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Research Article,

A Lab Simulation of Urinary Flow Changes during Cystometry of Immobile Male Patients with Bladder Outlet Obstruction

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Abstract:

The aim of this study is to investigate how male urinary flow is altered when measured from a supine posture relative to seated voiding. The theoretical impact of any changes on urodynamic diagnosis will also be considered. Water was poured from a calibrated device into a flow meter from geometry simulating seated male voiding, then supine male voiding through two different voiding aids; each condition was repeated nine times. Peak flow rate and its latency were marked carefully, and compared within and between conditions.

The primary outcome measures were changes in peak flow rate and its latency for supine voiding. Subsequent changes to diagnostic classification on the Schafer nomogram provided a secondary outcome measure- achieved by plotting the original and corrected pressure-flow coordinates of real patients and observing any category changes. Hydrostatic pressure was then estimated to assess factors unrelated to the patient or the apparatus that could influence the primary outcome measures. Finally, calculation of Reynolds numbers allowed the likelihood of turbulence to be judged, and the resultant effect this could have on flow recordings.

Recumbent flow was significantly slower than seated flow, and both its onset and its peak were delayed. However, the attenuation and lag observed by employing a modified Cystoaid were much smaller than when using a rectangular tube. Adjusting clinical data for these changes resulted in a reduction in the Schaefer Nomogram classification of detrusor strength for both aids. The changes lead to obstruction being underestimated or overlooked. A clinically significant re-categorisation (resulting in a change of management) is predicted when using the rectangular tube.

A component of the errors in both aided conditions is explained by a reduction in hydrostatic pressure as the source was tilted. Additionally, turbulence could be introduced by the Cystoaid during the fastest flows. The use of voiding aids could therefore convolute identification of clinical features and artefacts during qualitative analysis.

Introduction:

Causes of Bladder Outlet Obstruction in Males

Urinary flow rate is influenced by bladder volume [1], detrusor muscle strength [2], urethral resistance [3-5], pathological bladder outlet obstruction (BOO) [6], normal variations in urine composition [7], the presence of a urethral catheter [8] and unmeasured interactions among these factors. In men, anatomical obstructions include prostate cancer, benign prostatic enlargement (BPE), bladder neck contractures (usually following surgery), inguinal hernia [9] , urethra Stricture [10], epididymo-orchitis [11], prostatitis [12], posterior urethral valves [13-14]. Primary bladder neck obstruction [15], dysfunctional voiding [16], delays in sphincter relaxation (sphincter bradykinesia) [17], and detrusor sphincter dysynergia [18-19] can all cause functional obstruction. Of all these pathologies, BPE if the most common cause of BOO- in the USA it affects three-quarters of men in their seventh decade [20].

Diagnosis of Bladder Outlet Obstruction in Males

While clinical examination and imaging can identify anatomical compression, constriction or encroachment of the urethra, Cystometry is recommended to confirm the degree of functional obstruction (BOO) before considering surgical intervention [21]. It can elucidate anatomical and purely functional components and identify concomitant storage symptoms requiring additional management. Metrics calculated from various weightings of peak urinary flow rate, synchronously measured detrusor pressure, and post-void residual volume [22-24] are compared to pre-defined limits to objectively diagnose BOO. Alternatively, diagnostic limits derived from mathematical models of urethral resistance [3-4] are marked on pressure vs. flow plots forming the boundaries of a diagnostic nomogram [24-25]. The ICS nomogram [26] is similar to the A-G nomogram [25] and is considered the gold standard for diagnosing BOO by many clinicians [27]. The Schaefer nomogram (SN) [24] (Fig. 1) represents a compromise between the resolution of a continuous variable created by a metric, and the necessary diagnostic immediacy of a nomogram. It is also specifically applicable to patients with BPE making it ideal for an urban Urodynamics practice.

Modification of Diagnostic Tests in Immobility

When BOO occurs alongside neurological illness, spinal injury, or any condition affecting mobility, cystometry can be performed supine using a voiding aid. However, this is thought to introduce a delay in theonset of flow, and the time taken for the flow to reach its peak. It may also morphologically change the flow curve, including a reduction of amplitude. The aims of this study are to measure peak flow rate and its latency in simulated supine and seated voiding simulations for scientific and clinical comparison.

Methods:

Equipment and Experimental Protocol

A Medtronic Duet 9.0 Urodynamics system was used to acquire the data, employing a spinning disc flow meter with high and low pass filtering during acquisition between 1Hz and 50Hz provided by a 3rd order Bessel/Thompson filter and the sampling rate. The local convention for clinical cystometry is to be seated during the voiding phase, and its simulation provided the control condition. Two supine conditions were simulated using a length of rectangular tubing and modified cystoaid between the source and commode. In the seated condition, the bottle was held vertically over the commode at 44cm, while in the aided conditions, apatient bed was raised to 77cm with one end of the aid rested on it, and the other end secured to the commode seat (44cm) with tape (Fig. 2) . The upper end of the aid was held steady with the one hand while the other hand was used to tilt the bottle and direct fluid flow into a funnel at the top of the tube. For each experimental condition, 500ml of tap water at air-conditioned cool room temperature was poured into the flow meter from a device producing flow of 15 mls^{-1}[28], ten times.

Table 1: Peak Flow rate (Qmax) and time to peak flow rate (t Qmax) over ten flows

	Qmax (ml/s) Median (*95% CI's*)		t Qmax(s) Median (*95% CI's*)	
Seated	15.64	(15.37-15.82)	7.27	(5.33-10.01)
Rectangular Tube	12.27	(10.98-13.41)	41.13	(26.54-52.72)
Cystoaid	13.43	(12.72-14.61)	18.96	(9.33-20.80)

Table 2: Estimation of Hydrostatic Pressure given geometry.

	Seated condition	*Supine Conditions*
h= depth (m)	0.12	0.09
ρ = density of water (kg/m^3)	1000	1000
g = gravity (ms^{-2})	9.81	9.81
P_H= h ρ g	**1172.2 Pa**	**882.9 Pa**

Table 3: Calculation of Reynolds Number (R_e) describing the flow through a tube

	Rectangular Tube	**Modified Cystoaid**
v=velocity (ms^{-1})	0.015 (0.001-0.024)	0.054 (0.035-0.45)
d= tube diameter (m)	0.06	0.013
ρ = density of water (kg/m^3)	1000	1000
μ = viscosity of water (Pa s)	0.001	0.001
R_e = (v d ρ)/μ	**907 (600-1440)**	**696 (455-6500)**

Initial Signal Processing

The 30 flow curves were exported as .csv files then presented by an excel macro as an x-y scatter plot smoothed over a two-second window [29]. It was observed that this method of filtering introduced a systematic delay of 1.98s, and so the macro was re-programmed to shift the data to the left by the same amount and the raw data re-processed. For each plot Qmax and TQmax were marked and recorded in an analysis spreadsheet facilitating descriptive statistics and unpaired statistical comparisons.

Derivation of New Qmax

The adjustment to Qmax was simply the difference between the median Qmax during aided and unaided flow. Informed consent was given by three patients for use of their clinical CMG to illustrate any diagnostic effect of the experimental findings. An additional data point from a published study of normal males [30] was also utilised. The original pressure-flow co-ordinates were plotted on a Schafer nomogram and labelled: A: normative study; U: unobstructed case; M: mildly obstructed case; S; severely obstructed case. Any significant changes to Qmax found in the experiments were used to move the data points downwards, where they were giving a new, but linked, label (e.g., A').

Derivation of new PdetQmax

Indirect changes to Pdet.Qmax caused by experimental flow delays were derived on individual CMGs , then used to move datapoints horizontally where they were given another new label (e.g. A''). The separation ofthe original and double-dashed markers highlights the ultimate diagnostic effect of not correcting for the errors introduced by a change in measurement conditions.

Calculation of DAMPF

Finally, the detrusor amplitude modulated passive urethral resistance relation factor (DAMPF) was derived from the SN. Peak flow and its contemporaneous detrusor pressure are marked on the SN. Then and the smallest detrusor pressure allowing urinary flow to occur is identified on the CMG 10ml prior to the end offlow to account for the time taken for urine to traverse the male urethra. The second point is added to the nomogram and the two points are joined by a straight line whose right-most intersection with a detrusor contractility boundary is extrapolated vertically down giving the (unitless) DAMPF. This was calculated before and after the double correction of clinical data, and the two values were compared.

Consideration of Hydrostatic Pressure and Turbulence

The experimental design removes the influence of clinical factors, and variations in flow secondary to the presence of a catheter and voided volume. The variables are therefore the geometry of the fluid source and its physical path to the flow meter. Hydrostatic pressure (P_H= ρgh) is exerted by a liquid because of its potential energy and will influence flow- it is proportional to height which is invariably larger for our aided experimental conditions. Source P_H was calculated in each condition. Independent of height, phenomena introduced by rigid walled tubes on a Newtonian fluid (water), may add features to the flow recordings.

Knowledge of the viscosity of water and the physical measurements of each aid allowed calculation of the Reynolds number and characterisation of flow as turbulent, or not [31].

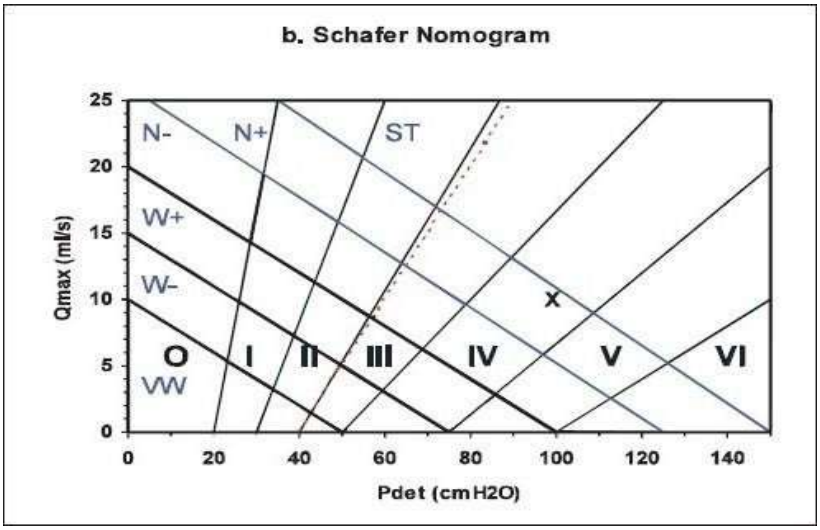

Figure 1: The Schafer nomogram for categorisation of BOO given detrusor strength.

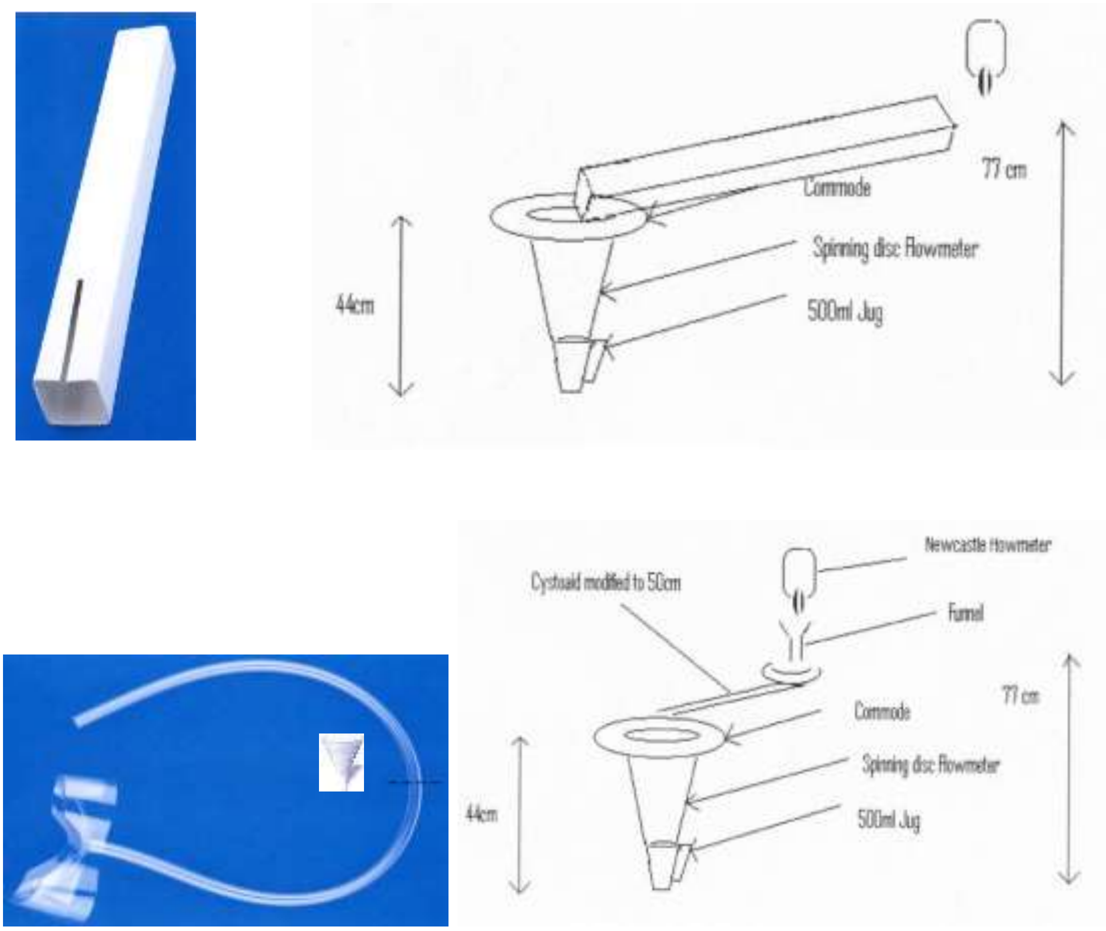

Figure 2: The two voiding aids and the geometry of the simulated micturition in each case. The rectangular plastic tube ((0.10m=0.01m) cut out of the upper surface to accommodate catheters. The tube of a Mediplus Cystoaid (1m x 0.013m) had a funnel inserted into it.

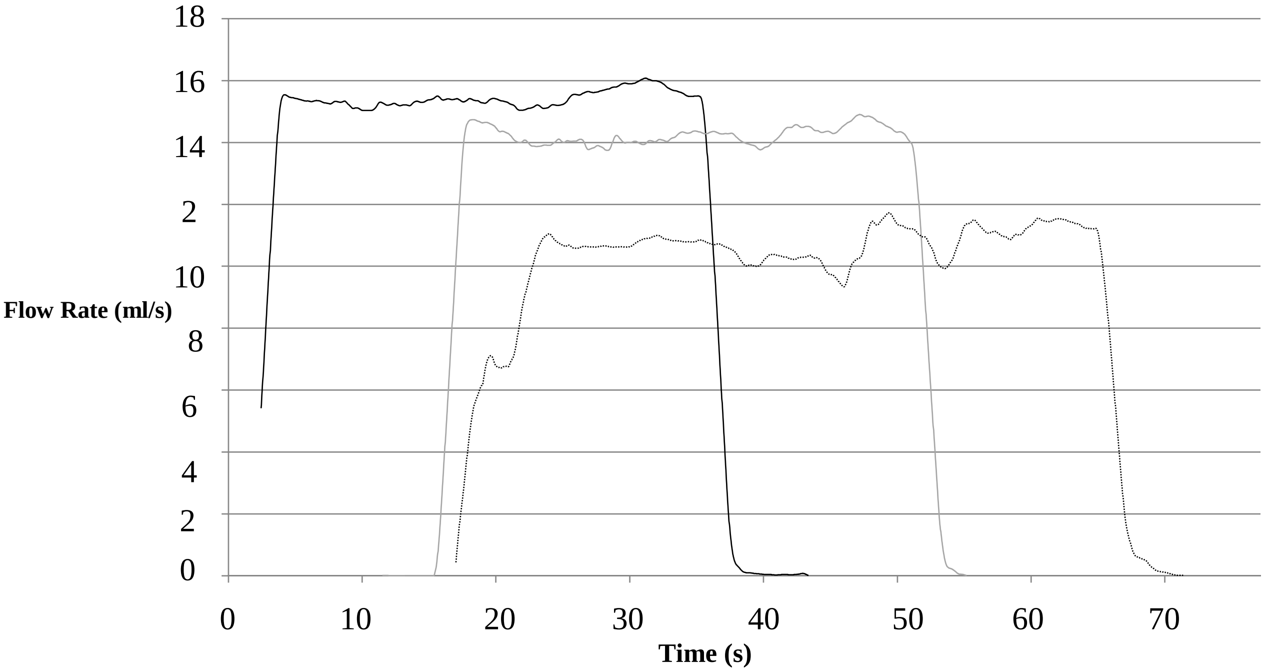

Figure 3 : The black, grey and dotted lines denote flow from simulations of seated and supine conditions with a modified cystoaid and a rectangular tube. The shape and duration of the first twocurves are similar. However, a small systematic reduction in flow rate and a substantial delay in flow beginning are introduced by the cystoaid. When the rectangular tube was employed, flow waseven more delayed and very slow (and therefore protracted). This condition also had more variability than the first two simulations.

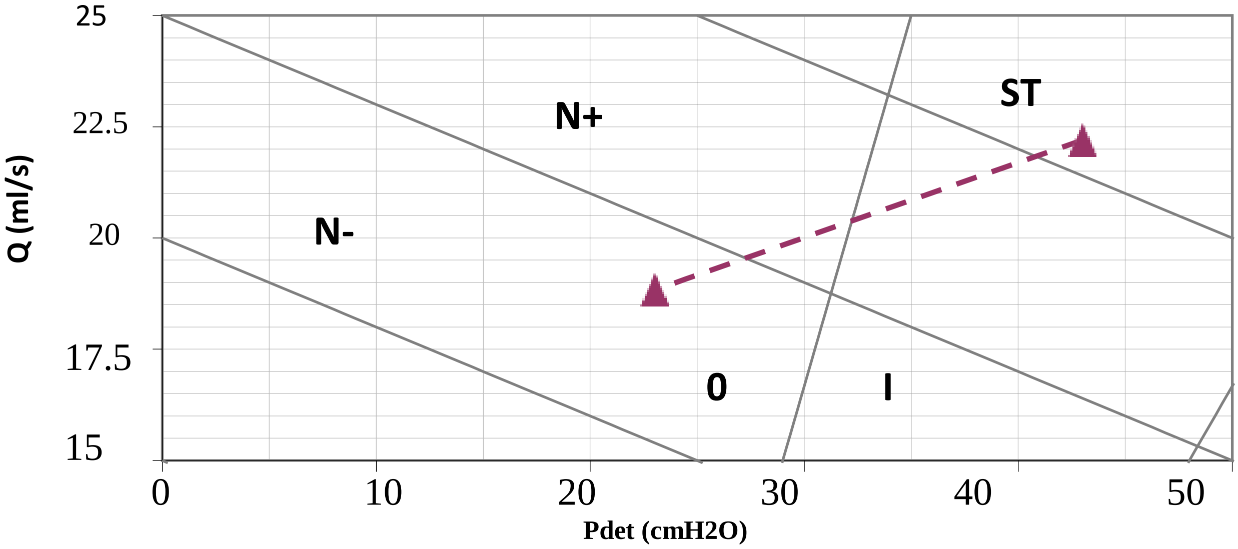

Figure 4: The effect of urinary flow attenuation, plus and a delay in its peak illustrated on a magnifiedSchaefer nomogram.

Results:

Attenuation and Variability of Qmax

Unsurprisingly, relatively fast flow was observed during the seated voiding condition, with flow through the voiding aids being slower and delayed (fig. 3); the flow curves also show that supine flow was more variablewithin each recording. The full experimental dataset is summarised in Table 1, and calculation of a non- parametric coefficient of variation (CV=interquartile range/median) showed variability of; 1.71%, 7.82% and 16.88% for Qmax in seated, RT and MC conditions, and

35.4%, 54.6% and 55.4% for TQ_{max} in the same postures. Median attenuation of 3.39 ml/s and 2.31ml/s by the RT and MC respectively were statistically significant according to a Mann-Whitney U test (U=0; p<0.01; U=0; p<0.01). Delays in Q_{max} of 33.06s and 9.33s for RT and MC were also statistically significant (U=0; p<0.01; U=10; p<0.01) .

The increased (apparent) height when the source was held vertically downwards resulted in a 25% larger P_H for seated voiding relative to the recumbent voiding simulation (1177 Pa and 883 Pa respectively) (Table 2)h. This will attenuate fluid flow in the aided conditions and accounts for much of the Q_{max} reduction. The smaller changes in all key parameters for MC may reflect a subsequent facilitation of flow by the narrower cylindrical tube.

Changes to Diagnostic Classification using the SN

The modification of flow we have demonstrated in the aided simulations caused shifts in diagnostic category on the SN for every real data point. Overall, use of the RT without correction is likely to cause underestimation of both detrusor strength and the degree of BOO (figure 4). The DAMPF was also reduced by 12 % which is clinically significant. The MC caused smaller shifts on the SN and the DAMPF that are unlikely to cause changes to the management of a patient.

Discussion

New diagnostic Insights applicable to all test centres

Locally, we see many immobile patients every year and while they may be more difficult to assess, their need for intervention may be greater than a patient who is able to manage their own symptoms. Where a patient is known to have BPH, the Shafer nomogram allows grading of the severity of BOO given Urodynamic measurements. This unique experiment has quantified changes in the rate and timing of fluid flow caused by voiding aids. We have also demonstrated how both underestimation of obstruction and detrusor contractility can occur during Schafer nomogram analysis, which is postulated to be clinically significant for the RT.

Our Findings in Context

The average flow rates for the unobstructed clinical example and the normative datum were 22.5ml/s and 24ml/s respectively, suggesting that the 15mls^{-1} flow rate provided by NFM is slower than average male flow, even when age is considered. It therefore undoubtedly mirrors obstructed urinary flow, and was adequate to reveal clinically significant changes to bladder pressure-flow studies. Good practice documents [29] and those describing the development of the Schaefer nomogram [24] do not stipulate a correct patient position; the former simply states that it should be noted. However seated voiding minimises variation due to gravity for very tall or very small patients, and prevents compensatory use of abdominal muscles (straining). It is therefore preferable for the voiding phase of Cystometry wherever possible.

Errors, Artefacts and Oversights

If a reduction in P_H reduces flow rate before it enters each aid, and flow rate is then enhanced by the MC, the parameter v used in calculation of the R_e may have been overestimated here. However, this error is small relative the three orders of magnitude by which the upper 95% confidence interval exceeds the turbulence threshold. The formula (table 3) reveals that the likelihood of turbulence is proportional to flow rate and tube diameter; a narrower tube may therefore be preferable. In the present study, high frequency filtering during recording, and the recommended post-hoc smoothing [29] applied by the macro reduced the appearance of turbulence in figure X and nay be sufficient to avoid misdiagnosis. It is recognised that temporal filtering caused by the voiding aids could obscure clinical features including flow modulations secondary to DSD, abdominal straining, and contractions of the urethral sphincter in dysfunctional voiding or sphincter bradykinesia. DESD occurs in progressive neuropathic conditions that may also render the patient immobile and so is very relevant to this experiment. Abdominal straining can be habitual in any obstruction and is also relevant, although minimised by avoidance of the standing during tests.

Broader Clinical Implications of Test Position

Recording the CMG in the supine position reduces the likelihood of observing DO in those suspected of having an overactive bladder [32]. It is therefore highly beneficial when the primary urodynamic question is of BOO because it will ensure a voiding phase by preventing involuntary leakage of the bladder contents.

Clinically useful bladder pressure and urinary flow measurements require appropriate selection of procedures and accurate analysis of results [29] which is increasingly possible because of this experiment and the interpretation of its results. Therapeutic decisions for those with neurogenic lower urinary tract symptoms aremade based on a comprehensive medical assessment, including urodynamics to identify the type of dysfunction [33] and the recording methods we have described make urodynamics possible in such a cohort.

Recording Insights from a Specialist Spinal Injury Centre

Voiding Cystometry in those with spinal injury can be made from a raised seated position, facing the commode where an electronically controlled bed with split legs is available. However, this option depends on the location of injury and the cognitive state of the patient. Staff expertise is also very relevant when performing any modified recording protocols. Experiments to identify any changes to measurements and nomogram classifications would be very useful for this configuration.

Conclusion:

We have described how Urodynamic testing can be modified where a male patient’s mobility is compromised, and how to adjust analyses to achieve accurate diagnosis. Our findings have implications for Uroflowmetry, Cytometry and non-invasive pressure-flow measurements [34] performed from a recumbent position. Similar lab experiments are necessary to calculate the necessary adjustments for spinal-injured patients assessed from a supported seated position. A prospective clinical study would allow full testing of the hypotheses that proven changes affect SN categorisation and clinical management.

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