Just as there are fashions, fads and fancies in Art, Music, Literature and Dress, so there are in the more academic pursuits of Science, Economics, Engineering and Architecture. Even Medicine is vulnerable to the vagaries of the vogue. “Fashion” sneered Ambrose Bierce cynically, “is a despot whom the wise ridicule and obey.” In Physic, a prime practice that has swung like a pendulum in and out of fashion is the performance of a physical examination as part of the diagnostic algorithm. Now, perhaps more than ever, with the availability of elaborate laboratory tools to analyze bodily fluids, the perception of high resolution imaging with sonic and electromagnetic vibrations, and the intimate glimpses afforded by microscopic, ultramicroscopic and molecular dissection of the tissues of the body, there seems to be little room for the tradition of inspection, percussion, auscultation and palpation. Auscultation of the heart has yielded to echocardiography; percussion of the chest to computer-assisted tomography; careful evaluation of the neural network with flashlight, pin, cotton wool, tuning fork and tendon hammer to magnetic resonance imaging of the brain and spinal cord; and inspection and palpation of the abdomen to endoscopic invasion of the gastrointestinal tract by flexible light-emitting tubes that propel charge-coupled devices, and with wireless capsules that relay their reconnaissance by radio transmission to the examiner. Whereas no one regrets the passing of gustation of sweat and urine in the diagnosis of jaundice and diabetes, respectively, is it any wonder that residents and fellows show little fascination or even interest, let alone respect, for the visual, auditory, tactile and olfactory examination of the tissues of the body, there seems to be little room for the tradition of inspection, percussion, auscultation and palpation. This lamentation is not expressed to imply that an extensive meticulous physical examination has always been the bedrock of clinical diagnosis — far from it, as we shall see. Rather it is an expression of nostalgia, that emotion of longing for temps perdu, which for several centuries was thought to be a truly disabling disease of young people forced to live far from their homes but now is a prerogative and a proof of senescence. But we digress, for the purpose of this exposition is to remind the reader that the physical examination not only has an illustrious pedigree but is still rewarding in hepatology, as it can indicate the presence of liver disease, assess its severity and, together with the patient’s history, give some intuition as to its cause.

Physicians of the Ancient World, in the East and the West, did not have the virtually unlimited access that we have today to the patient’s body, except perhaps at the time of the “ultimate physical examination.” Nonetheless, by carefully scrutinizing the accessible, i.e., the face, hands, body posture and movement, the rhythm and noise of breathing, behavior, demeanor and mood, together with some limited intrusive approaches, like feeling the pulse, inspecting the tongue, hearing the rumble of the abdomen and even shaking the patient, they made many astute observations. Witness Hippocrates and his facies, fingers and succussion. Hippocrates recognized jaundice and hepatic coma, and he could hear the succussion splash of fluid moving in the pleural space in his patients with pleurisy, whom he jolted to make the diagnosis. Galen, in 2nd Century CE Rome, could fill 16 volumes with his writings on observations, interpretations and prognostications of the pulse, a practice incidentally much favored in Ancient China too. Wang Shuhe, who lived during the Western Jin dynasty in the 3rd Century CE, compiled all available knowledge on pulse diagnosis in his manual on the pulse, Mai Jing. Galileo timed his pendulum from his pulse and vice-versa, while his Paduan contemporary Sanctorius Sanctorius (who had also improved on Galileo’s thermometer and dabbled in paracentesis) invented the pulsilogium, a pulse-watch dedicated to that purpose. The pulse, tongue, eyes, nails and skin were favorites of the Ayurvedic physicians too, dating from the early centuries of the current era in India, but here great emphasis was placed on the patient’s age, constitution, body proportions, and capacity for food and exertion, which were evaluated chiefly to allow them to estimate life expectancy. Yet though the practice of medicine in most cultures was vaunted as relying on the five senses, physical examination literally remained at a superficial level, by and large, until well into the late 18th Century. As Richard Gordon has sardonically remarked, the 17th Century physician was useless but decorative. With his satin gilt-decorated coat, buckskin breeches, silk stockings and buckled shoes, lace ruffles and full bottomed wig, he swung a long cane with a hollow gold head filled with Marseilles vinegar that he sniffed repeatedly to ward off infection. To Richard Mead (1673-1754), physician to Queen Anne and George II and Fellow of the Royal College of Physicians, the gold-headed cane was a badge of office to be carried with pride. To caricaturists, like Thomas Rowlandson and William Hogarth, it was an icon with which to identify individuals with medical pretensions, as in Hogarth’s 1736 cartoon “The Company of
Undertakers” that ridiculed leading physicians and quacks of the day who, with expressions that range from sour to stupid, are depicted either sniffing their canes or absorbed by the contents of a urinal. Successful and sought-after clinicians of the era, like Mead and Scotsman William Cullen,11,12 were often consulted by letter to which they replied in kind with a diagnosis, a prescription and a bill for services rendered. All of this was to change following the intellectual ferment of the French Revolution in 1789, which Iain Bamforth identifies as the event that turned medicine into a public utility.13 In place of mail order consultations, and diagnoses made by inference from a detailed, almost Freudian, interrogation and a Sherlock Holmes-like scrutiny of the patient’s face, physicians in the 19th Century added a structured physical examination to the narrative to help identify disease, using all the senses. There was at large a new doctrine of organ-based disease, arising from the discoveries of pathologists, microbiologists, physiologists and pharmacologists of the age, like Giovanni Morgagni, Rudolf Virchow, Robert Koch, Louis Pasteur, Claude Bernard, William Beaumont, Oswald Schmiedeberg, Paul Ehrlich, and so many others too numerous to tally here. And there were also innovations in the clinic that enhanced patient evaluation. The prevailing no-touch approach that was a product of social propriety and traditional diagnostic reasoning, gave way to the thoroughness of a physical examination that would have appeared impudent and embarrassing to patient and doctor alike in the 18th Century. In 1808, Jean Nicholas Corvisart, Napoleon’s personal physician, popularized percussion by publishing a translation of the 95-page booklet on the technique that had been produced in Latin almost 50 years previously in 1761, by the Graz-born Austrian Joseph Leopold Auenbrugger.14 Auenbrugger, who learned the percussion of patients as it had already been practised to some extent by Hippocrates, Galen, and even his teachers,15,16 and veterinarians in Switzerland were already percussing the heads of cattle to diagnose cysticerci.17 Auenbrugger’s contribution, and later that of Corvisart, was that he considered percussion to be an essential component of the physical examination. The second boost to physical diagnosis was, of course, the introduction by René-Théophile-Hyacinthe Laënnec of the stethoscope, which he developed from the rolled up quire of paper he had used to listen, from a respectable distance, to the heart of a buxom young woman.18 These devices for examination, together with the introduction of others such as the sphygmomanometer, the spirometer, the roentgenograph, the electrocardiogram, the ophthalmoscope and various forms of endoscopy, were seminal contributions made in the 19th Century to the practical science of clinical medicine.

In the realms of physical diagnosis, hepatology is a goldmine of lesions that typify moderate or advanced derangement of liver structure and/or function, granted, admittedly, that no physical sign is unique or pathognomonic. However, liver disease can affect each and every organ system, and since we have seen in the language of many cultures that “The body has a liver,”19 in the framework of the physical examination we can now safely say that, by its widespread effects, “The liver has a body” too. An organ system-oriented classification of the physical signs of liver disease would at first thought seem logical mechanistically, but a more practical tack would be to order the various signs as we come across them during the traditional conduct of the physical examination. For descriptive purposes, this is akin to taking a sightseeing expedition of the body, and here the analogy of another popular innovation of the 18th and 19th Centuries comes to mind, namely that of the Grand Tour. Whereas history is replete with the exploits of individual wayfarers who journeyed to distant lands to learn the terrain and the culture of the peoples there, like Benjamin of Tudela and his 12th Century itinerary from Saragossa to 300 cities in Greece, Mesopotamia, Syria, Palestine and Persia; Ibn Battutah and his 13th Century journey from Tangiers to India, China, Africa, Asia and Europe; Marco Polo and his trip from Venice to China in the 14th Century; and Cabeza de Vaca’s 16th Century foray into the interior of America, historians generally regard the so-called Grand Tour as having its beginnings in the late Renaissance and reaching its high point in the 18th Century. That prolonged sightseeing pastime abroad of the affluent continued well into the 19th Century, however, as travel became easier and more lands were colonized, and it is exemplified by the entrepreneurial activities of the 19th Century temperament campaigner Thomas Cook,20 whose name is now synonymous with the guided but cursory tour. Parenthetically, it was also implicit once that a Cook’s tour ensured home-away-from-home comfort for the well-to-do English while they were “touring” Europe, the Mediterranean, the Middle East, the Orient or the Far East, but that is hardly the case today.

In our Cook’s tour of the physical signs of the liver patient, we must first take in a colorful scenic view of the face before making our major stop at the hands. Is the patient conscious and coherent, or confused and even comatose? Are the eyes, mucus membranes and skin yellow, and if so shall we call it jaundice or icterus?21 Is there the bronzing of hemochromatosis or the hyperpigmentation of cholestasis or the whiff of fetor hepaticus22, the
gauntness of temporal wasting, and “paper money” skin where tiny superficial vessels resemble the finely chopped red and blue silk threads embedded in U.S. dollar bills; and are creamy periorbital excrescences, xanthelasmas, present? Is the corneal pigmentation visible that Drs. Kayser24 and Fleischer25 espied before Wilson described his eponymous disease,26 and do sunflower cataracts obscure our gaze into the patient’s soul? Are the teeth green from childhood cholestasis,27 or the lips, mucus membranes and tongue blue from hypoxemia that could hint at the hepatopulmonary syndrome? Is the tongue vitamin B deficiency red in the alcoholic or decorated like the skin elsewhere with the white lace-like pattern of lichen planus that sometimes accompanies chronic hepatitis C,28 primary biliary cirrhosis,29 primary sclerosing cholangitis,30 and other liver disorders too?31 Are we struck by the alcoholic’s elephantiasis des buveurs, i.e., the rhinophyma that is so popular in literature and the arts32; do his cheeks bulge from parotid enlargement33 and, of course, are spider nevi present too?34 (Fig. 1A). Does a flat forehead, widely-set eyes and a pointed chin suggest Alagille syndrome? There is much to delay us in the face before we move on to the hands.

Clubbing of the fingers (Fig. 1B,C), which occurs in liver disease and a host of other disorders, has fascinated physicians of all persuasions ever since Hippocrates described curvature of the nails and hot finger tips, the so-called “Hippocratic fingers,” in his patients with empyema more than 2000 years ago.4 When digital clubbing, palmar erythema and spider nevi are in conjunction (Fig. 1A-C), the presence of liver disease and especially cirrhosis is almost assured, yet the cause of clubbing (assuming that we even know how to recognize it without the use of an unguisometer35,36) remains enigmatic. As Samuel West wrote presciently in 1897, “Clubbing is one of those phenomena with which we are all so familiar that we appear to know more about it than we really do.” It has been hypothesized that clubbing occurs because of a noninflammatory vasodilatory hyperemia of the finger tips and nail beds, which results from a neurocirculatory

Fig. 1. Selected physical signs in liver disease, from head to toe. (A) Spider nevi. (B) Palmar erythema and finger clubbing. (C) Finger clubbing and Terry’s nails. (D) Toe clubbing and erythema of the terminal phalanges.
reflex that may originate in the cholinergic sympathetic autonomic innovation of the digits and the vagus nerve\textsuperscript{38}; transection of the latter does not reliably reverse clubbing but it has been known to resolve its painful bony counterpart, hypertrophic osteoarthropathy.\textsuperscript{39} Many cytokines and growth factors, like platelet-derived growth factor,\textsuperscript{40,41} vascular endothelial growth factor,\textsuperscript{42} growth hormone,\textsuperscript{43} and hepatocyte growth factor,\textsuperscript{44} have been impeached but the real culprit has yet to be caught. Some digitally-orientated philosophers have even suggested that these humors activate dormant genes that return the hand to an embryonic claw, or even restore the claws that humans have lost during evolution.\textsuperscript{44} Irrespective of the pathogenesis, however, when liver or lung disease is the cause, replacing the spent organ with a new one returns the digits to their pristine condition,\textsuperscript{55-57} unless rejection supervenes.\textsuperscript{48}

Even if the fingers are not clubbed and the hands are not disfigured with vitiligo or the rash of cutaneous porphyria, the nails may be thickened, ridged, brittle, flat\textsuperscript{59} or concave\textsuperscript{60} to indicate the presence of liver disease. Streaks of green in the nails testify to previous cholestasis, whereas the lunulae, with distal red or brown discoloration, define Terry’s nails\textsuperscript{53,54} (Fig. 1C), whereas the paired transverse white lines of Muehrcke\textsuperscript{55} that appear when there is hypoalbuminemia of any cause, must be distinguished from the transient white bands of alcohol abuse\textsuperscript{56} and from Mees’s white lines, those sinister marks of arsenic poisoning\textsuperscript{57} that transform hepatologists into criminologists. Inasmuch as impressions from onychomancy — divination from finger nails — conjure suspicions of liver disease and its cause, so much more does elicitation of the peculiar tremor known as asterixis that almost invariably indicates liver failure, even though this distinctive movement disorder occasionally stems from renal failure,\textsuperscript{58} respiratory failure,\textsuperscript{59} drug reactions\textsuperscript{60} and other nonhepatic causes.\textsuperscript{61,62}

That dramatic mental and neurological manifestations disturb patients with liver failure, has been known since the time of Hippocrates and Galen. Reference was made to the neuropsychiatric phenomena of what is now called hepatic encephalopathy (or portal-systemic encephalopathy) in all the more important writings on liver disease in the 18th and 19th Centuries, as appraised in detail by John Walsh more than 50 years ago,\textsuperscript{63} including his review of reports by such liver luminaries as Richard Bright, George Budd and Friedrich Theodor von Frerichs. Irregular jerky movements of the limbs, or jactitations, had been noted but the significance of the so-called “liver flap,” as it was colloquially called in the lingo of hepatic coma aficionados, was not appreciated until the publication in 1953 by Raymond Adams and Joseph Foley, of their landmark chronicle of the neurological disorder associated with liver disease.\textsuperscript{64} This publication, which was a comprehensive detailed extension of the preliminary account that they had reported a few years earlier,\textsuperscript{65} also contained biochemical, electrophysiological and exhaustive neuropathological data. Joe Foley, now a grand octogenarian but then a junior faculty member in neurology, performed repeated detailed neurological examinations on 60 patients who had been admitted with severe liver injury, two-thirds of whom had alcoholic cirrhosis, as he was looking for a harbinger of impending coma. More than 100 other patients were examined at least once too. Foley, who conducted these clinical studies initially at Boston City Hospital in collaboration with the renowned hepatic comatologist Charles Davidson and his colleagues, and later at the Massachusetts General Hospital, noticed that the liver flap appeared early in the course of the disease and in several cases was the first sign of looming coma. Foley considered this idiosyncratic movement disorder to be one of the most characteristic features of hepatic coma and one of the most useful in predicting disaster, since the vast majority of their deeply comatose patients died. Foley’s original description of the involuntary movement that some have hyperbolically likened to the beating of a bird’s wing, or flügelschlagen, as well as his description of hepatic coma itself, are unsurpassed. He described the appearances at irregular intervals of 1-7 seconds of rapid arrhythmic lateral deviations of the fingers, flexion-extensions at the metacarpophalangeal joints and flexion-extensions at the wrist, when the patient was asked to hold the arms and hands outstretched with the fingers spread apart. Flexion was always the most rapid of the movements that occurred in bursts every second or two, although there were also movement-free intervals. Comparable movements could be seen in the arms, legs and feet, tightly closed eyelids, corners of the retracted mouth, pursed lips and during sustained grasping by the hands; though bilateral, the movements were asymmetrical and asynchronous. The protruded tongue has picturesquely been described as showing “tromboning.” Foley also described a fine 6-9 per second tremor of the outstretched fingers that has only recently been termed “mini-asterixis,”\textsuperscript{66} which is thought by some to originate in the cortex, reflecting a pathologically slowed and synchronized motor cortical drive.\textsuperscript{67} Asterixis itself is technically-speaking not a tremor but rather a form of negative myoclonus in which there are irregular myoclonic lapses of posture caused by involuntary 50-200msec silent peri-
ods in muscles that are tonically active, as shown by electromyography.\textsuperscript{54,66} Notwithstanding, the exact mechanism remains elusive and many postulated explanations are yet to be explored.\textsuperscript{68} As for the term asterixis itself (which incidentally does not actually appear in the landmark publication\textsuperscript{64} but soon entered the neurological vernacular\textsuperscript{69}), this was Joe Foley’s invention too as he sought to substitute a universal neurologically-egalitarian nomenclature for the partisan term liver flap. He and another classics scholar, his Jesuit priest friend Father Cadigan, had repaired to a local hostelry in Boston, the Athens Olympia Café, to discuss neurological semantics. There, inspired by a splendid meal and fortified by an unspecified volume of the famous grape brandy invented just 60 years previously by the Greek silk trader Spyros Metaxas, Foley contrived the term \textit{an-iso-sterixis} (later shortened to asterixis for \textit{Hoi Polloi}) from the Greek, which means “a lack of [maintenance] of position,” which indeed it is.

Before we leave the bounding pulse and warm hands, flapping in dorsiflexion as if hesitantly bestowing a blessing, we cannot help but notice a curious flexion deformity of some of the digits, caused by shortening of the palmar fascia. Known as Dupuytren’s contracture, after the legendary but arrogant 19th Century French surgeon Baron Guillaume Dupuytren, Chief of Surgery at l’Hôtel Dieu in Paris and personal surgeon to both Louis XVIII and Charles X, this hand deformity had already been described around 1200 CE in the Icelandic sagas\textsuperscript{70} and was well known in Scotland too since the 16th Century, as the curse of the MacCrimmons of the Western Isles, whose preeminent bagpipe players were increasingly thwarted in their performances by progressive finger contraction deformities that were a frequent inheritance amongst members of that clan.\textsuperscript{71} Felix Plater, a Swiss anatomist in Basel, published the first account in the medical literature in 1614,\textsuperscript{72} when he described the contractures of the ring and little fingers of a master mason, and though Henry Cline at St. Thomas’s Hospital in 1808, and his famous former apprentice, Sir Astley Paston Cooper, in 1818, described the malformation too,\textsuperscript{70} it was Dupuytren who earned eponymous immortality after he delivered a lecture on December 5, 1831, on the topic of permanent retractions of the digits of the hand. Dupuytren later published in English in the Lancet\textsuperscript{73} without acknowledging the work of Cline and Cooper, about which he cannot have been oblivious. Yet, for all its time-honored history, neither the cause nor the pathogenesis of Dupuytren’s disease are clear, but fibroblast proliferation, chromosomal aberrations, immunological abnormalities, growth factor activity and androgen-responsiveness of Dupuytren palmar tissue are all thought to play a role.\textsuperscript{71} Dupuytren’s contracture occurs in both genders and all ethnic groups, but far and away it is predominantly an affliction of older men of northern European ancestry and, by repute, it is another genetic gift from the Vikings.\textsuperscript{70} Although typical liver patients with Dupuytren’s contracture have alcoholic cirrhosis,\textsuperscript{74} it is a feature of the alcoholism rather than the liver disease as such, and it also complicates diabetes, seizure disorders, cigarette smoking and probably vibration-induced hand injury too, especially in genetically-prone individuals.\textsuperscript{70}

Transfer to the chest by way of the arm, shoulder and neck offers more sights that bespeak of underlying liver disease. Muscle wasting is common in the upper arms, shoulder and around the scapula, tattoos give a clue to a high-risk lifestyle, xanthomas appears at the elbow and the ear, and this is definitely spider nevus country. Careful inspection of the neck, in the right light and at the right angle, may reveal portopulmonary hypertension-induced jugular venous pressure elevation, which can be enhanced by applying gentle manual pressure to the abdomen, anywhere but over a congested tender liver, to elicit an hepatojugular reflux. On the pruritic back, “butterfly distribution” sparing from hyperpigmentation, shows the limits of scratching.\textsuperscript{75} In the chest, gynecomastia\textsuperscript{76} may be the most prominent part of the feminization syndrome (together with sparse beard and soft skin),\textsuperscript{77} often painfully exacerbated or caused by a side effect (or should that be front effect?) of spironolactone treatment,\textsuperscript{78} and occasionally it may give an inkling of an underlying fibrolamellar hepatocellular carcinoma that synthesizes aromatase.\textsuperscript{79} Auenbrugger’s percussion confirms the presence of an hepatic hydrothorax without the need to shake the patient. Combining palpation of the precordium with auscultation through Laënnec’s invention, gives further evidence of the hyperdynamic circulation and/or pulmonary hypertension, both being relatively common in patients with cirrhosis. The abdomen has always been the domain of the hepatologist, and there is surely no need to wax lyrical to this readership on the virtue of bulging flanks, an everted umbilicus and shifting dullness (executed by Auenbrugger’s technique), nor to recall that even if the 3-hand trick of eliciting a “fluid wave” is possible, it is probably scarcely necessary because the presence of ascites is already obvious. And please, spare the patient the indignity of demonstrating the puddle sign. How fitting that the music of hepatology — the bruit of an hepatic tumor, the hum of Cruevelhier and Baumgarten,\textsuperscript{80} and the rare rush of a splenic arteriovenous fistula—can be heard, above the borbyrgmy, through Laënnec’s stereophonic device. Visible dilated superficial abdominal wall veins with cephalad flow are common in patients with cirrhosis but it is a rare chance to observe caudal flow in
these vessels, which is a sure sign of superior rather than inferior vena cava obstruction. Some say that the caput Medusa is as much a myth as the Greek legend from which its name derives. Abdominal hernias may not be all they seem; they may actually represent ascites rather than bowel extrusion, and in the inguinal region surgeons must beware of operating on what will turn out to be ascites or worse, a collateral vein filled sac.

And so to legs and feet, as 17th Century diarist Samuel Pepys might have said, for the culmination of the tour. In many ways the lower limbs are an anticlimax and simply mirror the upper ones, with their muscle wasting, sparse hair, and xanthomas on the knee. Spider nevi are never sighted here but the legs are, instead, the preferred location for edema. Dependency has its price, but perhaps therein lies the solution to the age-old riddle of how to grade and stage peripheral edema. Rather than being nonplussed by the usual arbitrary scale of “pluses” that some authors shun as meaningless, or foolishly trying to estimate the depth of the pit or the time that it takes to fill in without regard to the size or strength of the prodding fingers, why not grade the squelch of the waterlogged tissues as trace, mild, moderate or severe, and stage the encroachment of the legs by edema, plotting the extent upwards from the feet to the abdominal wall (with a correction for redistribution due to recumbency or loss of compressibility due to brawhiness). Muscle wasting occurs in the thighs, asterixis may be observed by simply letting them abduct as Foley recommended, and clonus may be elicited too. Petechiae may be seen when the high venous pressure in the legs conspires with thrombocytopenia, and the feet and ankles, the furthest cool reaches of the body, are also prone to the palpable purpura of cryoglobulinemic vasculitis of chronic hepatitis C. Finally, it may be possible to witness a recapitulation of changes that we have already seen in the hands, namely toe clubbing (Fig. 1D) and plantar erythema and even Dupuytren’s pedal counterpart, the lederhosen syndrome of plantar fibrosis, which is related to Peyronie’s disease by some cruel twist of fate.

Nowadays fashion in medicine is evidence-based and a few killjoys try to convince us that, despite the many landmarks we have seen on our tour, the physical examination is no longer worthwhile in patients with liver disease. However, neither the author nor skilled examiners like Joe Foley would agree (personal communication, November 2004). Admittedly, some arcane maneuvers in liver diagnosis, like the scratch test for detecting the liver edge, are unreliable, and clinicians often disagree about their physical findings. Why some cannot even find the mid-clavicular line. Yet, for all that, with practised hand and trained eye, seasoned clinicians looking for the physical signs described above, such as spider nevi, facial telangiectasias, white nails, abdominal veins, liver consistency, ascites, and the size of the spleen, are able to diagnose advanced liver disease and decompensated cirrhosis with a fair degree of certainty. Far from being a fad or a fancy, it seems most likely that a carefully performed physical examination will still be the fashion in clinical hepatology for many years to come.

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References

19. Reuben A. The body has a liver. HEPATOLOGY 2004;39:1179-1181.
41. Reuben A. The body has a liver. HEPATOLOGY 2004;39:1179-1181.