In November tests were carried out on another group of 19 subjects, all of whom had received 200 mg. of nicotinamide $1\frac{1}{2}$ to 3 hours previously. The test times were:

Control time, 122-26
Experimental time 1, 117-84; difference, -4-42. Significant
" " 2, 115-21; " -7-05. Highly significant

The suggestion was made by Dr. Platt that a single dose of nicotinamide should be given at specified times before the experimental tests, and the experiments were carried out in conjunction with him. It is noted that a somewhat different pattern in the results was obtained.

Having demonstrated that the effect of a single dose of nicotinamide resulted in a well-marked diminution of the time taken to complete the test and that this effect was most marked $1\frac{1}{2}$ to 3 hours after administration of the vitamin, it was essential to ascertain if similar effects would be obtained when tablets were given on six successive days and tests made on the seventh day. This investigation was therefore carried out on 24 I.T.W. subjects at Cambridge in November, and the results were:

Control time, 118-58
Experimental time 1, 116-54; difference, -2-04. Significant
" " 2, 114-62; " -3-96.

The pattern of these results is somewhat different from that of either of the other groups.

Summary

It has been shown in a series of carefully controlled experiments that the addition of nicotinamide alone, or of nicotinamide and certain other vitamins, to the diet of fit young men results in increased efficiency in carrying out a fairly severe test involving both physical effort and co-ordination.

The test chosen was severe, and called for the utmost co-operation from the subject, whose condition at the end of the test was just short of distress, as evidenced by his breathing and pulse rate.

In earlier experiments the subjects appeared to be less exhausted after the administration of vitamins.

Later experiments appear to indicate that continued heavy or exhausting physical stress may necessitate increasing the dose of nicotinamide.

Experiments which were carried out in conjunction with Dr. Platt and Prof. Ellinger will be reported jointly.

The whole of the work described in this report, and all the projects indicated, have been carried out or planned at the instance and with the support of the Medical Research Council.

I should like to acknowledge my indebtedness to Prof. F. C. Bartlett for his constant help and advice, to Sir Edward Mellanby for his interest and guidance in the administration of the vitamins, and to the many officers of the R.A.F. without whose unflinching help and co-operation this work would not have been possible. I should also like to thank Mr. E. G. Chambers, to whom I am indebted for all the statistical results, and to Sgt. J. M. Yallop (W.A.A.F.) for her assistance in the experiment and for all the clerical work.

ANXIETY STATES IN THE NAVY A CLINICAL SURVEY AND IMPRESSION

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A survey has been made of approximately 1,300 cases of anxiety state which have been under our care in a Royal Navy hospital during 1940 and 1941. These impressions have been amplified and modified by later experience in the hospital and in a naval depot.

The term "anxiety state" does not reflect the whole picture, but is a convenient designation; the basic condition is considered to be anxiety in its psychosomatic manifestations, and it is this reaction that is regarded as releasing the varied psychopathy of the constitutions affected. Depression in some degree was an almost constant finding in the more established cases, and for descriptive purposes the diagrammatic concept was formed of a straight line with a pure anxiety reaction at one extreme and a depression of the reactive type at the other; clustering around this line there is a big constellation of

symptoms and signs, including hysterical features, any of which may be present or absent. The syndrome may therefore present a very varied picture.

Points of prognostic import in the routine case-history are enumerated, stresses are discussed, the three main phases of development of the anxiety state are outlined, symptomatology as it affects the various systems is reviewed, and a brief summary of methods of treatment is made with a note on the chief elements in prognosis.

Anamnesis

In reviewing the cases an attempt has been made to assess significant factors emerging in the routine anamneses. In the direct family history—i.e., parents and siblings—there is in most cases a sufficient degree of instability to be realized, and quoted by the patient, as "nervous," "worrying," "hysterical." Psychosis is relatively rare. In infancy the more inadequate types produce with monotonous regularity claims that they "were difficult to rear," "have been given up," or "have had pneumonia" an astonishing number of times. By such reflections can one see the image of poor home conditions and an over-worried mother. During school years shyness, timidity, seclusiveness, fondness of reading as recreation or of swimming and walking as sports, all suggest a tendency to withdraw from the demands of schoolboy life and augur difficulty in adjusting later to the very similar claims of the fighting Forces. At the opposite extreme, "the young devil," "always in mischief," and "never out of trouble" indicated by these excesses a temperament often incapable of withstanding the threats and dangers of war.

The standard attained at school was used as a rough preliminary indication of the intelligence level. Truancy in the great majority of cases signified simply marked mental backwardness. Minor degrees of backwardness were by no means of bad import, but if breakdown did occur in such cases prognosis for recovery and return to duty was poor. More valuable, however, was the work record in rapidly assessing a man's prospects in the Service. Frequent changes of job justified in such phrases as "could not stand the heat (noise) in the factory," "had to give it up," "wanted a change," "got fed up," indicate a personality which will adapt poorly to Service conditions. Endless changes of job suggest marked mental defect.

Sexual maladjustment was conspicuously rare as an overt factor in breakdown compared with experience in civilian psychiatric practice. In part this is explained by Service psychiatry's dealing with a much wider group than would in peacetime attend a psychiatric clinic.

Previous organic illness was of importance in focusing anxiety on a system or the basis of hysterical phenomena. Age beyond middle life and arteriosclerosis facilitated the development of symptoms and impaired prognosis.

Stresses

The stresses to which the individual is subjected in the Service are remarkably constant. Separation from home and family bears heavily on the youth, particularly the only or youngest son, for whom the solicitude of the mother is still the criterion of what he may expect from the world: discomforts and hazards are magnified by too sympathetic an appreciation of their importance in her eyes. The older man experiences the rupture of recently established ties or the absence from wife and family, for years an integral part of his daily life. For certain men, to whom the establishment of a home has through the circumstances of their own early lives assumed a peculiar importance, its break-up through conscription and evacuation is often enough to precipitate breakdown. By no means rare, however, were the men in the later thirties for whom war meant a fresh lease of youth and an unacknowledged relief at sloughing, if only temporarily, the burdens and responsibilities of domesticity. For them Nemesis lay in the reaction and behaviour of a wife unreasonably, but with intuitive justice, resentful of the claims of duty.

Particularly difficult situations arise, too, where marriage has been the episode of a short leave and a young wife finds herself still living in the home of his or her parents, with but a wedding-ring to remind her of her altered state and that many barriers

have risen between her and the "good time" she has hitherto enjoyed. The mother, sisters, and men friends of the absent husband are watchfully ready to report and magnify to him her most casual association with a member of the opposite sex. Long watches give ample time for brooding and bitterness, which do much to break down his resistance to more concrete dangers. Similarly does the situation develop of the older man who learns that the mother of his children, to whom war has meant a doubling of her burdens and the withdrawal of support, has sought companionship in a dance hall or public-house, which she has possibly never before entered. The importance of such anxieties goes far beyond the relatively small proportion of cases in which the wife is actually unfaithful.

Physical hardship and discomfort are less obviously a factor in breakdown—the normal capacity for adaptation to them is very great. More important is the effect of lack of privacy and uncongenial company on the white-collar group of the population.

The problem of the "square peg in a round hole" is much more complex than is generally appreciated. During war the Service requires a vast number of men, physically healthy and of average intelligence, who may be trained to be the "working men" of the Service—the seamen, stokers, etc.; it is supplied with civilians accustomed each to his own occupation, trade, or profession. An adaptable individual of the required standard of physique and intelligence is readily trained for the business of war. A man of lesser endowment may have been employed as a civilian in the one sphere where the qualities he possesses are of value, and may have been relatively successful in that sphere. Should this limited type of qualification be one required in the Service, and he be so utilized, he is satisfied. If, however, his experience is not applicable to Service life, or should the number so qualified which the Service requires be small, the man is liable to be employed in a section for which he is not qualified, and his sense of inadequacy is often embittered by the belief that his fate is due to muddling and injustice.

Commonly labelled as "square pegs" are the youths for whom life has yet been too easy, and who are liable to dignify their distaste for continued effort by the belief that they are inappropriately utilized. Finally there are the psychopaths, inappropriate in any section, who too often regard failure in a job of little responsibility as an adequate recommendation for a position of greater trust.

Such maladjustments to the very rigid framework of Service existence are potent causes of anxiety and breakdown.

More intangible factors in maladjustment often present themselves during the period of training—these again more often in the youth who has not yet learned to subordinate himself to the task in hand, and who welcomed his civilian work as a source of livelihood but not his real interest in life. The Service assumes that the individual regards the job as more important than himself. Further, the tradition that only perfection is passable, with the corollary that explanation is no excuse for failure, is still acted on in the Service. These tacit assumptions lie behind much of the tradition of the Service, but to the new entry they may appear as callous disregard for himself as an individual, continual fault-finding, and an unfeeling refusal to listen to reason. In the early stages of training the stimulus and interest of a new life are sufficient to counterbalance these asperities, but in the second or third month, when familiarity has staled but habit has not yet accustomed him to the Service or involved him in the group spirit, the reaction may be one of rebellion, depression, or anxiety. Later, fellowship in responsibility in the smaller units of the ship and growing confidence restore injured self-esteem.

Once at sea the actual physical threats to life present themselves. To the imaginative the period leading up to action often brings the dread of proving inadequate: the inexperienced knows not what to expect; the experienced may dread failing in his responsibilities. The immediate stress, whether from air attack, action, exploding mine, or torpedo, produces a response which may be disability at the time or which by frequent repetition induces disability. Often overlooked are the stresses peculiar to the engine-room branch or stoker ignorant of what is happening above. For him a sudden reverberation, plunging him in darkness and throwing him among clanging and

shifting engine-room fittings, is as much a trauma, whether due to a mine dispatched by his own gear or by a near miss or a bomb or torpedo striking the ship. For the man below deck every possibility lies in the first concussion. At the other extreme lie the experiences of the man too long in northern waters, particularly in small ships. Here monotony of up to a week at sea with a small crew, with short visits to bases that offer no attraction to going ashore, and heavy weather in latitudes that in the winter months mean "darken ship" for 18 or more hours of the day, produce a severe reaction curiously similar to the anxiety-exhaustion and depressive syndrome presented by the sufferer from prolonged or severe stresses by enemy action in more southern latitudes.

Development of Anxiety State and Symptomatology

Subjected to the above-mentioned stresses, the individual tends to react with unexpected uniformity to an eventual state of anxiety which, however varied its manifestations, does in its essentials run true to form. The concept adopted regarding the development of these states was of the psychosomatic unit, subjected to a variety of stresses, endogenous and exogenous, and reacting to these at first physiologically: with undue prolongation of the demands disability supervenes. The less stable types or those in whom there is a smaller constellation of factors making for continued effort break down early; the more stable types and those in whom strong reinforcing sentiments are present do not come under medical care till a more advanced state is reached. The more inadequate types—the temperamentally unstable, the constitutionally inferior, and the mentally backward—often show up in training with mild depressive or hypochondriacal features. They complain of exhaustion, weakness, headaches, or "effort syndrome." (The more robust but maladapted frequently come into conflict with naval discipline at this period.) This may be regarded as the eliminating period of service. The vast majority who survive this test of adaptation may react to conditions of service or stress at sea with disability at three different stages.

Stages of Stress

Immediate stress of danger results at first in what may be regarded as a physiological adrenal-sympathetic response, with a mood of anxious expectancy (Cannon's (1929) "fight or flight" reaction). The physiological propriety of this response is not, however, apparent to the rating, aware only of blurring vision, beating heart, "stomach turning over," and tense or trembling musculature. In the stable, the need for action dissipates the discomforts of his state, and a mood approaching exhilaration often supervenes with gradual relaxation. The temperamentally unstable may over-react, however, to complete ineffectiveness. This may be regarded as disability supervening at the stage of *early stress*.

More commonly the repetition of such dangers leads to a state of heightened expectancy and somatic tension which, while appropriate and in fact synonymous with good morale, may become irreversible when threats are frequent. When relaxation does not occur with relief from strain on leave or ashore, and preoccupation with physical and mental discomforts develops, an anxiety state must be presumed to exist. Presenting himself, the patient may complain of the sense of tenseness or of palpitation, epigastric discomfort, or other correlates of his condition. The clinical picture is of dilated pupils, increased sweating, tachycardia, slight tremor, and increased tendon reflexes. Blood pressure is usually found markedly raised: readings of 170/100 or over are almost routine in the sick bay at this stage. This is regarded as the state of *established tension*.

In most cases of the more stable, conscientious, or experienced types the man may remain at duty for a prolonged period after the stage of established tension. Anxiety and somatic tension, though still present, become less obvious, and the presenting picture is more of depression and exhaustion, with emotional lability and loss of weight. Blood pressure is less elevated, or is even lowered, though tendon reflexes remain exaggerated. It is more commonly in this final state that misleading preoccupation with symptoms or signs in relation to one or other of the systems gives rise to the erroneous diagnosis of organic illness. This final state we have termed *anxiety with exhaustion*.

The concept of the development of anxiety state with disability developing at the phase of *early stress*, the state of *established tension*, or final state of *anxiety with exhaustion*, according to the stability of the constitution affected, is clinically valuable from the point of view of prognosis and treatment. In practice, however, the picture present is mixed, and an attempt has been made to discuss the whole range of symptoms. These may be psychic, somatic, or mixed, and vary from mild disturbances of function to gross hysterical features.

Psychic Symptoms

In the psychic sphere the anxiety varies from mild waves in the moments of stress to acute panic attacks. It has been found that even in the sheltered existence in hospital the latter occur, and they are very infectious. Anxiety itself is directed towards a number of different objects. In some, of course, it is the frank fear of danger, freely admitted. It is noteworthy, indeed, in our cases that refusal to admit fears to themselves, with consequential conflict, was very rare, and when it did occur appeared chiefly in the older, better-trained, and obsessional types. In others the object was family responsibility; fear of going insane, of blindness, of something being seriously wrong, especially in those who showed cardiac or gastric symptoms. There was also found the fear of heights, water, and trains, of being shut in or sleeping below at sea. With regard to the family, justification for anxiety often existed when dependent relatives were sick, alone, in poor economic circumstances, or exposed to raids on civilian population.

Sleeplessness was a very common symptom, and presented itself in varying aspects. There was difficulty in going to sleep, or the patient woke up at frequent intervals. Often sleep was disturbed by dreams, and he woke in the morning unrefreshed and with a headache. The dreams also varied. War dreams were common, and the patient often relived some horrifying experience, or woke up sweating after anxiety dreams. Many described their dreams by the phrase "mixed up."

Complaints of being easily tired, of lacking energy, and at the same time of restlessness and being unable to settle are frequently made. Coupled with this was a poor memory for recent events and forgetfulness. Characteristically also there was an inability to concentrate. Some patients found themselves unable to read more than half a page of a book at a time or to take in the gist of the subject-matter.

Loss of confidence and fear of responsibility or of "letting the others down" were both a symptom and a reason for augmented anxiety. Many complained of increased irritability. This appeared not so much with their fellows, since the dislike of company made them desire solitude, as with their home circle. The question, "Does your wife find you more short-tempered than usual?" often brought a rather sheepish reply, "I am afraid so, sir." Emotional disturbance was so constant that it was found advisable to have a small box of gauze squares at hand with which to supply the patient, who frequently broke down and wept during the interview. Increased consumption of alcohol was either an escape from reality or, in some cases, a spur to keep going.

Many of these symptoms explain themselves, and appear either in a setting of anxiety or, not infrequently, without much overt anxiety.

Somatic Symptoms

In the cardiovascular system symptoms were fairly common. Usually the tachycardia and palpitations became the focus of anxiety through ill-advised medical advice in earlier life or variously derived dreads of "heart disease." Precordial pain was often present in such cases and dyspnoea less commonly so. Frequently a man had entered hospital with a diagnosis of cardiovascular disorder based on those symptoms. In such cases no organic lesion was found. It was our experience, however, that the effort syndrome as such was rare in the Navy, and when present emerged generally in the training period and as an anxiety manifestation.

The blood pressure seems to vary at different stages in the illness. In acutely disturbed or shocked cases after some catastrophic event it was found to be low—just above or below 100 mm. systolic. In established cases there was a period when it was raised, while in later cases or those showing exhaustion it was lowered.

In the genito-urinary system frequency of micturition and even enuresis occurred in a number of cases, and may be either a symptom of a fairly severe state or a chronic manifestation without much apparent anxiety. In the former, we consider that both complaints clear up with general improvement, but as a chronic manifestation they have proved stubborn and difficult. Experience, however, has taught the necessity for checking a patient's own statements as to how often he micturates. In some cases these have been proved not wholly unconscious exaggerations. Impotence has been complained of in established cases in which the depressive element was strong, and is also found to clear up with treatment of the general condition.

Digestive disturbances are frequent. Morning nausea and often vomiting are complained of. Poor appetite is the rule rather than the exception, with the inevitable accompaniment of loss of weight. Functional dyspeptics were not as a rule admitted to a psychiatric ward. They usually are not recognized for what they are, and are admitted for gastric investigation. After negative results have been obtained the neuropsychiatric specialist has been asked to see them. Here, too, it is believed that symptoms are often considerably exaggerated. It is our opinion that gastric investigation should be undertaken in all cases and the psychiatric angle of the case then be tackled. There is usually no difficulty in finding other evidences of the anxiety state; where these did not exist the case was not regarded as psychiatric. Particular importance was attached to impressing medical colleagues with the difference between a dyspepsia in which no evidence of lesion had been shown by a fractional test meal and by radiographs—which remains a medical problem—and dyspepsia occurring as part of an anxiety syndrome.

Other Symptoms

Pain has been met with in every system, and in all parts of the body and all degrees of severity. There is little doubt in our minds that the anxious person is more aware of pain and that his mind, centred on his bodily sensations, has a lowered threshold for pain. A frequent complaint was of "shooting pains all over the body." Various muscular aches in the limbs were common, as was backache. Localization of pain often depended on an associated idea in the patient's mind.

Headaches were almost always present—sometimes accompanied by dizziness and sometimes based on a former head injury. It was often clear, however, that the injury had set the stage for, but was not organically responsible for, this symptom. The headaches, whatever their basis, may appear as a dull ache, a band of tightness, a feeling of vertical pressure, or an acute throbbing sensation in the temporal or occipital regions.

Grosser hysterical phenomena were rare and often occurred on the basis of mental backwardness or in a psychopathic constitution. We attach great importance to the necessity for regarding hysterical manifestations as but symptoms of the fundamental anxiety, and no attempt has been made to separate those cases which showed hysterical phenomena from the general mass of anxiety states. This evaluation of symptoms in true perspective avoided the temptation of spectacular "cures" and correspondingly dramatic subsequent conversion phenomena.

While functional weakness of a limb or part of a limb was observed fairly often, paralyses were relatively uncommon, and were certainly on a far smaller scale than was evident in the last war. In many cases the basis was an original organic lesion, and it became axiomatic to seek this organic basis.

Amnesias and fugues occur frequently. In not a few they begin while on leave or on the journey back to duty. Many of these were at a fairly conscious level, and in some cases were judged to be retrospective rather than to be true amnesias. It is considered that they often developed in a setting of mild depression. For a man to claim loss of memory as a reason for evading punishment for being absent over leave is only too easy a way out, from his point of view. A good deal of care was taken to avoid errors in assessing the man's responsibility. Repression and amnesia for painful experience have also been found to occur rarely, and, when present, related to such catastrophic events as being trapped below in a sinking ship; on one occasion they were related to guilty feelings in the patient, who had sought safety while his friend drowned.

Unexpectedly it was found that the conflict between duty and self-preservation was seldom repressed or the basis of a complex-determined symptomatology.

The ordinary man is, in this war, under no difficulty in admitting to himself that he is scared and would prefer to be elsewhere. That he does not give way to this feeling, but rises to the demands of a situation, may be the basis of later anxiety, though not of conversion symptoms. This fact, with the recognition of the anxiety state as such, doubtless explains the relative absence of conversion hysteria.

Anaesthesias and paraesthesias occurred with moderate frequency and varied in degree and situation. Here again there was often an original organic basis. Stammering appeared from time to time, and as a rule there was a similar history of this trouble in childhood.

Minor disturbances of vision were relatively common, although the grosser ones were less often seen than might have been expected—e.g., photophobia, occurring after exposure to explosion flash. Far more frequent were blurring of vision, with "spots before the eyes" and amblyopia. Night blindness was a common complaint, and in not a few instances functional failure to focus. This was chiefly demonstrated in those with a refractive error which was not improved by appropriate lenses. Visual complaints failing to improve with the general condition were in a significant number of cases found to be based on blindness in a relative and a corresponding fear in the patient.

Only a few cases of aphonia were seen; these usually clear up rapidly.

A history of "collapses," fits, and faints was commonplace, but occurrence of such in hospital was on the whole rare. They were not always easy to assess, for the classical hysterical fit was seldom seen. Some were undoubtedly syncopal attacks, others vasovagal, but there was a considerable group that did not fall into these categories, nor were they epileptic.

Treatment

Most cases seen in hospital are those which treatment from the ship's medical officer or in the local sick bay has failed to clear up. Briefly, such treatment has consisted of encouragement, reassurance, and sedation with short periods of rest in the sick bay. It must be emphasized that a large proportion of the milder anxiety states are adequately treated in this way and never reach hospital—treated often by medical officers who themselves experience corresponding stresses and are well able to judge the severity of the symptoms. The treatment to be discussed, however, is that of the cases that enter hospital.

Here the basic principle adopted has been that of resting the over-stimulated organism as a first measure and bringing it back to normal functioning as the second. Admission to hospital secures relief from the immediate situation; rest in bed, with the use of normal sedatives—i.e., bromides by day and barbiturates by night—and recourse to paraldehyde for the restless, is sufficient to ensure relaxation in the milder cases. Where loss of weight, debility, and exhaustion occurred without marked tension an effort was made to build up the physical condition and bring about an increase in weight. The usual methods were adopted, but a useful adjunct was the administration of insulin and glucose daily over a period. Small doses of from 5 to 10 units twice daily were employed with liberal carbohydrates. We did not use insulin sapor.

In cases in which exhaustion and loss of weight are marked and emotional tension is so severe as to prevent relaxation continuous narcosis has been found of great value. It has also been highly beneficial in cases admitted immediately after heavy raids or attacks, when the patient may show violent agitation, gross tremor, and somatic disturbance so pronounced as to render him inarticulate or even to produce a confusional element. The technique is a modification of that described by Mira (1939). For hyoscine, which frequently proved toxic, paraldehyde has been substituted. The treatment lasts for 72 hours; sleep is maintained by 1½ gr. of phenobarbitone 4-hourly during the whole period. This is reinforced by 2 drachms of paraldehyde, administered freely up to 10 to 12 drachms in the 24 hours. Ordinary light diet is given, with fluids "pushed."

Used as an immediate treatment in grossly agitated and acute cases this technique has proved spectacular in relieving

the patient's distress and subduing the gross physical disturbances that are otherwise apt to be hysterically prolonged. All cases, however, so treated have shown marked improvement in physical condition. Emotionally there is a sense of relaxation, sleep is re-established, tremors disappear, and the patient is encouraged by the feeling of relief and relative well-being. The improvement, however, is regarded as but a first step, most significant in men of good personality whose symptoms have been precipitated by prolonged or severe stress of active service. In the more inadequate and unstable types, whose anxiety is a reaction rather than the situation of war than to specific stress, the disturbing factors tend to come into play again as soon as full consciousness is regained. Cases showing depressive factors also react well.

Psychotherapy, as such, was of necessity superficial or symptomatic or limited in its application to problems of adjustment to Service life or conscious experiences. While an essential part of the treatment of every case, it is probable that by itself it seldom made the difference between a man's retention or discharge from the Service. In minor hysterical phenomena, such as tremor or spasm, treatment was firmly directed towards the underlying anxiety state, and, in the main, symptoms liable to be prolonged were found to clear up *pari passu* with the general condition. Suggestion and persuasion were occasionally of value as symptomatic treatment. A certain amount of relief is obtained with abreaction, and recovery of painful experiences with direct hypnosis or by the medium of narco-analysis as described by Mallinson (1940). Again, however, the general condition remained to be treated.

Occupational therapy, physical training, gardening, and hospital concerts were useful measures in returning to normal attitudes. The patients, too, were encouraged to go for afternoons outside the hospital grounds when possible.

The adjustment of concrete personal and domestic problems, where possible, was regarded as of such importance in promoting recovery that particular attention was paid to it. Too much stress cannot be laid on this. The recognition by the executive authorities of recommendations made was helpful, while the Welfare Officer and the Royal Naval Benevolent Trust invariably assisted when approached.

The prognosis of every case was assessed as soon as possible after admission and the patient informed. Those in which the outlook was thought to be unfavourable were recommended for consideration for invaliding as soon as they were well enough to be discharged to civilian life.

Hospital treatment beyond two to six weeks was required only in a small proportion of cases, and, in those, transfer to an establishment devoted to rehabilitation measures was effected. A moderate period of sick leave gave the stimulus of restored personal relations, relieved domestic anxieties, and revived a sense of independence; but prolonged leave was recommended with increasing discretion. The men returned to full duty, or frequently to service on shore preliminary to full service. While on shore service they were recommended to be under the eye of the neuropsychiatric specialist in their depot. He could then give the appropriate guidance to the executive authorities, maintain contact, and arrange for suitable employment in depot, or finally effect return to full duties at sea in an area of diminished stress.

Prognosis

In general it was found that the results of treatment were satisfactory. Prognosis was poorer in the cases described as constitutionally inferior or temperamentally unstable, particularly when allied with any degree of mental backwardness. It was also poorer where a prolonged state of tension had preceded a severe trauma such as being trapped in a sinking vessel. No close relation between age and prognosis was observed, except where the factor of arteriosclerosis entered. In such cases prognosis was bad.

The general result of our observations has been that there is a remarkable capacity for recovery from anxiety states in the averagely endowed and stable individual. Except where the above-mentioned factors operate, return to duty at sea with repeated stress can be anticipated.

Even in the cases of poorer prognosis return to some form of service in a position of diminished stress can be achieved in a large proportion of cases. Particularly has this been found

to be the case since a neuropsychiatrist has been established in the depot, with all his advantages in familiarity with conditions and demands and power to recommend disposal.

We wish to express our thanks to Sick Berth Petty Officers Orr and Winson for great pains in extracting the case material and copying the drafts on which this article is based.

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NITROUS OXIDE ANAESTHESIA: A CRITICAL EVALUATION

BY

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Nitrous oxide-oxygen is usually considered the safest and best anaesthetic agent. At the present time, when non-experts in increasing numbers are being called on to act as anaesthetists in both military and civil practice, a critical examination of this statement is necessary.

While quite suitable for many operations on susceptible patients, nitrous oxide, being the weakest of all anaesthetic drugs, is rather an agent for the production of unconsciousness than one which can provide any degree of muscular relaxation. The attempt to produce the former in many anaesthetic-resistant patients and the production of the latter in nearly all cases are usually accompanied by such a degree of anoxia as may often be dangerous. Thus Macintosh (1938) states that "its use by inexperienced anaesthetists for major surgery is fraught with disappointment if not carried out boldly, and with danger if it is"; while Clement (1939) in the standard work on the subject acknowledges that "deep, prolonged anaesthesia with nitrous oxide implies a drastic and continued curtailment of the oxygen supply which greatly augments any degree of anoxaemia that may be present" (p. 97); and, again, "The abnormalities" (of respiration) "occurring in the deeper planes are all evidences of oxygen want. . . . The symptoms produced in the nervous system by nitrous oxide-oxygen administration are in reality those of a gradually progressing state of anoxaemia" (p. 40).

Arguments against Nitrous Oxide

In these circumstances, why is nitrous oxide anaesthesia continually recommended when its use must often imply considerable oxygen want? The three main arguments are all propounded by Clement: (1) that anaesthetic agents in general produce their effects by reduced oxygen utilization, and nitrous oxide in particular "by the exclusion of the oxygen in the inspired air" (p. 98); (2) that nitrous oxide is an indifferent inert gas without any direct action or effect upon the body tissues (p. 23), and it is assumed, therefore, that any additional effect of anoxia on the tissues will be minimal, if not harmless; (3) that "the body shows a remarkable tolerance to moderate, and even temporary severe, degrees of oxygen want" (p. 97). In my opinion the weight of evidence is against each of these statements.

1. The theory that the narcotic action of anaesthetic drugs in general, or of nitrous oxide in particular, is due to depressed oxygen utilization is not supported by recent research. Henderson (1930), after reviewing considerable evidence, concludes that "oxidative processes and narcosis are separate phenomena. . . . No theory of anaesthesia will prove acceptable which is based on a proof of a depression of the resting oxidation of the cell." Pask (1941) reviews the recent work on this subject, and also concludes that under clinical and experimental conditions anaesthesia had no effect on the oxygen uptake of the intact organism or of isolated tissues.

2. Nor can it be assumed with certainty that the effect of nitrous oxide on the tissues is negligible. Clinical experience does not support this assumption, for short anaesthetics for minor surgery, even in the absence of anoxia, are often followed by headache, vomiting, and a feeling of distress and giddiness. Macintosh and Bannister (1941) state that they attempted to produce anaesthesia sufficient for dental extractions in 50 cases by nasal administration of nitrogen, and "although in all cases unconsciousness was reached, in the robust or anaesthetic-resistant type the full anaesthetic state

was not achieved. . . . If nitrous oxide has no anaesthetic effects, but acts only as an oxygen replacer, any inert gas would furnish as satisfactory an anaesthesia; actually, the anaesthetic properties of nitrogen are not as effective." Even were this assumption to be true, it is difficult to understand how it would render less harmful the effects of frank anoxia on tissue cells. Experience shows that the adoption of this assumption as a working basis often results in an anaesthetic technique which cannot be considered good practice.

3. The statement of Haldane (1922) that "anoxaemia not only stops the machinery but wrecks the machine" would appear to me to be as applicable to anaesthesia with nitrous oxide as to any other clinical condition. Indeed, recent research and clinical experience have not only confirmed Haldane's work but have demonstrated that the effects of anoxaemia may be insidious or delayed (Armstrong, 1939). Thus Samson Wright (1940) concludes: "A slight degree of oxygen lack may therefore act insidiously and only reveal its effects after a long latent period. . . . Following prolonged severe exposure to oxygen lack, very formidable after-effects occur." Courville (1936, 1939) has produced convincing evidence of the damaging effect which oxygen deficiency during anaesthesia, especially with nitrous oxide, may produce on the central nervous system, particularly on the cortex. He has shown how minor degrees of anoxaemia may cause permanent damage, which may not become apparent until after a considerable latent interval, while even a few minutes of severe anoxaemia may produce permanent damage. As Pask (1941) has emphasized, "immediate apparent recovery from a period of anoxia does not necessarily mean that a patient, particularly a shocked patient, has not suffered harm."

Cyanosis

Clinical experience does not support the view put forward by Clement: "The difference between the cyanosis associated with nitrous oxide-oxygen and that with other anaesthetic agents has been frequently overlooked" (p. 38); "cyanosis during nitrous oxide-oxygen anaesthesia has been given the same significance as with all other anaesthetics, thus the mode of action of nitrous oxide in producing anaesthesia by the exclusion of oxygen is ignored" (p. 103). The implication in these statements is that cyanosis is of a different nature when associated with nitrous oxide, and they have often been taken to justify its use in circumstances which must imply a considerable degree of anoxaemia.

Cyanosis depends on the absolute amount of reduced haemoglobin in the blood, the amount of oxygenated haemoglobin present being of little importance (Lundsgaard and van Slyke, 1923). Thus in plethoric individuals cyanosis may occur without anoxaemia, but such patients form a very small proportion of those coming to operation. Unless the haemoglobin concentration of any surgical patient is known to be above normal the possibility of cyanosis occurring without anoxaemia may be ignored.

Far different is the case with anaemic patients, who, in surgery, comprise the great majority. Here, the oxygen-carrying capacity of the blood being below normal, even when fully oxygenated there may be some anoxaemia, although the amounts of reduced haemoglobin present in the capillaries may not be sufficient to produce clinical cyanosis. But when the latter is present, the amount of haemoglobin available for carrying oxygen is further reduced and oxygen want intensified. Cyanosis therefore *must* be prevented in anaemic patients if anoxia is to be avoided.

McCarthy (1941) has described signs, affecting the respiratory and circulatory systems, by which he considers anoxia may be recognized, irrespective of the presence or not of cyanosis. Unfortunately, however, in my experience these signs do not occur in minor degrees of anoxaemia, where their value would be greatest; they are almost invariably late signs, indicating that circulatory and respiratory depression is already profound.

Prevention of Anoxaemia

It would appear, therefore, that the only method of avoiding anoxaemia is by maintaining scarlet blood in all cases. Where, however, anaemia is known to be present before operation, or is produced during operation by blood loss or other means, then not only must cyanosis be prevented but an increased concentration of oxygen must be given, over and above that necessary to produce scarlet blood, to compensate for the reduced haemoglobin, for by this means an increased blood-oxygen concentration may be produced (Boothby *et al.*, 1939, 1940; Wood, Mason, and Blalock, 1940).