Why Physiology Is Critical to the Practice of Medicine

A 40-year Personal Perspective

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KEYWORDS

• Diagnosis • Clinical reasoning • Intuition • Physical examination • Hyperventilation syndrome

KEY POINTS

- Accuracy in diagnosis trumps all other elements in clinical decision making. If diagnosis is inaccurate, management is likely to prove futile if not dangerous.
- The ability to apprehend clues that other clinicians miss depends on mental set (the prepared mind). Knowledge of physiology provides a periscope for identifying abnormalities beneath the skin responsible for clinical manifestations on the surface.
- Expert diagnosticians suspect disorders based on pattern recognition and automatic retrieval of knowledge stored in memory. Experts make decisions based on intuition rather than conscious analytical reasoning. Intuition is the fruit of years of book learning, analytical reasoning, and clinical practice.
- When making routine decisions, physicians typically do not cite mechanistic understanding, but they call on physiologic principles when confronted with challenging cases.
- A superior diagnostician looks at the same findings other clinicians see but thinks of causes that others have not imagined. Solving clinical mysteries depends on a clinician's power of imagination, not the capacity to recite an algorithm or apply a protocol.

My thoughts on the importance of physiology in clinical decision making represent a personal viewpoint based on more than 40 years of evaluating patients in outpatient clinics, hospital wards, and intensive care units (ICUs) while concurrently undertaking mechanistic physiologic research in patients and healthy subjects. The review is far from exhaustive, and I focus on items that stump present-day trainees and would have been far less challenging to residents in the early 1980s when I was hired as an assistant professor. The essay can be looked on as an *apologia pro vita sua*.

PROLOGUE

The 3 most important things in clinical medicine are diagnosis, diagnosis, diagnosis. As with a syllogism in logic, when the major premise is wrong, the elegance of ensuing deductions is irrelevant. The pivotal importance of diagnosis should be evident especially to pulmonologists. Despite deep understanding of the basic biology (chemistry, molecular biology) of venous thromboembolism and a slew of sophisticated diagnostic techniques, pulmonary embolism is the most frequently missed fatal diagnosis.

Conflict of Interest: M.J. Tobin receives royalties for 2 books on critical care published by McGraw-Hill, Inc, New York.

Dedication: This essay is dedicated to Professor Muiris X. FitzGerald, MD, University College Dublin, Ireland. M.J. Tobin served as M.X.F.'s registrar 1979-1980, and his approach to patient assessment and clinical decision making has served as the author's template throughout his career.

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Clin Chest Med 40 (2019) 243–257
https://doi.org/10.1016/j.ccm.2019.02.012

Fatal pulmonary embolism is found in more than 10% of autopsies. In 4 autopsy series, the diagnosis was missed in 55% to 70% of patients,[1–4] and in more than 80% of patients who had chronic obstructive pulmonary disease (COPD).[4] Mortality was 4 to 6 times higher in patients in whom the diagnosis was missed.[4] When promptly diagnosed and treated, pulmonary embolism rarely kills.

If formulation (and dissemination) of clinical-practice guidelines was the solution to a perplexing problem, fewer than 5% of pulmonary emboli should be missed. No other topic has attracted greater attention from the founders of evidence-based medicine (EBM), and it has been the subject of more guidelines than any other topic: the American College of Chest Physicians has published 10 editions of voluminous guidelines since 1986.

Elegant algorithms for the management of venous thromboembolism are of no value to patients if their doctor never suspects the diagnosis. This is the crucial stumbling block. For decades, physicians have been admonished to keep a high index of suspicion. Scolding is clearly not working. The fundamental problem is that symptoms of venous thromboembolism are far from unique, and many patients have atypical presentations. Most importantly, physiologic features are not consistent and are not readily detected at the bedside.

Every clinical encounter involves a search for clues that lead to a correct diagnosis. The task is to separate wheat from chaff, to spot pertinent clues and eschew distracting siren calls. Being able to ground one's thinking in physiology provides a roadmap that helps travelers reach the right destination. Pulmonary embolism presents a salutary example of what happens when clinical suspicion is not aroused by physiologic findings. It is not simply a case of being unable to navigate the road to the desired terminus; without a diagnostic trigger, physicians are not able to find the entry point, the feeder road, to get on to the correct highway.

> The search for the correct diagnosis remains the most crucial endeavor to assure the best possible care to patients.

MENTAL SET

When I stand at the bedside of a patient with a glaringly obvious physical sign, residents commonly cannot identify it. "To see what is in front of one's nose," Orwell averred, "needs a constant struggle."

Anatomy teaches that we see with the retina and visual cortex. This is true nominally, but incomplete. Immanuel Kant argued persuasively that the mind does not passively receive sense data.[5] Instead, it actively digests and structures what is being perceived. All cognition is channeled through the mind's categories, involving "a priori" forms of time and space. We look at what is in front of our eyes, but we discern with what is behind them, particularly through the prism of memory. "We see," mused Goethe, "only what we know."

In the *American Journal of Respiratory and Critical Care Medicine* series "How it *really* happened,"[6] most authors said their major discovery arose through serendipity. Many demurred that they did not discover anything, they were simply lucky. However, as Pasteur shrewdly observed, "Chance favors *only* the prepared mind."[7] The person making the serendipitous connection is already primed to appreciate its significance. An accidental event acquires significance only when it catches the attention of someone capable of putting it into scientific context. As with discovery in science, the same concepts apply to spotting clues in patients with obscure presentations.

The reason one clinician apprehends clues that other physicians miss depends on mental set: the set of beliefs that determines what a person perceives (the prepared mind).[8] Physiologic mechanisms provide a periscope for identifying what is wrong with a patient: pinpointing abnormalities in the machinery beneath the skin that are responsible for signs on the surface. A mental set forged through detailed knowledge of physiologic mechanisms selects and shapes what it is a clinician notices. Without a mental set, the obvious becomes invisible. The clinician is distracted and blinded by a blizzard of other possible diagnoses.

The word "physiology" has the same etymologic root as "physics": the study of things of nature. Many look on physiology as the application of physics to living organisms.[9] Ernest Rutherford, father of nuclear physics, quipped: "All science is either physics or stamp collecting," implying that soft activities such as surveys and categorization represent uninspired drudgework.

> A physiological mindset influences what a physician perceives and enables a physician to distinguish critically important processes from distracting findings.

WORK OF BREATHING

The most difficult cognitive challenge for intensivists is deciding whether (or not) patients can be managed without recourse to an endotracheal

tube. This dilemma arises at the point of placing a patient on the ventilator,[10] and it recurs at the point of deciding whether the ventilator can be discontinued.[11]

The dominant reason to institute mechanical ventilation is increased work of breathing, and it is also the principal cause of weaning failure.[12] Given the supreme importance of respiratory work, one might expect that inserting esophageal-balloon catheters would be routine in the ICU. It is not. This is not because catheter insertion is technically challenging or the discomfort it produces (doctors have little hesitancy in performing far more painful procedures). Instead, interpretation of the tracings is formidable.[13] Precise calculation of intrinsic positive end-expiratory pressure is taxing in patients contracting their expiratory muscles. Lining up esophageal-pressure tracings against the chest-wall recoil line to construct a Campbell diagram requires nuanced judgment. These skills are not found in the quiver of most intensivists. Instead of attempting such calculations, clinicians can profit more by becoming skilled in performing a sequence of carefully performed steps on physical examination.

In judging whether work of breathing is increased, I rely on palpation of the sternomastoid muscle more than any other sign. This emphasis is not widely accepted. There is no mention of sternomastoid activity in the chapter on physical examination by Dr Murray in *Murray and Nadel's Textbook of Respiratory Medicine*; indeed, palpation is explicitly judged "the least productive" part of physical examination of the respiratory system and "is not routinely performed by many physicians."[14,15]

Patients with COPD rarely contract their sternomastoids when in a stable state. Insertion of electromyography (EMG) needle electrodes into the sternomastoids of 40 patients with severe COPD (forced expired volume in 1 second [FEV_1], 0.69 ± 0.18 L; 17 having hypercapnia) revealed activity in only 4 (10%).[16] Conversely, sternomastoid contraction is common in patients experiencing acute respiratory failure. In a study of patients being weaned from mechanical ventilation, my colleagues and I recorded (EMG wire) activity of the sternomastoid in all of 11 weaning failure patients but in only 3 of 8 weaning success patients (the latter activity was modest).[17] Sternomastoid activity became evident within the first minute of the T-tube trial in 8 failure patients but only 1 success patient, signifying that it is a sensitive harbinger of respiratory deterioration.

McFadden and colleagues[18] observed visible sternomastoid contraction in 59% of patients experiencing acute asthma attacks. It was the only sign (or symptom) that identified severe pulmonary impairment (dyspnea and wheezing were much less reliable). In patients with sternomastoid activity, FEV_1 was less than half that in patients without contraction (0.65 ± 0.26 vs 1.34 ± 0.56 L).

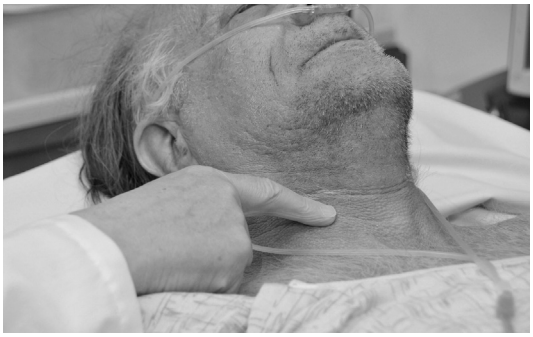

Fig. 1. Placement of the index finger (gently, barely touching) on the body of the sternomastoid muscle to judge the presence of phasic contraction and qualitatively determine its magnitude (mild, moderate, marked).

In the nineteenth century, French physicians considered sternomastoid contraction to be of such importance they dignified it the respiratory pulse.[19]

When gauging sternomastoid activity, I do not rely on inspection. Patients with minimal adipose tissue exhibit prominence of the sternomastoids without increased contractile activity, "sculpting," akin to the jutting sternomastoid in Michelangelo's *David*. Assessment requires placing the index finger, gently, barely touching, on the body of the sternomastoid, the finger pad mimicking an EMG electrode (Fig. 1). The examiner needs to focus solely on phasic muscle activity; tonic activity is used for posture and has no respiratory significance.

The second sign in judging work of breathing is tracheal tug, downward motion of the trachea with each inspiratory effort. Again, this sign should not be ascertained by inspection. Instead, the tip of the index finger should be placed on the thyroid cartilage (Fig. 2). Healthy subjects exhibit no

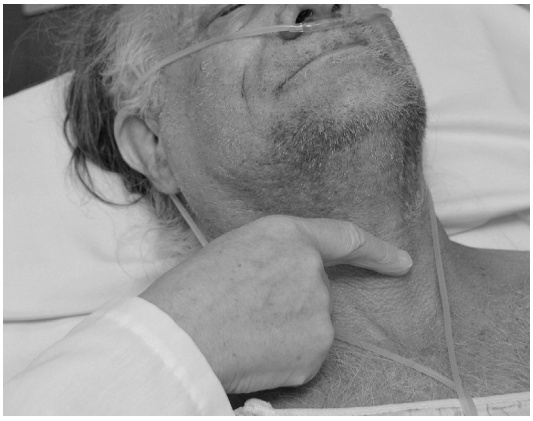

Fig. 2. Placement of the index finger on the thyroid cartilage to judge the presence of tracheal tug and qualitatively determine its magnitude (mild, moderate, marked).

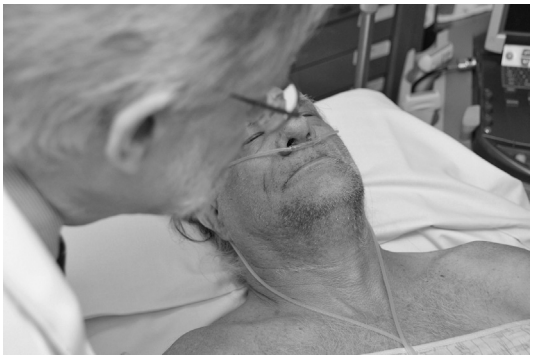

Fig. 3. Inspection of the suprasternal fossa to judge the presence of recession with each inspiration and qualitatively determine its magnitude (mild, moderate, marked).

tracheal tug. The degree of tug varies among patients, but its presence is always significant.[20] Because the respiratory muscles are not directly attached to the trachea, tugging is the result of the diaphragm pulling the entire mediastinum downwards with each inspiratory effort (like Quasimodo pulling the bell in Notre Dame) and, thus, signifying a marked increase in respiratory work.

The third sign involves careful inspection (not palpation) of the suprasternal fossa (**Fig. 3**). As swings in intrapleural pressure become more negative, the suprasternal fossa is visibly excavated with each inspiration. My colleagues and I demonstrated that recession of the suprasternal fossa, quantified using surface inductive plethysmography (a loop of wire fixed to the skin and excited by an oscillator circuit), was directly proportional to swings in esophageal pressure.[21] Supplementary evidence of increased pleural-pressure swings is obtained by inspecting the ipsilateral and contralateral hemithorax for intercostal recession[22] (**Fig. 4**).

Last, I check for diaphoresis, reflecting autonomic activation consequent to physiologic stress. I slowly move my index finger across the patient's forehead and then inspect the finger pad for moisture (this is more reliable than simply inspecting the brow for sweat) (**Fig. 5**).

With these 5 signs (sternomastoid contraction, tracheal tug, suprasternal-fossa recession, intercostal recession, diaphoresis), I form a judgment of whether work of breathing is increased or not and to what extent. There is no yardstick a physician can rely on for this assessment; discernment depends on having made the determination previously in thousands of patients (and storing them in the temporal lobe). The presence of signs of increased work is not necessarily bad (and absence is not necessarily good). If a patient has significant respiratory acidosis (or hypoxemia) and no signs of elevated respiratory work, the combination signifies respiratory depression. For clinicians harking after simple black-and-white rules, they do not exist and are never likely to exist. The signs need to be placed in overall context. There is no substitute for wisdom and experience when taking care of seriously ill patients.

Investigators have attempted to quantify physical signs and reported poor correlations with pulmonary function.[23,24] Such studies exemplify the McNamara fallacy (in logic): reaching conclusions based solely on quantitative data, discounting qualitative factors. Physical examination is a craft learned through apprenticeship. The essence of physical examination is its tacit coefficient; the explicit measurable components may be the least relevant.[10] As Georges Braque cautioned: "The only valid thing in art is that which cannot be explained."

The measurement I crave most in deciding whether to institute mechanical ventilation is

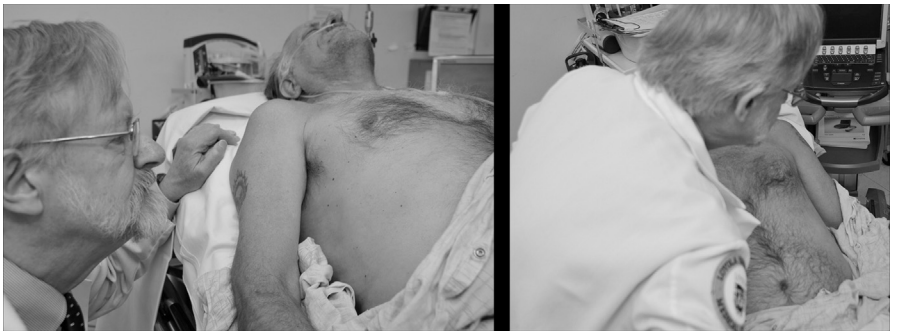

Fig. 4. (*Left*) Inspecting the ipsilateral intercostal spaces to judge for the presence of inspiratory recession. (*Right*) Sometimes recession is easier to detect upon inspecting the profile of the contralateral hemithorax. When inspecting each hemithorax, the clinician should also check for Hoover sign, a paradoxic inward motion of the lower rib cage during inspiration, signifying a flattened and disadvantaged diaphragm. (See Ref.[22])

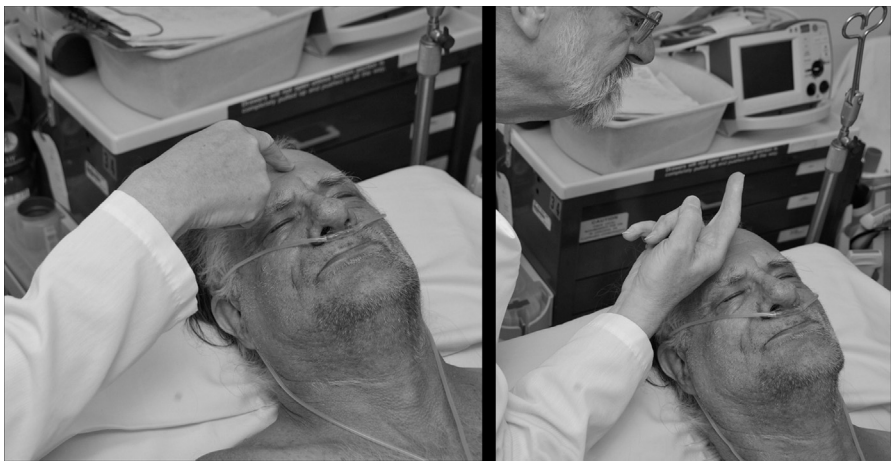

Fig. 5. To judge for the presence of diaphoresis, slowly move the index finger across the patient's brow and then inspect the finger pad for moisture.

spontaneous tidal volume (V_T).[25] This value cannot be gleaned from inspection, palpation, or auscultation.[26] In intubated patients, spontaneous V_T is visible on the ventilator screen, furnished by the pneumotachograph in the circuit. On switching ventilator assistance to zero, patients make little respiratory effort for 30 to 90 seconds because their respiratory centers are depressed consequent to relative hypocapnia and persisting mechanoreceptor stimulation. V_T increases gradually until it reaches a steady state. Eyeballing breath-by-breath values on the ventilator screen, the first 2 digits of the V_T should be higher than the respiratory frequency (f) (eg, *29*0 and *25*); if lower, this signifies a frequency/tidal volume ratio (f/V_T) greater than 100.[27] Patients commonly perform better than the charted f/V_T simply because respiratory therapists obtain measurements long before a patient has attained a steady state. (Further discussion on this topic is provided in The Control of Breathing during Mechanical Ventilation).

In nonintubated patients, it is virtually impossible to get reliable measurements of V_T. It has long been recognized that employment of instrumentation requiring use of a mouthpiece alters breathing pattern.[28] (The Heisenberg principle is an omnipresent cofounder when evaluating respiration in patients.) Clinicians rely instead on respiratory rate. Although rate is a cardinal vital sign, most physicians do not know its normal value, imagining 20 breaths/min to signify tachypnea. That threshold has been enshrined in SIRS criteria of sepsis guidelines.[29] The average respiratory rate in health is 17 breaths/min with a normal range of 12 to 22 breaths/min.[30]

Respiratory rate needs to be placed in the context of a patient's physiologic characteristics.[25] Patients with stiff lungs (low compliance) achieve a lower oxygen cost of breathing by breathing fast and shallow.[31] With elevated resistance, work is minimized by slow deep breathing. Rather than managing patients according to a protocol, each patient's unique physiologic characteristics need to be taken into account when making decisions regarding mechanical ventilation.

Recordings of peak airway pressure, plateau pressure, inspiratory flow, and delivered volume on a ventilator over 2 to 3 minutes provides greater insight into a patient's respiratory status than can be gleaned from an hour in a pulmonary function laboratory. Meaningful interpretation of the tracings (and their nuances) requires substantial grounding in physiology. I will not dwell on these recordings because I have discussed them too many times in the past: at length[12,32] and succinctly.[33–35]

> To reach a clinical judgment as to whether work of breathing is increased or not, the physician should palpate the sternomastoid muscles, palpate the cricoid cartilage to assess for tracheal tug, inspect the suprasternal fossa and intercostal spaces, and check for diaphoresis.

GAS EXCHANGE

Pulse oximetry has become the most widely used instrumentation after the sphygmomanometer. Although blood pressure is easily interpreted (given its linearity), the sigmoid shape of the O_2-disassociation curve can render pulse-oximeter interpretation similar to hieroglyphics. This is compounded by O_2 therapy. One of the commonest

orders is "Titrate supplemental oxygen to keep O_2 saturation above 92%." The order is viewed so benignly that it is included in preprinted admission orders.

When properly used, pulse oximetry is invaluable in alerting staff of a significant deterioration in a patient's condition.[36] An unexpected decrease in oximetry to 88% (equivalent to Pa_{O_2} 55 mm Hg) alerts staff of the need to determine the cause of a patient's deterioration. Because of the flatness of the upper O_2-dissociation curve, a patient with a saturation of 95% (equivalent to Pa_{O_2} 75 mm Hg) while receiving oxygen therapy may incur considerable deterioration in respiratory function yet exhibit minimal decrease in oximetry.[37]

When supplemental oxygen is administered, tissue oxygenation is optimally achieved at an oxygen saturation of 90%.[38] To allow for biological fluctuation, it is reasonable to aim for an oximetry target of 92%. Physicians should always specify the upper boundary of the target: rarely is it advisable to accept oximetry higher than 94% (equivalent to Pa_{O_2} 70 mm Hg). A saturation of 97% to 99% (often seen with supplemental oxygen) is consistent with a Pa_{O_2} anywhere between 90 and 500 mm Hg.[37] A 92% target minimizes the risk of oxygen complications (O_2-induced hypercapnia) while enabling oximetry to warn of significant deterioration in respiratory function (see also Physiologic Effects of O_2 Supplementation during Exercise in Chronic Obstructive Pulmonary Disease).

Using Pa_{O_2} in assessment of gas exchange requires knowledge of fractional inspired oxygen concentration. This is instantly available in intubated patients, but unknowable in nonintubated patients receiving supplemental O_2. Nostrums such as 2 L/min by nasal cannula is equivalent to 24% inspired O_2 concentration are delusive because of variable entrainment of air between patients. With a nasal cannula set at 2 L/min, inspired oxygen concentration ranges anywhere between 24% and 35%.[39]

Calculation of alveolar-to-arterial O_2 gradient can be invaluable in decoding veiled presentations.[32] Proving rapid-onset pulmonary edema can be challenging in ventilated patients. Pulmonary infiltrates commonly preexist, making it impossible to see superimposition of new edema. Hearing crackles is confounded by ventilator noise. I have taken care of patients who repeatedly failed T-tube trials for no obvious reason. The sole consistent finding was decrease in Pa_{O_2} associated with an increase in alveolar-arterial oxygen gradient; the finding of critical obstruction at coronary angiography, followed by stenting, led to rapid weaning and extubation.

Hypoxemia poses greater danger to patients than does hypercapnia. Pa_{CO_2}, however, provides deeper insight into what is going wrong with a patient than does Pa_{O_2}.

The respiratory controllers (respiratory centers, neurons and muscles that produce alveolar ventilation) maintain a stable Pa_{CO_2} across wide fluctuations in CO_2 production (further discussion on this topic is provided in Update on Chemoreception: Influence on Cardiorespiratory Regulation and Patho-Physiology).[12] CO_2 production can vary 10-fold during exercise, yet Pa_{CO_2} remains virtually unchanged. This stability is achieved by exquisite sensitivity of the chemoreceptor system, typically expressed as change in minute ventilation during CO_2 rebreathing. The normal range is 0.5 to 8.0 L/min/mm Hg (1.5–5.0 in 80% of subjects).[12] Thus, an increase in Pa_{CO_2} of 3 mm Hg should cause minute ventilation to increase by 10 L per minute (or double). Failure to observe such an increase signifies significant respiratory impairment, because the patient either will not breathe (secondary to significant respiratory center depression) or cannot breathe (consequent to mechanical load or muscle weakness).

I was recently consulted about a young woman admitted to a medical ward with acute pancreatitis, for which she was receiving morphine at frequent intervals. Five days after admission, the patient experienced a cardiac arrest that resulted in irreversible hypoxic brain injury. An arterial gas, obtained 2 days before the arrest, revealed pH 7.29, Pa_{CO_2} 44 mm Hg, Pa_{O_2} 76 mm Hg, bicarbonate 18 mEq/L, and oxygen saturation 93%. In the progress notes, the resident noted "Patient saturating well on 2 L of oxygen with nasal cannula. P_{CO_2} levels within normal limits. Continue present management."

It is true that the patient's Pa_{CO_2} was within the normal range. However, the recorded Pa_{CO_2} signaled considerable compromise. The marked metabolic acidosis was producing substantial stimulation of the central chemoreceptors.[12] Consequently, Pa_{CO_2} should have been much lower than 44 mm Hg, more like 31 to 35 mm Hg. The Pa_{CO_2} of 44 mm Hg signified considerable respiratory depression. When staff further increased the dosage of morphine, they markedly increased the patient's susceptibility to further respiratory depression, hypoventilation, and hypoxemia.

At the other extreme, high Pa_{CO_2} is commonly accepted as sufficient to explain change in mental status. Readers can still profit by reading

the 1956 article by Sieker and Hickam,[40] which provides details on 25 patients exhibiting varying degrees of hypercapnia and mental disturbance. If $Paco_2$ was less than 90 mm Hg (and pH >7.25), patients exhibited no change in mental state or only minimal drowsiness and intermittent confusion. Conversely, a semicomatose or comatose state was observed in every instance when $Paco_2$ was greater than 130 mm Hg (and pH <7.14). For $Paco_2$ between 90 and 130 mm Hg (and pH between 7.25 and 7.14), patients varied between consciousness and deep coma.

In patients proving difficult to be weaned from mechanical ventilation, it is profitable to relate $Paco_2$ to minute ventilation. If $Paco_2$ exceeds 45 mm Hg and minute ventilation exceeds 10 L/min, the pairing points to elevated dead space. The higher the minute ventilation (and higher $Paco_2$), the greater the dead space. Such patients will have great difficulty in making progress in weaning until improvements in lung disease lead to a decrease in dead space. There is rarely a unique therapy that dependably lowers dead space, and tincture of time is the safest prescription.

Interpretation of arterial blood gases is challenging enough without having ratiocination subverted by inaccuracies in venous blood gases.[41]

Evaluation of gas exchange involves relating arterial oxygen saturation to the shape of the oxygen-disassociation curve, relating arterial oxygen pressure (Pao_2) to inspired oxygen concentration, and relating arterial carbon dioxide pressure ($Paco_2$) to prevailing minute ventilation.

HISTORY AND PHYSICAL EXAMINATION

For patients attending a general-medicine clinic, studies show that correct diagnosis is made on the basis of history in about 82% of patients, by physical examination in 9%, and laboratory investigation in the remaining 9%.[42,43] Contributions differ with subspecialty referrals. Special investigations are more important than history or physical examination in patients presenting with gastrointestinal or endocrine problems.[44] Robust data on pulmonary clinics do not exist.

When taking a patient's history, it is imperative to ask open-ended questions, enabling the patient to drive the transfer of information. A new fashion has emerged among residents wherein they relate that a patient "endorses" something or other. Information gleaned from leading questions runs the risk of not only being worthless, but also dangerous.

The commonest symptom I encounter in clinic is dyspnea (further discussion on this topic is provided in The Pathophysiology of Dyspnea and Exercise Intolerance in COPD).[45] Most referrals to my clinic have COPD or asthma, but a substantial number have dyspnea out of proportion to pulmonary function. Many of these patients have hyperventilation syndrome (psychosomatic dyspnea), yet trainees (and attendings) miss this diagnosis even when it stares them in the face.

The combination of substantial dyspnea with normal (or near normal) pulmonary function serves as an alert. The diagnosis is made primarily on history taking. The physician must listen in silence, allowing the patient to speak freely without interruption. Skillful listening involves hearing what a patient wants to communicate, as contrasted with getting the patient to tell you what you want to hear. Interrupting a patient's account early in the encounter backfires.

The characteristics of the dyspnea is different: patients typically describe a sense of being unable to take a deep enough (satisfying) breath, greater difficulty in breathing in than out, a sense of oppression (suffocation) in the chest. Unlike patients with pulmonary or cardiovascular dysfunction, dyspnea in hyperventilation syndrome has a less clear-cut relationship to exercise and is less likely to improve with rest. Chest pain is frequent and sometimes mimics angina pectoris. Some patients attribute symptoms to a life-threatening disorder, such as myocardial infarction, and, fearing death, rush to the emergency room.[46] Erroneous attribution sets off a vicious circle, causing more dyspnea and anxiety, leading to a sense of doom.[47,48]

Physical examination helps by excluding organic disease. While interacting with the patient, the clinician should be on the lookout for sighs. Healthy people take up to 4 sighs per hour,[30] whereas up to 100 sighs per hour are seen with anxiety[49] (**Fig. 6**).

Empathetic interaction (while elucidating the history) and explanation of what is causing the symptoms is the primary therapy. Patients have a long history of alarming symptoms for which no clinician has been able to offer an explanation. Many doctors consider these patients hysterical or anxious. Patients fear their symptoms will be considered imaginary, which further contributes to their distress.

When I make the diagnosis, I explain to patients that the cause of their symptoms is hyperactivity of the respiratory control system. I

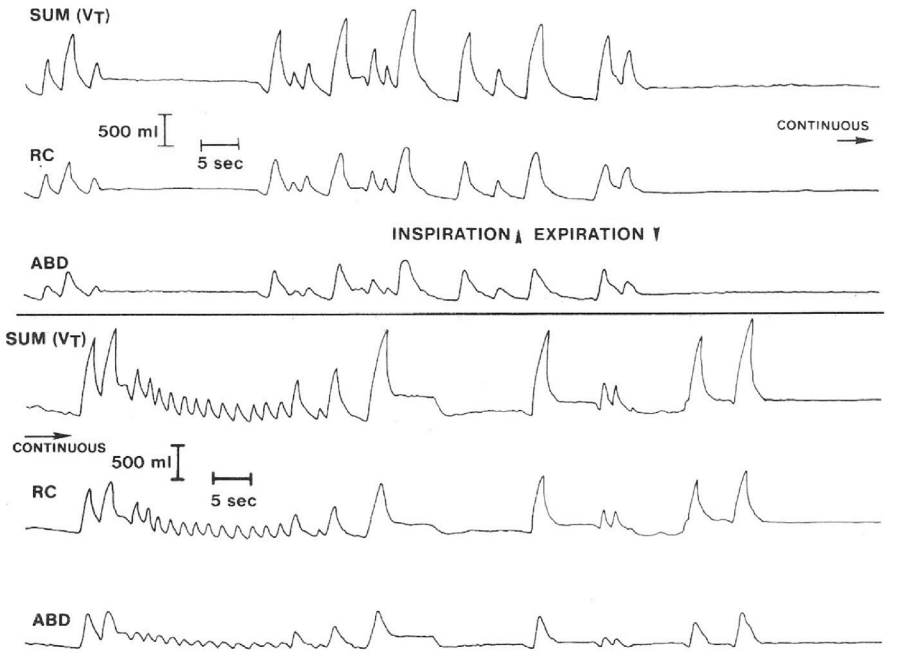

Fig. 6. Chaotic breathing pattern in a patient with chronic anxiety. Deep sighing respirations alternate with periods of rapid, shallow breathing and prolonged apneas at different lungvolumes. ABD, abdominal excursion; RC, rib cage excursion; SUM(VT), the sum of rib cage and abdominal excursion, equivalent to tidal volume.

explain that people differ in the number of signals sent from receptors in their lungs to the respiratory centers and that patients with hyperventilation syndrome are more aware of these signals than are people without dyspnea. Research shows that these patients have elevated respiratory motor output and other abnormalities of respiratory control.[47,48,50]

I emphasize to patients that the condition does not signify a psychiatric disorder (patients resent any insinuation that their symptoms are "mental" in nature). I communicate that they have a "lung condition" that is likely to continue, and the primary treatment is for a patient to understand its origin (increased signals to respiratory centers). I emphasize that despite repeated feelings of imminent demise, the condition never threatens life. The aim is to break the vicious circle that drives the symptoms by providing the patient with insight into the physiologic basis of the condition.[46–48] I never prescribe pharmacotherapy. Talking to the patient, words, is the most effective therapy.

A physician making the diagnosis of previously undetected hyperventilation syndrome has a greater opportunity of alleviating dyspnea than in patients with any other pulmonary disorder (as illustrated in Case # 7 in Unraveling the Causes of Unexplained Dyspnea: The Value of Exercise Testing).

Inspection, palpation, percussion, and auscultation constitute a time-hallowed quartet. I rely on inspection more than the other 3 and find inspection the component most often misapplied by trainees. Clinicians commonly miss Cheyne-Stokes respiration because they do not engage in a few minutes of silent inspection. Many devote less than 1 minute to inspection: axiomatically, the diagnosis of Cheyne-Stokes respiration cannot be made.

In patients with respiratory disorders, it is invaluable to surreptitiously creep up and watch their breathing pattern (**Fig. 7**). Spying is best accomplished when the patient is in a state of reverie or asleep (further discussion on this topic is provided in Pathogenesis of Obstructive Sleep Apnea). This golden opportunity is undone when some clodhopper announces loudly "we just want to watch your breathing."

The importance of palpation in assessing work of breathing has already been emphasized.

> Elucidation of the cause of dyspnea requires asking open-ended questions, relating the degree of patient discomfort to the severity of pulmonary dysfunction, and surreptitiously observing the patient's pattern of breathing.

Fig. 7. Watching breathing pattern surreptitiously in order to evade the cofounding influence of the Heisenberg principle, wherein the technique of measurement changes the very entity being measured.

CLINICAL JUDGMENT

The naming of illnesses has become ostensibly less onerous because of widespread use of tags linked with *ICD* codes that empower clerks to claim reimbursement but are empty of cognitive content. Examples include *hypoxic respiratory failure*, an elastic term that begs more questions than it answers, *ventilator-dependent respiratory failure*, an appellation that connotes predestined defeat, and *acute respiratory distress syndrome (ARDS)*, a ragbag that subsumes multiple idiosyncratic conditions. When clinicians affix jejune epithets like these, they delude themselves into believing they have reached a diagnosis, whereas the designations obfuscate more than they illuminate. In a patient presenting with infiltrates and hypoxemia, a physician may diagnose ARDS and conclude that ARDS is causing the hypoxemia. Given that ARDS is defined by hypoxemia, the reasoning is circular (and vacuous).

For intensivists, the major challenge is to make decisions grounded on careful characterization of the patient: delineations derived from physiologic assessment (it is not based on procalcitonin titers or playing musical chairs with antibiotics). Rather than simply appending a diagnostic label, the cognitive task is: "What is *really* wrong with this patient, and how can I fix it?" A surgeon has steel, but a pulmonary and critical care physician has only thoughts. Fresh thinking that breaks free from circular reasoning and clichés is vital. Each patient is unique: not the next specimen on a conveyor belt awaiting treatment by protocol.[51]

We teach medical students (and we should) to search for all relevant information, weigh it, and formulate it into a differential diagnosis. However, expert clinicians do not use differentials when arriving at most diagnoses. Instead, they aim for a bull's-eye. On a list of 5 differentials, the 4 that do not match the actual diagnosis are of no value to a patient.

Cognitive-psychology research reveals that experts solve problems rapidly, *augenblick*, at the blink of the eye. Decisions are automatic, often nonverbal.[52] Much of daily practice consists of seeing patients who closely resemble previously seen cases. Diagnoses are based on pattern recognition and automatic retrieval from a well-structured network of stored knowledge.[53] Experts are generally not aware of solving problems and making conscious deliberations; rather, they do what normally works.[54]

The hallmark of an expert is sound intuition, which can be defined as a judgment that appears quickly in consciousness, whose underlying reasons we are not fully aware of, and is strong enough to act on.[55] Intuition is characterized by use of heuristics, mental shortcuts learned through experience, which saves time and effort.[56]

Intuition overlaps with tacit knowledge, as contrasted with explicit (conscious) knowledge. The central epistemological thesis of tacit knowledge is: "We can know more than we can tell and we can tell nothing without relying on our awareness of things we may not be able to tell."[57]

In *Thinking, Fast and Slow*, the Nobel laureate, Daniel Kahneman, brings together 5 decades of research on human decision making.[58] Kahneman presents human thinking as involving 2 independent systems. (Dual-process terminology has mutated, and the present preferred nomenclature is type 1 and type 2 processing.[59]) Type 1 is amazingly fast, intuitive, and effort free; it operates automatically with no sense of voluntary control. Type 2 does the slow work of forming judgments based on conscious thinking and deductive reasoning.[58] Doctors like to believe they mostly use type 2, but all humans use type 1 for about 95% of daily decisions.[60]

Evidence in support of dual-process theory is substantial and includes anatomic localization based on functional MRI. Intuition-based decisions by experts are associated with activation of the precuneus of the parietal lobe and the caudate nucleus of the basal ganglia.[61]

A second Nobel laureate, Herbert Simon,[62] did extensive research on perception of experts by studying what might seem to be the least intuitive of fields: chess. To develop the intuitive skill of a chess master required at least 10,000 hours of dedicated practice (5 hours a day for 6 years). From hours of intense concentration, a chess master becomes familiar with thousands of combinations and sees pieces on the board differently from the rest of us. Simon concluded that intuition is a form of pattern recognition: "The situation has provided a cue; this cue has given the expert access to information stored in memory, and the information provides the answer. Intuition is nothing more and nothing less than recognition."[62] Simon reduces the magic of intuition to the everyday phenomenon of memory.

Memory holds the vast repertoire of skills we acquire over a lifetime of practice. In a recent article, I discuss the differences in comprehension of material presented on paper versus online, and that material read online is stored in a weaker form of memory than material on paper.[63,64] Given the importance of memory for expertise, trainees are best advised to lay down the foundations for their storehouse of knowledge by deep reading on the printed page as opposed to scanning online resources. It is memory that enables wise decisions and skilled performance, involving the ability to deal with vast amounts of information swiftly and efficiently.[65,66]

The idea of intuition appeals to the lazy who think that true expertise is nothing more than a random guess or inspiration of a mystic. Guessing involves reaching a conclusion when one does not have sufficient knowledge or experience to do so. True intuitive skill (type 1) is the fruit of many years of deliberative analytical thinking (type 2): it is knowledge hard earned and shaped by experience.

> Experts reach diagnoses based on pattern recognition and automatic retrieval of knowledge stored in memory. Experts make decisions based on intuition (or tacit knowledge) employing mental shortcuts learned through repeated experience.

The following case illustrates the role of intuition, tacit knowledge, and memory. A nurse sees a patient fighting the ventilator and calls a resident to evaluate. The resident finds no obvious cause for distress and plans to administer lorazepam. An expert looks at the airway-pressure waveform and spots a bump at end-inspiration, causing her to suspect activation of the expiratory muscles during inflation (**Fig. 8**).[67] During pressure support, the switch between inflation and exhalation is delayed in COPD because of prolonged time constant. The delay fosters activation of the expiratory muscles while the ventilator is still trying to push gas into the patient.[68] On switching from pressure support to assist control, the patient stopped fighting the ventilator.

The bump at end-inspiration activated information stored in the expert's memory, causing a particular diagnosis, expiratory-muscle activation, to spring to mind. The expert was not so much thinking as reacting. Over years, experts build up a bank of experiences, stored in memory, that shapes how they perceive new information. The skill is not the result of conscious reasoning, but pattern recognition: a feat of perception and memory, not analysis.[62]

Although a clinician suspects a diagnosis within milliseconds (type 1), he or she still subjects the thought to analytical reason (type 2). The initial intuition may not feel right. When a decision carries considerable risks, a prudent physician asks: "What else might this be?" There are no pure type 1 or type 2 tasks in medicine, and no single approach can be applied across all diagnostic problems. The final judgment is typically a synthesis of the 2 systems.[69] An enlarged distal phalanx suggests clubbing, but the nail fold must be brought to eye level to check if the angle approaches 180°.

Speed in making decisions will arouse suspicion that a clinician is slipshod. The doctor conducting laborious rounds is viewed as more dependable and conscientious. However, the critical point is not the means used to reach a decision, but whether the decision is the right one (and that is why creative imagination is the key ingredient: see later discussion). Several experimental studies show that experts reach correct diagnoses very rapidly (type 1), and slowing down and deliberate use of type 2 reasoning do not improve accuracy.[70–74] This does not mean that trainees should be encouraged to make speedy diagnoses: diagnoses rarely need to be made with alacrity. That is not the point. Among experts, the speed at which they reach a diagnosis is linked with accuracy, and longer processing time is associated with more, not fewer, errors.[69] The irony here is that payment to physicians is proportional to time spent, rather than accuracy of decisions.

Mistakes that result from use of heuristics (type 1 mental shortcuts) are termed cognitive biases, and more than 100 have been described.[60] "Availability bias" is the disposition to consider a diagnosis more likely if it readily come to mind. "Premature closure" is the tendency to stop

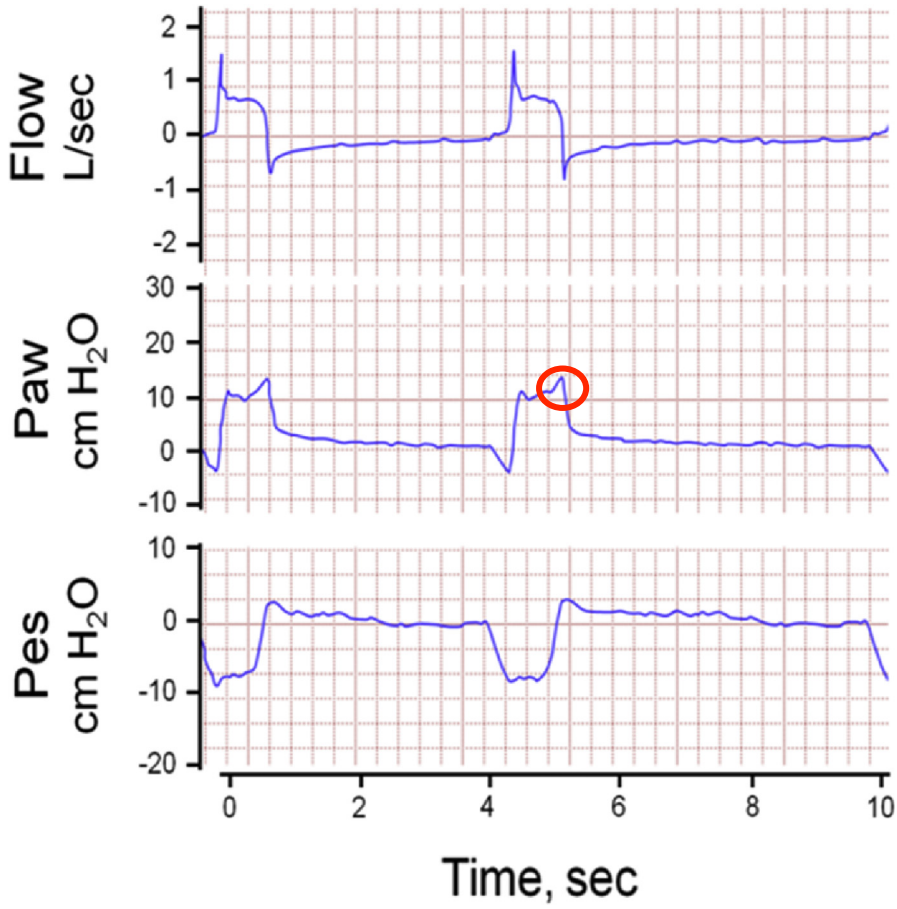

Fig. 8. A patient with COPD receiving pressure support 10 cmH_2O, with tracings of flow (inspiration directed upward), airway pressure (Paw), and esophageal pressure (Pes). The increase in airway pressure above the preset level resulted from activation of expiratory muscles.

decision making too soon and fail to gather additional critical information.

Some researchers claim that cognitive biases are responsible for more diagnostic errors than are deficiencies in knowledge.[75,76] If, however, a physician is not aware that positive airway pressure fosters persistence of a bronchopleural fistula, the problem is knowledge deficit, not a faulty thinking process. Despite repeated chidings about cognitive biases, experimental studies evince that knowledge is the key determinant of diagnostic accuracy.[70,74,77,78]

Some investigators recommend use of specific rethinking steps (metacognition) to minimize the normal human predisposition to cognitive biases, these are termed debiasing strategies.[75] Reflecting on one's decision making is commendable, but studies disclose that systematic employment of debiasing strategies does not reduce diagnostic errors.[79–81] It makes little sense to posit that diagnostic errors originate primarily with type 1[75,76] or type 2 processing because both operations are involved in most medical judgments.

Physicians acquire 2 types of knowledge: *formal* (book learning) and *experiential* (from clinical encounters). Book knowledge provides the foundation on which experiential knowledge is constructed. Although physicians may not cite mechanistic understanding in routine decisions, they revert to physiologic principles when confronted with obscure or ambiguous situations.[53] In a study of complex electrolyte problems, nephrology faculty made more extensive use of physiologic principles than residents and reached correct diagnoses more than 90% of the time contrasted with 25% for residents.[82] Pathophysiologic knowledge relating to disease mechanisms serves as a theoretic framework for the organization and recall of clinical knowledge, and it persists longer in memory than information devoid of physiologic underpinning.[83]

Every so often, clinicians encounter problems whereby knowledge is incomplete, and they

need to reason from first principles. In such a situation, it is better to base deductions on physiologic mechanisms as opposed to probabilistic outcomes based on chance.[84] The number of physiologic principles necessary for managing patients is endless: examples are listed in **Box 1**.

Box 1
Some physiologic principles that apply to patient management

- A fragile respiratory control system predisposes to life-threatening hypercapnia when supplemental oxygen is targeted to oxygen saturation greater than 94% (see also Update on Chemoreception: Influence on Cardiorespiratory Regulation and Patho-Physiology).
- Patients with sleep apnea are vulnerable to profound hypoventilation after small doses of sedatives (see also Update on Chemoreception: Influence on Cardiorespiratory Regulation and Patho-Physiology and Pathogenesis of Obstructive Sleep Apnea).
- A decrease in pulmonary artery pressure after pharmacotherapy may signify right-ventricular failure rather than improvement of pulmonary hypertension (see also Clinical and Physiological Implications of Negative Cardiopulmonary Interactions in Coexisting COPD-Heart Failure).
- In patients with elevated respiratory motor output, the default inspiratory-flow setting on a ventilator results in an increase in work of breathing (see also The Control of Breathing during Mechanical Ventilation).
- Patients with a prolonged time constant (COPD) typically recruit expiratory muscles during the inflation (inspiratory) phase of pressure support (see also The Control of Breathing during Mechanical Ventilation).
- Using low V_T on a ventilator is necessarily accompanied by shortening of mechanical inspiratory time, and, when this decreases below neural inspiratory time, double triggering (and delivery of high V_T) is inevitable (see also The Control of Breathing during Mechanical Ventilation).
- Airway pressures during compression of a bag-valve mask (Ambu) frequently reach 100 cm H_2O and can be responsible for cardiac arrest during resuscitation attempts (see also Clinical and Physiological Implications of Negative Cardiopulmonary Interactions in Coexisting COPD-Heart Failure).

A third Nobelist, Peter Medawar,[85] founding father of transplantation immunology, wrote more sagaciously about intuition than any other hands-on scientist. He emphasized that transformative advances in science depend on imaginative intuition (type 1), not the use of apparatus and the ritual of fact finding (type 2). Much writing on clinical reasoning cleaves to the 2-step hypothetic-deductive method, whereby a hypothesis is first advanced and then ruled in (or out). Clinical expertise resides more in dreaming of fertile hypotheses (type 1) than in doing tests (type 2).[86] Confronted with an inscrutable case, the imperative is to look at findings that other clinicians have seen and think of causes none have imagined.

In the past, it was believed that expertise was closely related to years of experience. In reality, the 2 are poorly correlated (skill commonly decays over time).[87] Expert performance, however, can be traced to active engagement in deliberate practice. Superior diagnostic performance is linked with repeated exposure to challenging cases, involving unusual presentations that draw on a rich understanding of pathophysiologic principles.[88] Repeated engagement with thousands of difficult cases, and ability to recall these from memory, is strongly related to expertise.[54,59,89]

Doctors are familiar with the truism that each patient is unique. Likewise, the reasoning of experts is unique because memory of cases is, by nature, idiosyncratic.[90] There is a positive-feedback loop between type 1 processing and expertise: the acquisition of expertise results in a better developed type 1 and sophisticated use of type 1 is what distinguishes an expert from a nonexpert.

If I were to pick the biggest deficiency in trainees, it is lack of imagination. Even worse is failure to appreciate the importance of creativity in solving vexing problems. When a physician is challenged with an enigmatic case, what he or she yearns more than anything else is to figure out what is happening beneath the patient's skin. Cracking these riddles depends on a clinician's power of imagination (type 1 processing). The solution of conundrums never rests in the capacity to recite some algorithm or apply a protocol. Unraveling mysteries depends on a clinician's capacity to imagine internal biologic happenings that explain external clinical findings. This is where physiology comes in. Faced with a perplexing patient, my mind conjures simulacra of machines with chambers and tubes, cogwheels, and pumps, and what happens when a spanner gets thrown into the works.

A superior diagnostician looks at the same findings that other clinicians see but thinks of causes that other clinicians have not imagined. Solving clinical mysteries depends on a clinician's power of imagination, the capacity to imagine internal biologic happenings that explain perplexing clinical manifestations.

CODA

When launching EBM, the founders specified their goal was to deemphasize all reasoning based on pathophysiologic rationale in the practice of medicine.[91] They have surpassed expectations of even the most starry-eyed devotee. Trainees of the 2010s possess a fraction of the pathophysiology known by residents of the 1980s. What did we get in exchange? The promise that grading of articles (into a hierarchy) would improve patient care, an epistemological strategy that had been demolished by far brighter brains (Karl Popper and critics of the logical-positivism movement) more than 40 years before.[92,93] Randomized controlled trials are invaluable in evaluating drugs and other therapies, but provide zero help with the principal impediment in all clinical encounters: perceiving the right diagnosis concealed beneath confounding camouflage (pulmonary embolism). Creative thinking depends on neurons nourished by scientific understanding, not on grading of articles. From the nineteenth-century onward, the epoch of Virchow, Bernard, and Starling, the practice of medicine had been grounded on physiologic principles. To barter science for sophistry is an exchange that even Faust would not have contemplated.

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