Active toe movements on the left and the power of the left anterior and posterior tibial muscles were diminished.

After five minutes at ground-level toe movements reappeared in the left foot, but the power of the anterior and posterior tibial muscles of the left leg was still diminished and the left leg was still cooler than the right. All leg reflexes and both plantar responses were normal. B.P. 120/80.

After one hour at ground-level the general examination revealed nothing abnormal apart from some slight residual weakness in the left leg. B.P. 120/80. The patient was then admitted to R.N. Hospital, Haslar.

Investigations on Admission.—Serum electrolytes (mEq/l.): Na 138, K 4, Cl 120; HCO_3 23.6. Blood urea 17.5 mg./100 ml. Next day the figures were Na 148, K 5.2, Cl 103, HCO_3 27.2, Hb 107%. Chest x-ray picture was normal on admission. An E.E.G. showed asymmetrical slow activity in the theta and delta frequencies over the left hemisphere. There was also an isolated burst of moderate-to-high-voltage delta activity in all areas. Two days later the E.E.G. was repeated: this record was within normal limits and showed no focal or paroxysmal features. The slight residual weakness of the leg disappeared within 24 hours of admission to hospital and the patient was discharged the next day. (A preliminary report of this case has been published elsewhere (Coburn, Gould, Young, Hatfield, Colley, and Boyd Martin, 1962).)

Case 2

A 31-year-old observer, height 73 in. (185 cm.), weight 191 lb. (86.6 kg.), was found on initial examination to have a B.P. of 110/75 and pulse 72/min. Chest x-ray picture was normal, and skinfold measurements were subscapular 14 mm., triceps 15 mm., suprailiac 22 mm.; calculated endomorphic index $5\frac{1}{2}$. He had undergone a high-altitude selection test four years previously and had been placed in category A.

Thirteen minutes after the beginning of his first decompression run at an altitude of 37,000 ft. (11,277 m.) he complained of a dull ache in the upper abdomen, of feeling "hot and cold all over," "pins-and-needles" across the chest, and of difficulty in focusing. Deep inspiration produced pain in the chest and choking. Descent was begun immediately. At 20,000 ft. (6,096 m.) he felt dizzy and faint and had to be supported; at ground-level there was only slight improvement in his condition.

On examination his B.P. was 90/50 and pulse 60/min. On deep inspiration choking persisted with discomfort in the chest, and he still said he was "unable to focus his eyes." His pupils were moderately dilated and reacted briskly and equally to light and accommodation. Visual fields were normal to confrontation. No abnormality was detected in the cranial nerves. Limb power, tone, co-ordination, and sensation to light touch and pain were normal.

Six minutes after the onset of symptoms, compression to a pressure depth of 60 ft. (18.3 m.) of water was carried out. At this pressure he was subjectively much improved although he still choked slightly on deep inspiration. B.P. was 105/70.

Nine minutes later B.P. was still 105/70 and his signs and symptoms had completely disappeared, with no abnormality on general examination.

Thirty minutes after the onset of compression the pressure depth was reduced to 50 ft. (15.2 m.). After 30 minutes at this depth, B.P. was 115/80 and he was symptom-free. Slow ascent was then made to 15 ft. (4.6 m.) over a period of one hour with no recurrence of signs and symptoms. The ascent to ground-level from 15 ft. was made over a further period of one hour. He remained symptom-free throughout this decompression. After observation for two hours with no recurrence of signs and symptoms, he was admitted to hospital.

Investigations on Admission.—Serum electrolytes (mEq/l.): Na 135, K 3.8, Cl 109, HCO_3 25. Total protein 7.3 g./100 ml.; blood urea 25 mg.; P.C.V. 47%. Chest x-ray picture was normal. An E.E.G. record was within normal limits and showed no focal or paroxysmal features. The patient was discharged next day.

Case 3

A 23-year-old trainee observer, height 70½ in. (179 cm.), weight 174½ lb. (79 kg.) showed no abnormality on initial examination; B.P. was 120/80 and chest x-ray picture normal. Skinfold thicknesses were subscapular 10 mm., triceps 18 mm., suprailiac 15 mm.; calculated endomorphic index 5. He had not previously been exposed to altitudes above 27,000 ft. (8,230 m.). After 15 minutes of his first run at 37,000 ft. (11,277 m.) he developed a "bend" in the right hip which radiated down to the right knee. This was followed by the onset of a constricting pain across the chest with uncontrollable coughing. Descent was begun immediately. At ground-level the coughing persisted, respirations were shallow, with pain on deep inspiration, which also accentuated the coughing. In addition, he complained of "tingling" in the tips of the fingers of his left hand. He was restless and pale, and was perspiring freely. Supine B.P. 105/70, pulse 100/min.

Immediate compression was carried out to an equivalent pressure of 40 ft. (12.2 m.) of water. Coughing persisted, with pain in the chest on deep inspiration, at this depth. Compression was continued to a pressure of 60 ft. (18.3 m.) of water, which produced some improvement in his breathing, but he still coughed on deep inspiration and complained of chest pain. B.P. 102/68, pulse 74/min. The paraesthesiae of the left hand had disappeared and there was no muscular weakness. Cranial nerves were normal. There were no abnormal neurological signs in the limbs.

Compression was continued to an equivalent pressure depth of 90 ft. (27.4 m.) of water, at which depth the tightness in the chest had gone and he was feeling very much better. On deep inspiration there was no cough or pain in the chest. B.P. 104/70, pulse 72/min.

After 15 minutes at 90 ft. there had been no return of signs or symptoms and he was decompressed over a period of 10 minutes to 30 ft. (9.1 m.). At this depth his chest felt tighter and he began to cough again. He was again recompressed to 60 ft. (18.3 m.), where he felt well, with no cough or tightness of the chest on deep inspiration. B.P. 120/70, pulse 72/min. After 30 minutes at 60 ft. decompression was carried out over a period of four and a half hours with no return of signs or symptoms. Stops were made of increasing length at 40 ft. (30 minutes), 30 ft. (one hour), 20 ft. (one hour), and 10 ft. (two hours). After this decompression B.P. was 126/80 and pulse 80/min.; no abnormality could be found in the chest or the central nervous system, and the patient was admitted to hospital for observation and investigation.

Investigations on Admission.—Serum electrolytes (mEq/l.): Na 142, K 5.3, Cl 110. Blood urea 23 mg./100 ml.; total proteins 7.7 g./100 ml. Blood picture: Hb 106% (15.4 g./100 ml); P.C.V. 47%; E.S.R. 4 mm./hour (Wintrobe); W.B.C. 6,000/c.mm. (polymorphs 58%, lymphocytes 34%, monocytes 5%, eosinophils 2%, basophils 1%). Chest x-ray examination demonstrated no air in the pleural cavity or mediastinum and the lung fields were clear. Urine: S.G. 1012; reaction neutral; no sugar; albumin, faint trace. Microscopical examination showed 8 R.B.C.s per one-sixth field with some epithelial cells and amorphous debris.

The patient was discharged from hospital the next day.

Case 4

An 18-year-old midshipman, weight 161 lb. (73 kg.), height 68 in. (173 cm.), showed no abnormality on initial examination. Resting B.P. was 120/80, pulse 72/min. Chest x-ray picture was normal. Skinfold measurements were subscapular 12.5 mm., triceps 10 mm., and suprailiac 18 mm., calculated endomorphic index 4½. He had not previously been exposed to altitude.

After 37 minutes on his first run at 37,000 ft. (11,277 m.) he complained of "being unable to keep his eyes open." On further questioning he admitted having had a "bend" in his left wrist for some 10 minutes. The visual symptoms were followed by a feeling that his left leg "did not belong to him." He was recompressed to ground-level within two minutes.

During the descent to ground-level his condition deteriorated and he became semiconscious, pale, and clammy. At ground-level B.P. was 50/0, pulse 84/min. Within two minutes at ground-level he vomited profusely, complained of a constricting pain in the chest, and was unable to inspire deeply without coughing or severe pain. Examination of the central nervous system revealed no abnormality. B.P. 50/0, pulse 84/min. He was taken by ambulance to a recompression chamber 5 miles (8 km.) away. On the journey he showed

a slight improvement but still complained of a retrosternal pain, which was worsened by deep inspiration. On arrival at the recompression chamber supine B.P. was 110/80, pulse 80/min., but the chest pain and cough still persisted.

Thirty-nine minutes after the onset of symptoms he was compressed to a pressure depth of 40 ft. (12.2 m.) of water, developing a bilateral aural barotrauma on descent. At 40 ft. all his chest symptoms had disappeared and he felt well. B.P. 120/80, pulse 68/min. No abnormality was detected in the respiratory, cardiovascular, or central nervous systems.

After 27 minutes at 40 ft. his condition remained good and decompression to ground-level was performed over three minutes without incident, his B.P. and pulse remaining constant throughout the ascent. He was then admitted to hospital for investigation and observation.

Investigations on Admission.—Serum electrolytes (mEq/l.): Na 138, K 3.5, Cl 101, HCO₃ 26. Blood urea 40 mg./100 ml.; total protein 7.3 g./100 ml. Blood picture: Hb 113% (16.5 g.); P.C.V. 45%; M.C.H.C. 36.6%; W.B.C. 12,500/c.mm. (polymorphs 90%, lymphocytes 4%, monocytes 4%, eosinophils 2%). Chest x-ray examination demonstrated normal lung fields with no air in the pleural cavity or mediastinum; an E.E.G. was within normal limits. He was discharged two days later.

Discussion

The success of compression in the treatment of these four cases suggests that this form of therapy can be as important in the treatment of decompression sickness in aviators as in its counterpart in divers. However, comparison with a control series, such as that of Malette *et al.* (1962), is difficult because of the unpredictable course of the post-decompression collapse syndrome, and a substantially larger number of cases treated by compression is needed to establish its value beyond doubt. Compression is well established in the treatment of decompression sickness in divers, and there appears to be general agreement that bubble formation is the primary lesion in decompression sickness in both aviators and divers, but direct evidence of bubble formation at high altitude is rare, and this view is based mainly on the effect of denitrogenation (Bazett and Burton, 1941; Behnke, 1955; Marbarger, Kemp, Kadetz, Variakojis, and Hansen, 1957). The site of bubble formation and how its effects are produced remain in considerable doubt (Fulton, 1951; Mason, 1962), and, although the clinical picture of decompression sickness is similar in both aviators and divers, since there are many fundamental differences in the circumstances under which they occur (Sproule, 1951) any direct comparison between the two may not be justified.

The incidence of decompression sickness in flight is difficult to estimate. Mason (1962) could find only seven fatal cases reported in the English literature; however, minor symptoms often go unrecorded and some accidents attributed to pilot error may in fact be due to decompression sickness. During exposure in a decompression chamber the incidence of decompression sickness is determined by altitude, time of exposure, pre-oxygenation, and exercise at altitude (Fulton, 1951), and therefore varies in different series (Brown, 1946; Fulton, 1951; Morant, 1952; Cotes and Gronow, 1952; Samuel, 1955). The incidence of decompression sickness in 365 subjects undergoing the Royal Naval high-altitude selection test was category A, 238 (65%); category B, 109 (30%); category C, 18 (5%).

The association between age and susceptibility to decompression sickness is generally agreed (Fulton, 1941; Morant, 1952; Cotes and Gronow, 1952), although Samuel (1955) failed to confirm this association by the results of a less severe test than that used by previous workers. The relationship between age and susceptibility to both "bends" and severe decompression sickness in the Royal Navy subjects is shown in the Chart. Since category C cases are not retested by the Royal Navy, the incidence of severe symptoms is somewhat higher in the youngest age-groups undergoing their first test than subsequently; however, the incidence rises again as age increases.

This pattern is shown by the four cases reported. Two of these were undergoing their first test; the others had been tested previously and had been symptom-free. It is of interest that if cases developing severe symptoms were retested (assuming that the results of subsequent tests would be the same), the incidence of severe symptoms in the over 36 age-group would be approximately 30%.

Relationship between age and the incidence of decompression sickness in 365 subjects undergoing the Royal Naval high altitude selection test.

All four cases reported above were overweight and had endomorphic indices above the average. Obesity appears to be definitely associated with a greater susceptibility to severe decompression sickness, especially in young subjects (Haymaker and Davison, 1950; Hornberger, 1950; Gray, 1951; Cotes and Gronow, 1952; Samuel, 1955; Berry and King, 1959). All cases of severe decompression sickness in the Royal Naval series occurred in overweight subjects, although there is no correlation between the incidence of severe symptoms and the degree of obesity and no such association with the incidence of simple "bends" (Table I). Age and increased weight appear to be independent in their effects since they themselves are not significantly correlated in this series (Table II). However, this apparent lack of association between age and weight may not be genuine. The life insurance tables on which the degree of obesity has been based in these figures allow for a "normal" increase in weight with age, and since category C cases are not

TABLE I.—Relationship Between Weight and the Incidence of Decompression Sickness in the Royal Naval High-altitude Selection Test

	No. of Subjects Tested	% Incidence of Decompression Sickness		
		Cat. A	Cat. B	Cat. C
More than 15% overweight ..	62	56	36	8
10-15% " ..	41	64	29	7
5-10% " ..	63	60	29	11
Less than 5% " ..	84	69	27	4
Less than 5% underweight ..	56	73	27	Nil
5-10% " ..	41	66	34	"
10-15% " ..	14	71	29	"
More than 15% " ..	4	75	25	"

TABLE II.—Relationship Between Age and Weight of Subjects Undergoing the Royal Naval High-altitude Selection Test

Age	Percentage of Subjects								No. of Subjects Tested
	Overweight				Underweight				
	> 15 %	10-15 %	5-10 %	< 5 %	< 5 %	5-10 %	10-15 %	> 15 %	
17-20	22	18	13	26	15	5	1	Nil	82
21-24	11	11	18	27	18	9	5	1	132
25-28	23	6	17	19	15	15	4	1	69
29-32	9	16	25	19	9	16	3	3	32
33-36	35	Nil	8	15	15	23	4	Nil	26
Over 36	8	13	25	16	13	17	4	4	24

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retested, overweight subjects are progressively eliminated. It is possible that neither age nor obesity itself is important but that they are merely indications of some common predisposing factor such as a lack of physical fitness.

Fatality after decompression is due to the onset of post-decompression collapse, the main feature of which is severe irreversible shock (Adler, 1950). It is usually preceded by the development of symptoms of decompression sickness at altitude (Romano *et al.*, 1943; Cotes, 1952; Halbouty and Long, 1953), especially if symptoms persist after return to ground-level (Cotes, 1953), but it may follow a symptomless ascent (Fryer, 1957). The onset of collapse may be acute or insidious, and either neurological or hypovolaemic symptoms may predominate or occur in combination (Malette *et al.*, 1962). Cotes (1953) recognized three phases—haemoconcentration, pulmonary oedema with normal blood-pressure, and circulatory failure. The prognosis depends mainly on early recognition (Berry and King, 1959; Berry, 1961), and the mainstay of previous therapy has been the maintenance of circulating plasma volume (Malette *et al.*, 1962). Findings on investigation have included pyrexia, leucocytosis (Mason, 1962), elevation of haematocrit (Goggio and Houck, 1945) and raised blood sugar (Dominguez *et al.*, 1960). Hyperkalaemia has also been reported (Mason, 1962), although few measurements of serum electrolytes in this condition are available.

The aetiology of post-decompression shock is unknown. Mason (1962) concludes that frank air or fat embolism is unlikely to be an essential part of the syndrome. It has been suggested that shock results from liberation of "toxic substances" following cellular disruption by gaseous expansion at altitude (Sproull, 1951; Mason, 1962) and that other features of the syndrome—for example, the presence or absence of a latent interval and associated central nervous system symptoms and signs—are secondary to the vascular disturbance (Mason, 1962).

The four cases reported above suggest that the post-decompression collapse syndrome can be promptly terminated, at least in its early stages, by overcompression. The small increase in total oxygen carried by the blood in subjects breathing air at three atmospheres pressure absolute (approximately 1.6 vols. %), although possibly contributory, is unlikely to be significant in producing this reversal, especially as the administration of 100% oxygen to these cases at normal ambient pressures has never been shown to have this marked effect. It appears likely that compression produces its effect by aiding the dissolution of bubbles which have persisted after descent to ground-level and that the concept of post-decompression shock being secondary to a single traumatic event at altitude (Sproull, 1951; Mason, 1962) is incomplete.

Mason (1962) notes that in the cases reported after actual flight, those who show the most rapid onset of irreversible collapse have all remained at altitude for a minimum of 20 minutes since the onset of symptoms, and it is likely that the longer bubbles are allowed to persist the greater is the chance of developing the fully established shock syndrome. It is clear that if compression is to be effective it must be instituted early, while the condition is still reversible. Early compression is likely to prevent not only subsequent secondary shock but also the persistent sequelae which may result in these cases (Berry and Smith, 1962). The delay before compression was begun in Case 1 probably accounted for the persistence of abnormal signs and abnormalities in the E.E.G. following treatment. This case also showed a slight rise in serum potassium, otherwise the investigations in all four cases were normal, but some hours elapsed before these were performed, and it is possible that more complete investigation at an earlier stage would have revealed changes.

The unpredictable course of the post-decompression collapse syndrome and the need to avoid any additional hazards introduced by the treatment itself makes the selection of cases for

treatment by compression difficult. In our view, all cases in which local symptoms and signs persist at ground-level, with or without a drop in blood-pressure, should be compressed. This we feel is justified by the dramatic symptomatic relief produced alone. In addition, if the full picture of post-decompression shock is allowed to develop, then compression is much less likely to be effective although it may still be a valuable adjunct to therapy.

The pressure depth to which these cases should be compressed should, in our opinion, be the minimum which produces relief of symptoms in order to avoid the risk of further hazards during subsequent decompression. Sixty-five feet (19.8 m.) of water appears to be the optimum depth initially. At this depth the pressure is 12 times that at which bubble formation presumably occurred. Even the most severe symptoms in divers yield to much lower relative pressure increases than this. After recovery, times for subsequent decompression must be somewhat empirical until there is more evidence on which decompression schedules can be designed.

Post-decompression collapse is undoubtedly rare. The introduction of the pressurized cabin, however, has not entirely eliminated decompression sickness in flight, and cases like those above still occur in decompression chambers. Like decompression sickness in divers, it is of general interest because cases with a prolonged latent interval between flight and development of symptoms could be seen by virtually any doctor in the country.

Summary

Four cases of the post-decompression collapse syndrome are described in aviators who have been exposed to a simulated altitude of 37,000 feet (11,277 m.) in a decompression chamber. The factors which predispose to the development of this condition are discussed. In all four cases compression to pressures greater than atmospheric produced immediate relief, and theories of the aetiology of post-decompression collapse are discussed in relation to this effect.

The success of compression in these four cases and in two cases treated elsewhere by this method suggests that this form of treatment should be generally adopted for these cases, and a scheme of treatment is outlined.

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Clinical and Biochemical Features of a Case of Hartnup Disease

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A disease characterized by "pellagra-like skin rash, with temporary cerebellar ataxia, constant renal amino-aciduria, and other bizarre biochemical features," was first described by Baron, Dent, Harris, Hart, and Jepson (1956). This disorder, now known as Hartnup disease, is transmitted as a recessive autosomal trait and at the time of writing we were able to find reports of 13 known cases of this syndrome in nine families. One of the most striking features of the disorder is the renal amino-aciduria without evidence of any other tubular dysfunction. Because of the associated pellagra-like rash, Baron *et al.*

(1956) postulated that the immediate biochemical lesion was an abnormality of nicotinic acid metabolism. On the basis of their investigations in two Hartnup cases, Milne, Crawford, Girao, and Loughridge (1960) have suggested that Hartnup disease is primarily a disorder of amino-acid transport—across both the mucous membrane of the jejunum and the renal tubule. In addition, a defective conversion of tryptophan to nicotinic acid has also been postulated. The latter defect, it is claimed, fully explained the pellagra-like rash.

The clinical features and the results of investigations on a subject with Hartnup disease and his asymptomatic sister are reported here. The clinical manifestations are identical with the reported cases, but results of biochemical investigations seem

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