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Autonomic neuropathy in anaesthesia

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1. Introduction

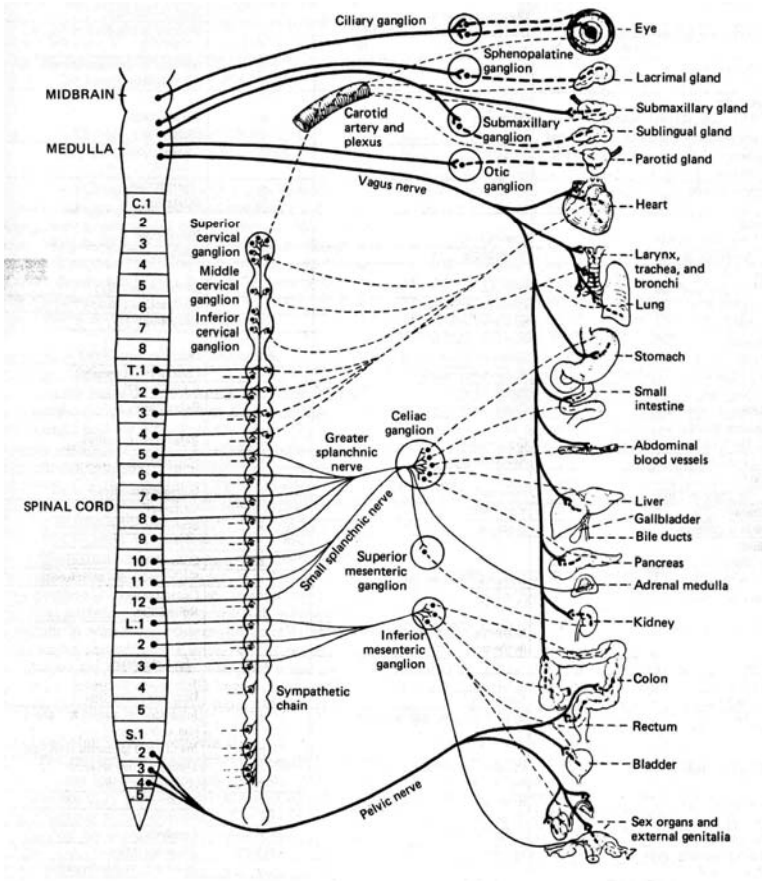
Autonomic Neuropathy is a common problem encountered by anaesthetists, both in operating theatres and in the critical care setting. There are a wide variety of causes, many of them associated with significant co-morbidity. It is clear that it is a problem which involves every system on a number of levels, and many of the issues are of particular significance to the anaesthetist. This review will cover briefly the aetiology and diagnosis of autonomic dysfunction, before discussing the clinical manifestations and consequences of the disorder. The major focus will be on cardiovascular autonomic neuropathy (CAN) and its implications for the perioperative phase. In addition, it will briefly look at the involvement of the enteric nervous system, as well as deal with some of the new concepts emerging in the literature.

2. The Autonomic Nervous System

The word 'autonomic' originates from two Greek words meaning 'self' and 'law'. It regulates the unconscious, involuntary control of automatic bodily functions. There is close interaction with motor and sensory nervous systems, and it may be influenced by higher centres with some voluntary control. It is traditionally divided into the parasympathetic system, arising from cranio-sacral outflow, and the sympathetic system, which is thoracolumbar in origin. The dominant neurotransmitters are acetylcholine and noradrenaline. For a more detailed look at the structure and functioning of the autonomic nervous system, read Prof James' lecture.[1]

When one looks at diagrams of the ANS anatomy, such as the one illustrated overleaf, it becomes immediately apparent that the ANS is involved in the control of almost everything in the body. It innervates the entire neuraxis and permeates all organ systems. It regulates blood pressure, heart rate, sleep, and bladder and bowel function.[2] Pathology in the ANS thus has potential to cause significant and widespread effects, in particular during the perioperative phase. Consider the stress response, which is a complex series of mechanisms aimed at optimizing circulation and metabolism for short-term survival. Sympathetic outflow alters blood distribution, cardiac output, renal function and metabolic pathways, all of which are parameters which could have a significant impact on perioperative morbidity and mortality. Responses to sympathetic and parasympathetic stimulation are frequently antagonistic. The disruption of balance between sympathetic and parasympathetic systems, as well as

inappropriate responses to stress could potentially have devastating consequences.



3. The Autonomic Neuropathies

The autonomic neuropathies are a group of disorders in which the small, lightly myelinated and unmyelinated autonomic nerve fibres are selectively targeted. Autonomic features occur in varying combinations with these disorders, and may involve the cardiovascular, gastrointestinal, urogenital, sudomotor, and pupilomotor systems. Diabetes is the most common cause of autonomic neuropathy in developed countries.[3] Autonomic neuropathies may also occur after acute infection, as part of a paraneoplastic syndrome,

after exposure to certain neurotoxins or as a result of amyloid deposition. Conditions such as Guillain-Barre syndrome, porphyria and botulism cause acute/subacute autonomic neuropathies. There are also several familial autonomic neuropathies with varying patterns of inheritance. Of particular significance in Kwazulu-Natal is the growing awareness of the prevalence of dysautonomia in HIV infection. It should also be recognized that causes of autonomic neuropathy may be central as well as peripheral. For example, a lesion of the medulla produced by a posterior fossa tumour can impair BP responses

Selected Causes of Autonomic Peripheral Neuropathy

- Diabetic autonomic neuropathy
- Amyloid neuropathy
- Acute and subacute autonomic neuropathies
- Immune-mediated and paraneoplastic neuropathies
- Hereditary autonomic neuropathies
- Autonomic neuropathies due to infectious diseases
- Toxic neuropathies

4. Making the Diagnosis

In looking for the presence of autonomic neuropathy, many physicians chose to evaluate just one component of the autonomic nervous system – the cardiovascular system. Cardiovascular autonomic neuropathy (CAN) is a valid method for routine screening and monitoring of autonomic neuropathy in a wide variety of conditions, with the implication being that where CAN is present, there will be autonomic dysfunction in other systems as well.[4]

The diagnosis of CAN should be based on the results of a battery of autonomic tests rather than one single test, and the function of both branches of the autonomic nervous system should be evaluated. The current standard for diagnosis of CAN is that at least 3 of the following seven parameters should be abnormal (specificity 100%):

1) Valsalva Maneuver (Valsalva ratio)
2) Orthostatic test (30:15 ratio)
3) Deep breathing test (E:I ratio)
4) Orthostatic hypotension test (OH)
5) Spectral analysis of HRV – very low frequency
6) Spectral analysis of HRV – low frequency
7) Spectral analysis of HRV – high frequency

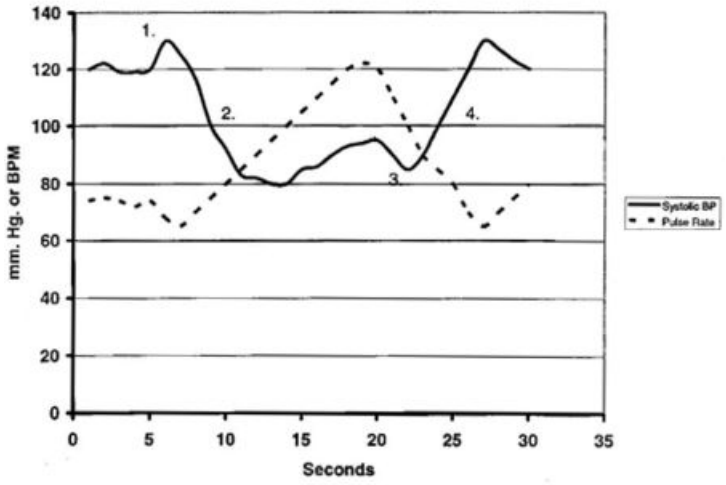
The last three criteria require computerised analysis. In the absence of a computer system, the first four tests can be performed and 2 or more positive results indicates a positive diagnosis, with a specificity of 98%.

Ewing and Clark described a method for the evaluation of cardiovascular autonomic reflexes, involving five simple tests which could be performed with routinely available equipment and in 20 minutes.[4] While their method was described for diabetic autonomic neuropathy, they stated that the tests were "equally applicable in the diagnosis of autonomic damage caused by other disorders". Essentially the tests look at the response of blood pressure and heart rate to a number of stimuli, and evaluate the integrity of both parasympathetic and sympathetic components of the autonomic system. These tests are outlined below according to Ewing and Clarke's description. Each response is categorised as normal, borderline or abnormal.

Tests evaluating cardiac parasympathetic function

Heart rate response to Valsalva Manoeuvre

The usual response to the strain period of the Valsalva manoeuvre is a drop in blood pressure and a rise in heart rate. After release of the strain the blood pressure rises to a higher level than its resting level and the heart rate slows. In patients with autonomic dysfunction, the blood pressure falls more slowly, does not overshoot its resting value, and there is no change in heart rate. Practically, a patient must exhale against 40mmHg of pressure for 15 seconds. The heart rate is recorded and the Valsalva ratio is calculated, which is the longest R-R interval (or slowest heart rate) divided by the shortest R-R interval (or fastest heart rate). This test is repeated three times, each a minute apart, and the mean of the three ratios is the final result. The following diagram illustrates the four phases of the Valsalva manoeuvre.



Heart rate (R-R interval) variation during deep breathing

Normal variation in heart rate with breathing is dependent on an intact parasympathetic nerve supply. This variation is more marked in younger patients and with deeper breathing. For this test, patients breath at six breaths a minute while heart rate is recorded. Each breath should consist of five seconds inspiration and five seconds expiration. Heart rate is recorded with the breathing phases marked onto the ECG trace. The result is the average of the differences between the minimum and maximum heart rates for all six breaths.

Immediate heart-rate response to standing

On rapid standing, there is a characteristic increase in the heart rate, followed by a decrease which is mediated by the vagus nerve, and which commonly is referred to as a relative overshoot bradycardia. The heart rate at the 30th beat (when the heart rate is slowest) is compared to that of the 15th beat (when the heart rate is quickest) to give a 30:15 ratio. The test is independent of age or the resting heart rate.

Test evaluating cardiac sympathetic function

Blood pressure response to standing

The usual response to standing is a slight drop in systolic blood pressure which is minimised by peripheral vasoconstriction, a sympathetically mediated phenomenon. In patients with sympathetic dysfunction, this response is blunted, and postural hypotension occurs. The postural drop is

the difference between the systolic pressure in the supine position and in the standing position. An abnormal result is reflective of advanced peripheral sympathetic damage.

Blood pressure response to sustained handgrip

In patients with a normal autonomic nervous system, the response to a sustained handgrip is a rise in blood pressure secondary to an increased heart rate with unchanged peripheral vascular resistance. The lack of an adequate rise in blood pressure may signal damage to the sympathetic nervous system. The blood pressure is measured three times before testing. Handgrip is then maintained at 30% of the maximum handgrip for as long as possible, to a maximum of five minutes, while blood pressure is measured at one minute intervals. The result is the difference between the highest diastolic pressure reading during handgrip and the mean of the three diastolic readings prior to handgrip.

Interpreting Test Results

Ewing and Clark recommended that all five tests be conducted in order to obtain as much information as possible about both parasympathetic and sympathetic pathways.[4] They grouped their results into one of four categories:

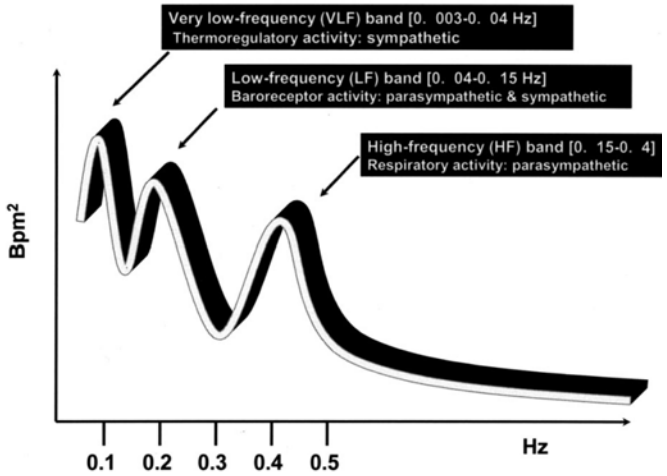
1. Normal (no tests abnormal)
2. Early parasympathetic damage (at least one test abnormal)
3. Definite parasympathetic damage (At least 2 tests abnormal)
4. Combine parasympathetic and sympathetic damage (Positive results in both categories)

	Normal	Borderline	Abnormal
Tests reflecting parasympathetic function			
Heart-rate response to Valsalva manoeuvre (Valsalva ratio)	⩾1·21	1·11–1·20	⩽1·10
Heart-rate (R-R interval) variation during deep breathing (maximum-minimum heart rate)	⩾15 beats/min	11–14 beats/min	⩽10 beats/min
Immediate heart-rate response to standing (30:15 ratio)	⩾1·04	1·01–1·03	⩽1·00
Tests reflecting sympathetic function			
Blood-pressure response to standing (fall in systolic blood pressure)	⩽10 mm Hg	11–29 mm Hg	⩾30 mm Hg
Blood-pressure response to sustained handgrip (increase in diastolic blood pressure)	⩾16 mm Hg	11–15 mm Hg	⩽10 mm Hg

The natural history of autonomic damage in diabetics appeared to be parasympathetic damage first, followed by sympathetic damage. This was the primary reason that Clark and Ewing gave for the grouping which is described above.

Heart Rate Variability: A little more detail

Power spectral analysis of HRV is a commonly used method to evaluate for the presence of cardiovascular autonomic dysfunction and to differentiate between sympathetic and parasympathetic components.[5] Three main frequency peaks are identified (high, low and very low). The high frequency peak is principally determined by respiration, mediated by the vagus nerve, the essential manifestation of this being sinus arrhythmia. The low frequency peak is a reflection of baroreceptor activity, mediated by both the parasympathetic and sympathetic pathways. The very low frequency peak is more complex, affected greatly by external influences, as well as peripheral vasomotor and chemoreceptor activity and the renin-angiotensin system. Total power is a global measure that incorporates the combined influence of all three peaks. The ratio of low frequency power to high frequency power is often used as a measure of heart rate variability. Numerous factors may influence the test results: age, heart rate, respiratory rate, BP, eating, drinking coffee, smoking, body position, volume status, mental stress, drugs, exercise, and time of day.



Do we have to do all the tests?

As mentioned above, Ewing and Clark recommended doing all these tests, in order to obtain a more complete view of the ANS. This is unlikely to be done on a premed visit. Either the patient must be referred for formal testing – something which could be set up if the need was felt to be significant enough – or we need a shortcut. There are various alternatives to the method described above, from relying on one test such as heart rate variability or postural hypotension – which may test just one arm of the

autonomic system, to making assumptions based on the duration and severity of diseases such as diabetes, which are inaccurate at best. Essentially, for a complete picture one must do all the tests, but many clinicians and researchers are choosing to use just one measurement – heart rate variability.

Questionnaires

Is it possible to ascertain whether a patient has autonomic dysfunction from a history? Various questionnaires have been designed for this purpose, such as the Autonomic Symptom Profile (known as COMPASS – the composite autonomic symptom scale), from the Mayo Clinic in Rochester.[6] It consists of 169 questions, although 57 of these relate to demographics. It was designed predominantly as a research tool, and is unlikely to be administered on the premed visit! It also relies on symptoms to make the diagnosis, and will thus miss more subtle levels of dysfunction that autonomic testing may elicit.

Problems with testing

Autonomic tests are affected by a wide variety of conditions, and testing needs to be standardised in order to ensure correct interpretation. All cardiovascular tests should be performed in the morning, under fasting conditions, with a capillary blood glucose level lower than 180 mg/dl and all cardiovascular medication, anxiolytics, antidepressants, caffeine and decongestants discontinued for at least eight hours and optimally 24 hours before (because it will depend on the half-life of each drug in particular). Normal values always depend on the age range of the patient and are standardized. When comparing populations, homogeneity needs to be ensured with regard to ethnic group, daily physical activities and pharmacological therapy. Temperature may also affect readings.

It is important to consider drugs that may affect autonomic function. There are a large number which affect various systems, but some of the more important ones include:

- Tricylic antidepressants
- Beta blockers
- Calcium channel blockers

All of these factors make it difficult to simply test patients in the ward on our own initiative. Testing needs to be done in a more formal manner and with adequate standardisation in order to avoid inaccuracy.

5. Cardiovascular Autonomic Neuropathy (CAN)

CAN is one of the most clinically significant complications of diabetes mellitus, but one of the least frequently diagnosed.[6] It refers to damage to the autonomic nerve fibers that innervate the heart and blood vessels, resulting in abnormalities in heart rate control and vascular dynamics. It is associated with higher cardiovascular morbidity and mortality and poor quality of life in diabetic individuals. The following clinical manifestations may be associated with CAN: resting tachycardia, severe orthostatic hypotension, syncope, exercise intolerance, perioperative instability, asymptomatic myocardial ischemia and infarction, left ventricular diastolic and systolic dysfunction, and increased risk of renal diseases, chronic renal failure, stroke, and sudden cardiac death.[6] CAN is present in approximately 25% of the patients with type-1 diabetes mellitus and in 34% of those with type-2 diabetes mellitus. The prevalence of CAN progressively increases in a direct proportion to age, duration of DM and poor glycaemic control.[5]

The Natural History of CAN

Most of our knowledge on this subject is derived from the diabetic population, and caution needs to be used in applying this to other causes of CAN. Some of the features in diabetics are[5]:

- It can often be detected at the time of diagnosis.
- Neither age nor type of diabetes are limiting factors in its emergence; it has been found both in young people with newly diagnosed type 1 diabetes and in older people newly diagnosed with type 2 diabetes.
- Poor glycaemic control plays a central role in development and progression.
- Intensive therapy can slow the progression and delay the appearance of abnormal autonomic function tests.
- Subclinical autonomic neuropathy can be detected early using autonomic function tests.
- Autonomic features that are associated with sympathetic nervous system dysfunction (eg, orthostatic hypotension) are relatively late complications of diabetes.
- There is an association between CAN and diabetic nephropathy that contributes to high mortality rates.
- Type 1 and type 2 diabetes may have different progression paths.
- The relationship between autonomic damage and the duration of diabetes is not clear, although numerous studies support an association.
- Prevalence and mortality rates may be higher among individuals with type 2 diabetes, possibly because of the longer duration of glycaemic abnormalities before diagnosis.

6. Clinical Manifestations and Consequences of CAN

Resting tachycardia

Heart rate control is relatively complex, but is generally governed by a parasympathetic mechanism. Whereas abnormalities in HRV are early findings of CAN, resting tachycardia and a fixed heart rate are characteristic late findings in diabetic patients with vagal impairment. Resting heart rates of 90 to 100 bpm and occasional heart rate increments up to 130 bpm occur. The highest resting heart rates have been found in patients with parasympathetic damage, occurring earlier in the course of CAN than sympathetic nerve function; in those with evidence for combined vagal and sympathetic involvement, the rate returns toward normal but remains elevated. A fixed heart rate that is unresponsive to moderate exercise, stress, or sleep indicates almost complete cardiac denervation. Thus, heart rate may not provide a reliable diagnostic criterion of CAN in the absence of other causes unless it is increased by more than 100 bpm.[5]

Heart Rate Variability

Physiologic systems constantly change over time and respond to stimuli. In young, healthy subjects they exhibit marked physiologic signal variability and complexity, whereas aging or diseased systems show a loss of variability, decreased complexity, and increased regularity.[7] It has been hypothesized that decreased variability of heart rate dynamics may occur over a broad range of critical illness and injury and may be inversely correlated with disease severity and outcome in both adult and pediatric patients. Stein et al.[8] examined the value of HRV measurements in predicting clinical course in patients undergoing abdominal aortic surgery. Decreased HRV was shown to be an independent predictor of prolonged hospitalization (>7 d) after surgery.

Filipovic et al. showed that an altered low-to-high frequency power ratio before induction of anaesthesia was a strong and independent predictor of both all-cause mortality and major cardiac events within 2 years in patients with documented or suspected coronary artery disease undergoing major noncardiac surgery. This result confirmed their previous findings about the prognostic value of heart rate variability for 1-year mortality in a similar population and is consistent with findings in the general population and in non-surgical patients with acute coronary artery disease and congestive heart failure.[9]

Several studies with cardiac patients suggest that decreased HRV as well as baroreceptor dysfunction are more powerful predictors for cardiovascular mortality than established clinical predictors, such as left ventricular ejection fraction and ventricular premature complexes.[10]

HRV is also altered in a number of neurological conditions. It appears that HRV may reflect the functional state of the central nervous system in the setting of severe brain damage, and has been correlated with severity, survival and neurological outcome.[7] HRV has also been suggested as a complementary tool in the diagnosis of brainstem death.

Cardiac autonomic dysfunction is associated with mortality in patients with end-stage renal disease.[11]

It has been hypothesized that septic shock resulted in an uncoupling of organ system interconnectivity, and that the uncoupling phenomenon could be quantified as a loss in HRV.[12] Studies in paediatric critical care, as well as in healthy volunteers administered endotoxin (!) have supported this hypothesis.[13] These results correlate well with early study results showing evidence of 'decomplexification' in experimental models of sepsis. This is dealt with in greater detail later on in this review.

Exercise Intolerance

Autonomic dysfunction impairs exercise tolerance, reduces response in heart rate and blood pressure, and blunts increases in cardiac output in response to exercise. This is important if one considers that the perioperative phase is in many ways analogous to exercise.

Intraoperative and Perioperative Cardiovascular Instability

Perioperative cardiovascular morbidity and mortality are increased 2- to 3-fold in patients with diabetes. Compared with nondiabetic subjects, diabetic patients undergoing general anaesthesia may experience a greater degree of decline in heart rate and BP during induction of anesthesia and less of an increase after tracheal intubation and extubation. Vasopressor support is needed more often in diabetic individuals with CAN than in those without CAN.[14] Recent studies have shown that high LF/HF ratios can identify patients at risk of developing severe hypotension during spinal anesthesia for caesarean delivery or for prostate gland procedures in ASA I or II patients.[15,16] The normal autonomic responses of vasoconstriction and tachycardia do not completely compensate for the vasodilating effects of anesthesia.

In addition, there is an association between CAN and more severe intraoperative hypothermia[17] that results in decreased drug metabolism and impaired wound healing. Reduced hypoxic-induced ventilatory drive may also occur.

Orthostatic Hypotension

Orthostatic hypotension is defined as a fall in BP (>30 mm Hg systolic or >10 mm Hg diastolic BP) in response to a postural change from supine to standing. A change from lying to standing normally results in activation of a baroreceptor-initiated, centrally mediated sympathetic reflex, resulting in an increase in peripheral vascular resistance and cardiac acceleration. In patients with diabetes, orthostatic hypotension is usually attributable to damage to the efferent sympathetic vasomotor fibers, particularly in the splanchnic vasculature. Patients with orthostatic hypotension may respond poorly to changes in position in theatre.

Orthostatic Tachycardia and Bradycardia Syndromes

The hallmark of these abnormalities is the absence of a fall in BP with standing, but a tachycardia or bradycardia with the change in posture. The pathogenesis of these conditions has not been fully elucidated.

Silent Myocardial Ischemia/Cardiac Denervation Syndrome

Reduced appreciation for ischemic pain can impair timely recognition of myocardial ischemia or infarction, thereby delaying appropriate therapy. The mechanisms of painless myocardial ischaemia are, however, complex and not fully understood. Altered pain thresholds, sub-threshold ischemia not sufficient to induce pain, and dysfunction of the afferent cardiac autonomic nerve fibers have all been suggested as possible mechanisms. Patients with CAN warrant more careful attention, and cardiovascular autonomic function testing may be an important component in the risk assessment of diabetic patients with coronary artery disease.

Preoperative QTc dispersion is prolonged in patients who subsequently go on to develop postoperative silent myocardial ischemia, early cardiac morbidity, and all cause early adverse cardiovascular events. Despite this, it performs poorly as a predictive test and cannot be currently recommended as a screening tool for identifying those patients at risk for cardiovascular morbidity and mortality who would warrant more thorough cardiac investigation.[18]

Increased Risk of Mortality

A number of studies have suggested an increased relative risk of mortality in patients with CAN, although the underlying mechanism of death is not

always clear.[5] Some have shown a 2-3-fold increased risk of CAN in diabetic patients showing a prolonged QT interval, leading to speculation that CAN might also predispose to malignant ventricular arrhythmias and to sudden death from cardiac arrest caused by torsades de pointes, as in long QT syndrome. It should be remembered that It is difficult to determine the independent effects of CAN on mortality because of the coexistence of cardiovascular disease. Mortality rates after an MI are higher for diabetic compared with non-diabetic patients. A simple bedside test that measured 1-minute HRV during deep breathing was a good predictor of all-cause mortality for 185 patients (17.8% with diabetes) after a first MI.[19]

Heart Failure

There is abundant evidence linking sympathetic nervous system activation to outcomes in patients with heart failure. Parasympathetic activation has complex cardiovascular effects that are beginning to be recognized in heart failure. Recent studies have shown a close relationship between cardiac dysfunction and autonomic dysregulation during development of heart failure.[20] Evidence is also emerging that some of the existing treatment for heart failure may exert its effects through a favourable effect on parasympathetic tone. ACE-inhibitors may have a muscarinic effect. Statins may alter heart rate variability and heart rate in a beneficial fashion.

Autonomic Cardiopathy

CAN may be associated with abnormalities in LV systolic and particularly diastolic function in the absence of cardiac disease in diabetic patients. Echocardiographic studies have shown a significant correlation of the severity of CAN with reduced peak diastolic filling rate and with an augmented atrial contribution to diastolic filling as assessed by Doppler echocardiography.

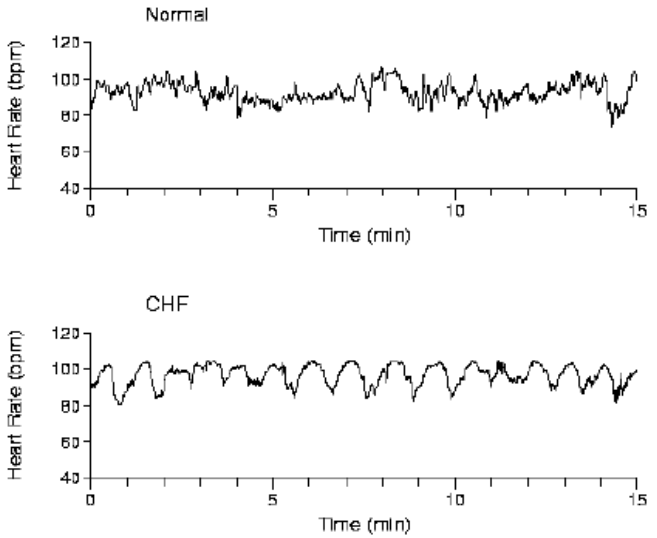
Induction and Intubation responses

Increased cardiovascular instability during anaesthesia and abnormal cardiovascular responses to intubation and induction of anaesthesia have been described in patients with diabetic autonomic neuropathy.[21] Interestingly, in many of the studies where intubation response in patients with documented autonomic neuropathy is being evaluated, the method of induction is fentanyl (2ug/kg), Thiopentone and Vecuronium. Many specifically state that the patients were intubated 180 second after the administration of vecuronium. This is in sharp contrast to teaching about the necessity of a rapid sequence induction in patients with autonomic neuropathy.

7. Variability: a bit more depth

According to classical concepts of physiologic control, healthy systems are self-regulated to reduce variability and maintain physiologic constancy. Contrary to the predictions of homeostasis, however, the output of a wide variety of systems, such as the normal human heartbeat, fluctuates in a complex manner, even under resting conditions.[22] A hallmark of physiologic systems is their extraordinary complexity. A defining feature of healthy function is adaptability, the capacity to respond to unpredictable stimuli and stresses. New techniques of analysis are providing remarkable insights into the way physiological systems function. In particular, there is growing interest in nonlinear dynamics, often referred to as chaos theory.

The heart rate plots of two different patients are shown below. They have nearly identical means and variances, suggesting no clinically relevant differences. Yet, visual inspection indicates that the two sequences of data display a markedly different organisation.[23] Classical teachings about homeostasis often assume that ‘noise’ should be dampened, but it is the ‘noisy’ signal depicted below that represents health.



This loss of nonlinear variability may signal aging, or the onset of disease. In critical care medicine, it has been observed that the loss of fine variability may herald the onset of multiple organ dysfunction syndrome, and that its return may signal the return to health. This is sometimes also referred to as

uncoupling, or *de-complexification*. This uncoupling of autonomic regulation has also been witnessed in healthy athletes, and investigators speculate that it may rather be a failure of *re-coupling* that is being observed in the critically ill patient. Regardless of mechanism, this information is being used to diagnose and prognosticate as well as to inspire new forms of therapy. The new therapies, many of them theoretical, have exciting names like chaos control and chaos anti-control[24] – the principle being that external stimuli can be used alter physiological dynamics and hopefully improve patient outcome. In essence, the problem reflects a lack of reserve, and a decreased ability to adapt or to compensate, and these are issues that anaesthetists need to be mindful of.

8. Gastroparesis: RSI?

One of the principle concerns for anaesthetists when considering patients with autonomic neuropathy for surgery is the degree of gastroparesis. Discussions often centre around the need for a rapid sequence induction to prevent aspiration. In answering this question, one firsts needs to consider the manner in which the diagnosis of autonomic neuropathy was made. Does CAN provide any information about the integrity of the enteric nervous system? It should be remembered that the enteric nervous system is a hugely complicated network involving many splanchnic and central reflexes mediated by a large number of peptides, as well as neurotransmitters such as acetylcholine. Thus it does not necessarily follow that the existence of CAN will mean that gastroparesis is present.

In diabetic patients, gastrointestinal symptoms are relatively common, but may be more likely due to other factors than to autonomic dysfunction.[25] Oesophageal dysfunction results at least in part from vagal neuropathy. Approximately 50% of patients with longstanding diabetes have delayed gastric emptying.[26] Gastric emptying is largely dependant on vagus nerve function, which can be severely disrupted in diabetics. Gastroparesis in diabetics is usually clinically silent, and the presence of symptoms should prompt investigation for other causes.
Gastric emptying in HIV positive patients is often delayed, but this may not necessarily correlate with autonomic dysfunction, and is multifactorial in nature.[27]

Even if we assume that there is some degree of gastroparesis present, should this lead to a rapid sequence induction in fasted patients? To assist in answering this question, it is instructive to look back at Mendelson's original paper on the subject.

Mendelson and Aspiration

Mendelson's classic paper on aspiration during obstetric anaesthesia was published in 1946.[28] He became interested in aspiration after a personal experience following a 'night of relative intemperance'. He examined 44016 cases of women who underwent general anaesthesia for caesarean section. They were anaesthetised with nitrous oxide and ether administered by a face mask. There were 66 cases of aspiration (0.15%), 2 of which subsequently died (0.005%). This is a population group with a classically high risk of aspiration, having increased residual gastric volumes and delayed gastric emptying during labour, as well as a number of physiological and anatomical changes which predispose to reflux and regurgitation.

Rapid Sequence Induction?

So what should we do in fasted patients with documented autonomic neuropathy? We know that the risk of aspiration is low even in a high risk group. It is apparent that many researchers are choosing cardiovascular stability over RSI in their studies. In particular in diabetic patients, autonomic neuropathy is likely to be accompanied by macro- and micro-vascular pathology – often resulting in coronary artery disease. This applies to many of the other diseases associated with autonomic neuropathy as well, such as renal failure. There is little evidence to provide clarity on the subject. It does seem reasonable, however, that in the absence of other risk factors for aspiration, an RSI is not necessarily essential, particularly if other co-morbidity suggests that haemodynamic stability is particularly important.

9. HIV Infection

Autonomic dysfunction is known to occur in patients with HIV.[29] Although it seems to be more frequent and severe in patients with AIDS, several reports have suggested that HIV-seropositive patients and those in the early stages of infection also show evidence of dysautonomia. The severity of autonomic dysfunction seems to show a continuum from the early to later stages of HIV infection. In addition to direct viral effects and interactions between virus and host, toxins, drugs, vitamin deficiency and malnutrition could have roles in the manifestations of this syndrome in the later stages of illness. Autonomic testing shows abnormalities of sympathetic and parasympathetic systems.[3]

There are very few studies which look at the prevalence of autonomic neuropathy in African patients, and only one that specifically examine the prevalence in sub-Saharan Africans. Compostella et al recently looked at CAN in HIV-positive patients in Mozambique. In a well-designed study, they

found the prevalence to be 27-30%, but looked at just 30 patients. Its prevalence in the literature ranges from 5% to 77%, depending on the population studied and on the definition of autonomic dysfunction used.[29]

Given the impact of CAN in other settings, it may well prove that CAN in the HIV patients confers significant additional risk. Currently approximately a third of people in Kwazulu-Natal are living with HIV, and it is likely that more than a third of our surgery is performed on this population, given their predilection for a wide variety of illnesses. The impact of CAN in this group on morbidity and mortality is unknown, but is likely to be significant.

10. Conclusion

Autonomic neuropathy is thus a disorder that involves every organ system and has a wide number of clinical consequences. Testing, while reasonably simple, is time consuming, requires specialised equipment and may be difficult to obtain. It has been shown to be predictive of significant cardiovascular risk, both in the intraoperative and postoperative phases and in addition, other complications relating to gastroparesis and temperature management may occur. New techniques of analysis are allowing a greater insight into aging and many disease processes, and it is possible that in the future, measures of autonomic function may become routine. Anaesthetists need to be aware of the issues surrounding autonomic neuropathy in order to anticipate and possibly prevent perioperative complications.

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