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EDITORIAL

Can you diagnose hyperventilation?

Hyperventilation can be conveniently defined physiologically as breathing in excess of metabolic requirements.[1] At sea level the drive to breathe is principally derived from the requirement to keep the arterial carbon dioxide tension within the normal physiological range. This is achieved via central (medulla and brainstem) and peripheral (aortic and carotid body) chemoreceptors which effect changes in ventilation themselves via the respiratory centres.[2] At high altitude, however, ventilation may also be driven by hypoxia rather than via this CO_2 pathway.[3] From a clinical point of view, hyperventilation is used to describe the clinical syndrome or syndromes associated with the subject's breathing in excess of their metabolic requirements. The syndromes relate to the symptoms produced and the signs which are present on examination.

There are two main clinical syndromes which occur in subjects who hyperventilate. There is a syndrome which involves acute episodic hyperventilation (which has also been described as 'panic attacks') and a syndrome which involves more chronic hyperventilation. In reality, whilst there are subjects who display the two syndromes in their pure forms, there appears to be a spectrum of disease between these two extremes and most patients will have some features of both.[4]

The terminology used for patients who have respiratory symptoms which cannot be easily explained by organic disease has become somewhat confusing. The term 'dysfunctional breathing' has been adopted as an all-encompassing diagnosis. Dysfunctional breathing is difficult to define as an entity but probably includes patients with symptoms related to a variety of causes. There will undoubtedly be some patients who hyperventilate within any group of subjects with dysfunctional breathing.[5] There will however, also be subjects whose symptoms relate to chronic fatigue,[6] vocal cord dysfunction[7] and also thoraco-abdominal paradoxical movement.[8] There are studies which demonstrate that these conditions can exist alongside hyperventilation or in isolation to cause respiratory symptoms not related to lung disease *per se*.

The term dysfunctional breathing therefore should be used with caution and where possible, subjects should be defined more clearly as to whether they hyperventilate, have chronic fatigue, thoraco-abdominal paradox, vocal cord dysfunction or all of these. This is especially important in the context of clinical trials, and particularly ones where a treatment intervention is being studied in these groups of subjects.

A further complication of all of the conditions described above which may comprise dysfunctional breathing is that they may co-exist with what one may describe as organic respiratory or cardiac disease such as asthma,[9] COPD[10] and ischaemic heart disease.[11] Whether or not there is a causal link between the organic and the 'functional' condition (as has been suggested in subjects with both asthma and hyperventilation) remains to be proven in most cases.

Terminology and co-existent organic disease aside, how does one diagnose hyperventilation?

In the case of episodic acute hyperventilation it is usually very clear from simply observing the subject that they are acutely hyperventilating. Panic attacks such as this are associated with a feeling of fear and the acute hyperventilation is easily documented by demonstrating a low arterial or end-tidal CO_2 level.[12] There may be concomitant relative hyperoxia in addition. The history of episodic attacks coupled with the demonstration of ventilation in excess of their CO_2 drive (ie, the low arterial or end-tidal CO_2) along with exclusion of other pathology such as asthma is usually all that is required for diagnosis.

Subjects with chronic idiopathic hyperventilation (CIH) however can be much more difficult to diagnose. They often present through respiratory or cardiac clinics in secondary care with breathlessness on exertion. Classically they describe breathlessness and chest tightness during low level exercise, particularly during their activities of daily living such as housework, shopping and walking up and down stairs. Parasthesia, whilst common in acute hyperventilation is seldom a feature of the more chronic condition. During consultations the subjects may be tachypnoeic, however this is not a consistent feature and should not be relied upon. The clue to the diagnosis comes from the normalcy of the tests performed of cardiac and respiratory function. Exclusion of significant cardiorespiratory disease in a patient with breathlessness on exertion should therefore alert the clinician to the possibility of

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underlying CIH. Tests to confirm the diagnosis are however still required.

What about symptom questionnaires and symptom scores for diagnosis? Patients with CIH have significant anxiety when assessed using the Hospital Anxiety and Depression Score questionnaire.[13] This however, is neither sensitive nor specific for CIH. The Nijmegen Questionnaire has been suggested to be able to diagnose hyperventilation. The questionnaire was however devised as a research tool to score symptom levels in a group of subjects already defined with physiological testing to demonstrate hyperventilation.[14,15] Many symptoms on this questionnaire are common to 'organic' respiratory diseases and on an individual level in the absence of physiological testing this questionnaire is neither sensitive nor specific.

Which tests should we therefore use to confirm the diagnosis of CIH? In my own unit, the gold standard for confirmation is the demonstration of a low end-tidal CO_2 level which is sustained at low work rate during a ramp incremental cycle ergometer cardio-pulmonary exercise test (CPX). An additional pattern also seen is a high baseline ventilation level with variability in minute ventilation during exercise and also during the recovery phase.[16] The recovery phase is also frequently prolonged. Despite their hyperventilation during early exercise subjects often exercise to reasonable levels of work rate (although reduced compared to normals) and often achieve anaerobic threshold.

We have recently described the exercise response on a group of subjects with CIH, they appear to have abnormal and sustained ventilatory drive which persists throughout exercise, even at high work rates when the subject is anaerobic.[17]

In centres without cardiorespiratory exercise equipment, a low end-tidal or arterial CO_2 may be demonstrated after a corridor walk test either using capnography or by assessing arterial blood gas tensions. The latter test should be interpreted with caution as the procedure of taking an arterial blood sample can induce acute hyperventilation secondary to the pain induced by the test. With the correct history and otherwise normal cardiorespiratory function however, this is usually sufficient to confirm the diagnosis.

Hyperventilation provocation tests (HVPT) are tests in which subjects are asked to volitionally hyperventilate. This can be done effectively by asking the subject to either take 20 consecutive maximal deep breaths or to have them breathe rapidly (usually at a rate of 40 breaths per minute) for three minutes.[18] Studies have investigated the symptoms produced during volitional hyperventilation and have concluded that this test is not sensitive at differentiating normal subjects from those who have hyperventilation.[19] Adding CO_2 to the inspired air to maintain the CO_2 level at the pre-test level does not add any further sensitivity to the test.[20] What does appear to be a useful discriminator however between normal subjects and those with CIH is what happens to ventilation levels after the period of volitional hyperventilation ceases. In normal subjects due to them reducing their arterial CO_2 levels during volitional hyperventilation, there is often a period of apnoea or hypopnoea during the recovery phase. In subjects with CIH however there seems to be an inability to stop hyperventilating after the period of volitional hyperventilation. They continue to hyperventilate above baseline pre-test levels for a period of time during recovery. Anecdotally from my own laboratory subjects are often still hyperventilating 30 minutes after the volitional period has ended.

The exact mechanism of this phenomenon is unknown but it may be related to an abnormal feedback mechanism at airway, chest wall or brainstem level. This mechanism may be attributable to altered corollary discharge/after discharge response in these patients.[21,22] To demonstrate this persistent hyperventilation however, centres will require facilities to measure ventilation (such as a pneumotachograph). These centres will therefore usually also have access to full cardio-respiratory exercise testing which is likely to be more sensitive.

Breath-hold time (BHT) is also abnormal in subjects with CIH. We have recently reported BHT in a group of CIH subjects as being only 20 seconds compared to a control group whose mean BHT was 60 seconds.[17] Breathing pure oxygen should (and indeed does) increase BHT in normal subjects by 50–100%, however it did not alter BHT in the CIH subjects. BHT may therefore offer a simple test which requires nothing more than a timepiece to suggest CIH. BHT can be reduced in patients with respiratory and cardiac disease, therefore exclusion of these conditions is essential before a reduced BHT can be implied to suggest CIH.

In summary therefore hyperventilation can in some circumstances be diagnosed on clinical grounds only, however in the vast majority of patients physiological testing for confirmation is required. There is no questionnaire which will reliably diagnose CIH in an individual subject. Cardio-pulmonary exercise testing appears to be the most sensitive test to confirm the diagnosis, however arterial blood gas estimation, capnography, persistent ventilation following HVPT and breath hold assessments may all aid diagnosis.

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