Abstract

Post-stroke pneumonia (PSP) is common after stroke in the geriatric population. Acutely, it causes significant mortality and institutionalisation and over the long term, patients show poor functional outcome. The main implicated factor in PSP is dysphagia and the development of aspiration. Other significant risk factors include older age, dependency, COPD, cognitive impairment and mechanical ventilation. The location of the stroke lesion has also been shown to predict PSP with larger, multiple and vertebrobasilar lesions showing a significant association.

Prompt treatment of PSP has conventionally proved adequate in preventing unfavourable patient outcomes thus negating the need for antibiotic prophylaxis. Currently, limited evidence suggests that prophylaxis is beneficial. It reduces infection rates by 15% and is thought to additionally reduce stroke-induced immunodepression, a recently proposed phenomenon. Prophylaxis may be made more efficient by identifying and targeting those at risk of aspiration. Specialised tests such as videofluoroscopy are effective but have disadvantages including radiation exposure and compliance issues. Thus, simple bedside measures e.g. pulse oximetry measuring hypoxia have been implicated in detecting aspiration risk; but their sensitivity is questionable. A combined test including a water-swallow test and pulse oximetry has shown promising sensitivity and specificity.

This review considers the evidence for the prophylactic treatment of PSP. Identifying mechanisms and risk factors for PSP supports the need for targeting a select group of patients who would benefit from prophylactic intervention; potentially via a screening tool. Further prospective multi-centre evaluation is needed to validate the acute and long-term effects of antibiotic prophylaxis in stroke patients.
Background

Stroke is a serious vascular emergency which is common and significantly debilitating. In England and Wales alone, it accounted for 11% of all deaths in 1999 [1]. The annual incidence of stroke is 110,000 with more than 900,000 living with the effects of stroke. This national health burden is compounded by the significant dependency of these patients. Data from the National Audit Office Report estimated stroke’s cost to society being £7 billion annually with major expenditure from direct healthcare costs (£2.8 billion) being primarily from diagnosis and inpatient care [1].

Stroke is a focal or global disturbance of cerebral function greater than 24 hours or leading to death with an apparent vascular cause [World Health Organization, 2008]. An extension of this clinical syndrome includes various post-stroke complications including mood disturbances, falls, chronic pain, venous thrombembolism and infection – especially urinary infections and pneumonia [2]. Pneumonia is the commonest infection being reported as up to 30% of which occur within 48 hours and most developing within a week [3]. A large cohort study found pneumonia being associated with a relative risk of 3.0 for mortality when adjusted for stroke severity [4]. Given significant mortality and morbidity associated with this pulmonary complication, prophylactic management has been the subject of relative interest in the literature as medical complications rates dictate prognosis.

Current national guidelines advocate the appropriate treatment of diagnosed infections. However the value of antibiotic prophylaxis has been disputed with no definitive conclusion regarding its benefits on overall mortality. Hence this review aims to address some of the pertinent issues surrounding chest infection post acute stroke and whether there is indeed a case for the use of antibiotic prophylaxis. Additionally, considering evidence implicating hypoxia as an indicator of aspiration risk will highlight potential measures to target this patient group.

The Impact of Post-Stroke Pneumonia

There is no clear definition of post-stroke pneumonia (PSP); one classification divides PSP into acute and chronic forms, with 1 month post-stroke being the cut off-threshold [5]. Clinically, this definition doesn't accurately capture the urgency of post stroke pneumonia and the need for intervention. A separate trial adopted CDC (Centres for Disease Control and Prevention) criteria [6] where a diagnosis of stroke-associated pneumonia required new-onset clinical (i.e. auscultation, percussion, fever, secretions), microbiological (e.g. sputum cultures) and radiological signs. Such heterogeneity between studies investigating PSP accounts for the wide range of quoted prevalence rates. Pneumonia may occur in 7-22% of stroke patients [7] compared to 3.5% of controls (elderly inpatients on a medical ward aged 65 and over) [8]. It is important to briefly discuss the burden of PSP if the requirement of a prophylactic antibiotic protocol is to be established. There have been studies considering both the acute and chronic effects on patient morbidity after stroke associated infections.

Patients who develop concomitant chest infection do worse acutely. In a sample of patients admitted with stroke (n=439), 91% were clinically diagnosed with confirmed stroke [9]. 17% of the sample had a post stroke infection by the fifth day and of these, 11% had pneumonia with just over 1% suffering pneumonia with UTI. These rates are consistent with previous works in the field. Infection had a significant association with inpatient mortality and institutionalisation post discharge; odds ratios were 2.5 and 1.9 respectively. This effect was also reported as being associated with TIAs (transient ischaemic attacks). The authors argue this because both groups had a similar proportion of TIA patients (8-9%). Hypothetically, small ischaemic cerebral insults can predispose to pneumonia, further highlighted in the mechanisms section. However, as PSP was
diagnosed within 5 days of admission and given the definition of a TIA being less than 24 hours, a causal relationship is difficult to argue. There is no information regarding percentage of TIA patients having a subsequent stroke which would help explain this trend.

Similarly, the prognosis for stroke associated infection is equally poor over longer term follow-up. One cohort study [10] considered the longer term patient outcomes of PSP with data from the Netherlands Stroke Survey (n=521). Patients were followed up at discharge and 1 year, where PSP was defined as infection within a week of admission and Rankin scores were used to monitor outcome. 7.5% of the sample had PSP with 4.4% having a urinary tract infection. Poor outcome was reported in 88% of stroke associated infections with a 47% mortality rate. Despite adjusting for confounding variables, outcomes were poorer in the infection group both at discharge and at 1 year. Not only was pneumonia the most prevalent infection in the sample, it also showed a greater correlation with negative patient outcomes in a year. Therefore the debilitating impact of post stroke infections, especially pneumonia, cannot be understated.

Thus, briefly understanding the reasons behind this phenomenon and identifying risk factors is logical, not only to target these patients, but to identify and rationalise preventative measures such as prophylactic antibiotics.

Mechanisms & Risk factors for Post-Stroke Pneumonia (PSP)

The pathophysiology of PSP is probably multifactorial (see table 1) but the main implicated factor, one of the significant results of stroke, is dysphagia [11]. If dysphagia is conceptualised as a difficulty of the transmission of the bolus from the mouth to the pharynx, it is easy to understand that the prime complication is the transfer of bolus particulate into the airway, termed “aspiration” [12]. Dysphagia is commonplace (up to 50%) however the range of prevalence rates given in the literature highlights the problems in concordance between methods of assessment and study design [12]. Fundamentally, dysphagia leads to pulmonary complications via aspiration, particularly pneumonia [13].

Dysphagia is a direct risk factor for the development of PSP. However there are other factors mentioned in the literature. One group [9] found that older age and pre-morbid dependency of the patient were characteristic of the infection group. Other risk factors for developing infections included pressure sore development, presence of seizures and urinary catheter use. In this instance, there was no proven association with past medical history and delay from onset to admission. General limitations included the inability to accurately diagnose post-stroke infections, with pre-stroke infection confounding results. Specific limitations included data extraction from patient notes at day 5 not being blinded to outcome hence leading to observer bias. There was also a lack of statistical power given the small sample size.

A separate prospective study (n=124) reported an incidence of PSP as 21% on a Neurology Intensive Care Unit (NICU) over a period of 1 year [6]. In their analysis, they report several risk factors for PSP including dysphagia, mechanical ventilation (MV) and multiple lesions/vertebrobasilar stroke as risk factors. These findings merit further discussion. Firstly it is worth highlighting that this study represents a specialised population of stroke patients, being on the NICU, hence is not representative of acute stroke patients as a whole. This also is related to the fact that the authors found mechanical ventilation to be a risk factor for developing PSP, as it is offered to an even smaller subset of acute stroke patients. The fact that these patients are in respiratory failure in the first place may be due to hypoxia secondary to infection. On closer inspection, less than 30% of patients were classed with having dysphagia, which emphasises the
prevalence of ventilation-associated pneumonia significantly contributing to the overall PSP prevalence.

Table 1: Risk Factors Reported in the Literature for Development Of Post Stroke Pneumonia

<table>
<thead>
<tr>
<th>Pre-Stroke Factors</th>
<th>Post-stroke Factors</th>
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<tbody>
<tr>
<td>o Age &gt; 65 years[9]</td>
<td>o Dysphagia[6] / Abnormal water swallow result [15]</td>
</tr>
<tr>
<td>o Pre-morbid dependency[9]</td>
<td>o <strong>Lesion-dependent factors</strong>[6] – size of lesion, vertebrobasilar lesions, multi-hemispheric lesions, MCA-I territory</td>
</tr>
<tr>
<td>o Oral health status[14]</td>
<td>o Cognitive impairment e.g. AMTS &lt;8[15]</td>
</tr>
<tr>
<td>o COPD[15]</td>
<td>o Mechanical ventilation[6]</td>
</tr>
<tr>
<td>o Diabetes mellitus[16]</td>
<td>o Dysarthria[15]</td>
</tr>
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</table>

Risk factors have been compiled by various studies and classified into (a) factors prior to the stroke onset and (b) factors related to/as a result of the stroke. All risk factors reported are significant (p<0.05).

The location of the stroke lesion itself may predict PSP. The lesions that were predictive of PSP in one study included the middle cerebral artery I (MCA I; sphenoidal segment), multiple hemispheric lesions (>1 major vascular territory), vertebrobasilar stroke and multiple vertebrobasilar stroke i.e. additional cerebellum and brainstem compromise [6]. Dysphagia wasn’t controlled for in this trial but we can hypothesise on a fundamental level. Swallowing is a complex physiological mechanism and strokes can affect the process at a number of levels. Lesions in the pre-central gyrus for example interrupt oral, facial and lingual motor co-ordination contralaterally [11]. Strokes may compromise elements of cognitive function including attention and concentration leading to inefficient execution of swallowing [17]. Brainstem strokes are renowned for their association with dysphagia [11]. This is due to the complex interconnection between facial musculature, bulbar nuclei, swallowing centres and innervating suprabulbar neurones. This damage may herald aspiration pneumonia; further study is warranted to identify any neuroanatomical risk factors by functional imaging.

Impaired consciousness has been proposed as a confounding variable in the post-stroke infection literature [18]. It is thought to degrade protective reflexes, impaired function of the lower oesophageal sphincter and ineffective overall co-ordination of breathing and swallowing, increasing the risk of aspiration. It could be argued that these features are difficult to separate entirely from the cerebral damage resulting from stroke. Nevertheless, controlling for GCS (Glasgow Coma Scale) values as an independent variable may address this point in future studies.

Other limitations in the above literature include lack of congruency between studies when controlling for overall stroke severity, which exacerbates all the discussed mechanisms. This was directly addressed in a recent prospective study that considered 591 stroke patients, 72 of which subsequently developed pneumonia [19].
This trial adjusted for appropriate variables utilising logistic regression models unlike the NICU study of PSP [6]. Given that lesion size was an independent predictor of PSP in these patients, this probes into alternative mechanisms for PSP as part of its multi-factorial causation. The authors implicate a putative model based on a CNS injury-induced immunodeficiency syndrome (CIDs). Connections with the sympathetic nervous system and hypothalamic-pituitary axis may modulate cytokine production, with a greater production of cytokines with larger lesions. Hence, targeting prophylactic interventions specifically at patients with larger lesions could prevent negative outcomes. This concept was addressed in a recent trial, discussed in the treatment section.

Other mechanisms thought to be involved in the causation of PSP include dysfunction of gastrointestinal motility precipitating aspiration [20]. Essentially however the main mechanism and risk factor leading to PSP is dysphagia via aspiration. There are clearly some other risk factors for the development of PSP. Some of these are pre-morbid factors such as age and COPD. Others are stroke associated factors such as resulting cognitive impairment and consciousness. Having considered these factors and processes leading to PSP, the current evidence for any beneficial effect of antibiotic prophylaxis must be evaluated.

### Treatment of PSP – A Niche for Prophylaxis?

Post stroke infection has been shown to have a close association with the severity of stroke. However, PSP’s effect on independent patient outcomes when treated promptly has been questioned. Such evidence supports current guidelines promoting the prompt diagnosis and treatment of post stroke infections such as pneumonia as opposed to prophylactic intervention.

One prospective study (n=229) defined PSP as presence of fever, respiratory symptoms and a blood leucocyte count >11,000 cell/ml or <4000 cell/ml [21]. After excluding subjects with infection on admission, PSP was diagnosed if symptoms presented within a week of stroke onset. A poor outcome was defined if the modified Rankin Scale was >2 at day 7. Significant univariate predictors of early infection included age, nasogastric tube feeding (strongest predictor), non-lacunar infarcts (as distinct from lacunar) and high baseline NIHSS score - consistent with previous studies. Post diagnosis, prompt antibiotic regimens were administered included amoxicillin (53%), levofloxacin (38%), cefalosporins (5%), tazobactam-piperacillin (3%) and vancomycin (2%). A logistic regression model showed only NIHSS score and tube feeding to remain associated with poor outcome. In terms of prophylactic intervention within 7 days of stroke, this did not significantly affect improve poor outcome of patients. Hence post stroke infection when promptly treated did not present as an independent predictor of outcome in this particular trial. This may not be true for all patients and there is a case of for identifying a subset of patients that may benefit from prophylaxis.

### Table 2: Relationship Between Stroke Lesion Size and PSP

<table>
<thead>
<tr>
<th>Lesion size</th>
<th>n</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1.5 cm (%)</td>
<td>14</td>
<td>0.5*</td>
</tr>
<tr>
<td>1.5 - 5 cm or 1.5 - 1/3 MCA (%)</td>
<td>16</td>
<td>0.6</td>
</tr>
<tr>
<td>&gt;5 cm or &gt;1/3 MCA (%)</td>
<td>42</td>
<td>3.5***</td>
</tr>
</tbody>
</table>

Adapted results showing the relationship between lesion size and incidence of infection. NB: * p<0.05, **p<0.01, ***p<0.001, OR - adjusted odds ratio, MCA - middle cerebral artery territory.
Current Guidelines

There is a lack of clarity regarding the exact micro-organisms contributing to PSP. A “community-acquired aspiration syndrome” has been described in the literature [22]. This implicates Haemophilus influenzae, Pneumococcus, Staphylococcus aureus and Enterobacteriaceae which predominate within 4 days post after stroke admission. Alternatively, given the acute onset of PSP, 50% being within 48 hours [3], the current treatment of PSP could follow the guidelines of hospital-acquired pneumonia (HAP; [23]). Early-onset HAP (<4 days after admission [24]) encompasses these organisms but late-onset HAP (>4 days after admission [24]) may be attributed to antibiotic resistant strains of gram negative organisms. These include Pseudomonas aeruginosa, Acinetobacter spp and gram positive organisms including MRSA [23]. This clearly has implications for an appropriate treatment regime. For early-onset HAP in the UK (<5 days post admission), a standardised empirical regimen is administered [25] which consists of intravenous cefuroxime or co-amoxiclav (depending on the trust and local antibiotic resistance). If resistance is suspected or for admission greater than 5 days, an antipseudomonal drug (e.g. Tazocin®) or broad-spectrum cephalosporin (e.g. ceftazidime) or quinolone (e.g. ciprofloxacin) [25]. Longer than a week treatment may be needed if Pseudomonas is isolated and an aminoglycoside (e.g. gentamicin) may be required if this infection becomes severe [25].

Despite these guidelines, there are limited UK trials considering antibiotic prophylaxis for stroke with lack of concordance between antibiotic regimens in international studies.

Evidence for Prophylaxis

At a fundamental level, pneumonia in stroke has been studied in mouse models [26]. A 60 minute stroke was simulated by occlusion of the MCA and the intervention group received moxifloxacin either immediately or 12 hours post stroke. The subjects were followed up for 14 days. Prophylaxis was shown to decrease mortality, prevent the development of infections including pneumonia and improve neurological outcome. Moxifloxacin administered at 12 hours post-stroke was associated with a significantly lower infarct size. Notably this study was investigating the theory of stroke-induced immunodepression and hence these results are unrelated to aspiration pneumonia syndromes. Preliminary data from animal models are merely suggestive and need to be explored in the clinical setting.

A recent meta-analysis of the most significant works that have examined antibiotic prophylaxis for post-stroke infections [27] showed the viability of prophylactic intervention in PSP. Randomised patients were considered from 4 clinical trials (n=426) including the landmark ESPIAS trial (Early Systemic Prophylaxis of Infection After Stroke; [28]). The interventions included fluoroquinolones in 2 trials as well as combinations of tetracyclines and beta-lactam with beta-lactamase inhibitor in one of the trials (see table 3). Prophylaxis was commenced 24 hours after the onset of stroke and the treatment was between 3-5 days. In terms of outcome measures, 2 studies considered infection rates directly [28, 29], with one trial looking at proportion of subjects with fever [30]. The remaining trial [31] actually investigated the neuroprotective effect of minocyclidine and did not have a blinded outcome assessment. The primary outcome for this trial was change in NIHSS (National Institute of Health Stroke Scale) scores of patients at baseline and at 90 days.

The meta-analysis revealed that prophylactic intervention reduced the incidence of infection in acute stroke from 38.1% to 23.5%, the most common infection being pneumonia (complicating one in three of the acute strokes). There was no significant reduction in overall mortality between groups. Adverse effects in this analysis were low with only one trial describing exanthema and elevated liver enzymes [30]. Only one trial measured antibiotic resistance with no
significant differences between intervention and control groups [29].

**Table 3: Results Of Studies In Meta-analysis with Interventions, Mortality and Infection Rates [27]**

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients (n) &amp; Controls (n)</th>
<th>Mortality Rates (Treatment vs. Controls)</th>
<th>Odds Ratio</th>
<th>Infection Rates (Treatment vs. Controls)</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chamorro et al</td>
<td>Levofloxacin (67), Placebo (69)</td>
<td>6% vs. 1%</td>
<td>4.32</td>
<td>16% vs. 19%</td>
<td>0.85</td>
</tr>
<tr>
<td>Lampl et al</td>
<td>Minocyclidine (74), Placebo (77)</td>
<td>7% vs. 12%</td>
<td>0.55</td>
<td>Not reported</td>
<td>-</td>
</tr>
<tr>
<td>Harms et al</td>
<td>Moxifloxacin (39), Placebo (40)</td>
<td>3% vs. 8%</td>
<td>0.32</td>
<td>15% vs. 33%</td>
<td>0.38</td>
</tr>
<tr>
<td>Schwarz et al†</td>
<td>Mezlocillin + Sulbactam (30), Placebo (30)</td>
<td>0% vs. 0%</td>
<td>-</td>
<td>50% vs. 90%</td>
<td>0.11*</td>
</tr>
</tbody>
</table>

†Adverse effects of the intervention: Exanthema (n=1) and elevated liver enzymes (n=1)  
* = p<0.05

There are certain original features of the trials included in this analysis. One of the trials included [29] is one of the few to appreciate and control for the effect of lesion location and severity, discussed earlier in the mechanisms section. Uniquely, this particular trial’s inclusion criteria specified non-lacunar ischaemic infarcts. Excluding small lesions and lacunar infarcts is a step towards targeting patients at risk of pneumonia and enhancing the effect of prophylactic treatment. This trial also added weight to the theory of stroke-induced immunodepression by finding a positive association with monocytic HLA-DR expression, predictive of infection. A similar neurobiological approach was considered by the trial employing the minocyclidine regime. The investigators evaluated the neuroprotective properties of antibiotic prophylaxis in stroke and achieved improved patient outcomes. This was attributed to minocyclidine’s anti-apoptotic effects, reinforced by previous animal models [26]. However, minocyclidine does not adequately cover the common organisms responsible for aspiration pneumonia and the trial failed to evaluate infection rates.

Overall, the meta-analysis results concluded the number needed to treat (NNT) to prevent infection was 7 whereas the NNT to prevent death was 63; although, these figures represent all types of infection. Such figures may be expected in prophylactic interventions but potentially improved through effective screening of risk factors. Despite these results, the meta-analysis is not without limitations. The general flaw is heterogeneity between trials on a number of different levels. For example, the definition of infection varied significantly between studies and timing of infections may not strictly be true cases of PSP. One major factor already discussed as influencing infection rates is stroke severity and this analysis utilised the NIHSS (National Institute of Health Stroke Scale) to measure this. Variation in NIHSS inclusion criteria ranging from scale 4-11 in 3 trials limits the comparison between trials. One trial employed the modified Rankin score instead. Trials were also graded accorded to the Jadad scale measuring methodological quality. This again ranged from 2-5 limiting comparability. Withdrawal post-randomisation introduces selection bias due to knowledge of outcome. A major tenet in evaluating the effect of preventative interventions is the long term functional outcome of patients. These were not included in the trials over long term
follow-up and should be considered in future studies.

Essentially, current trials do conclude a beneficial effect of antibiotic prophylaxis on reducing infection rates. Antibiotic prophylaxis does not however convincingly reduce patient mortality rates. Furthermore a lack of long term follow-up measures including those of functional outcomes necessitates further large cohort studies. Paralleling this need for future research is the benefit of identifying further indicators of PSP to identify at-risk groups whom could benefit from preventative antibiotics. One theory is that recognising hypoxia can identify those at risk of aspiration who subsequently develop PSP.

**Hypoxia as an Indicator of Aspiration Risk**

Dysphagia has been identified as a primary cause of an increased risk of aspiration. There are several methods available for identifying dysphagia. These can be classified into (a) bedside tests such as clinical examination and pulse oximetry and (b) specialised tests such as videofluoroscopy [12]. Current specialised methods to detect aspiration are accurate but do have limitations. Videofluoroscopy is currently the 'gold-standard' for detecting aspiration and uniquely allows the evaluation of posture and dietary modification as therapeutic interventions [1]. Disadvantages of videofluoroscopy include a lack of corroboration regarding it's implication in PSP, adequately mobilising stroke patients to radiology departments, radiation exposure and the fact that it provides a mere “snapshot” of swallowing function [2].

A separate method, fibre-optic endoscopy, has been validated yet patient outcomes with respect to pneumonia development may be indifferent regardless of using videofluoroscopy or fibre optic endoscopy [32]. Fibre-endoscopy is portable and reliable however does require compliance of the stroke patient which is not always practical [1]. The idea of simple bedside tests having a comparable accuracy in the detection of aspiration risk is alluring as it avoids the disadvantages of specialised techniques. Desaturation or reduced arterial oxygenation has been implicated as an indicator of aspiration risk [33]. This can be measured by pulse oximetry, a simple bedside observation. Aspiration is thought to induce bronchoconstriction leading to ventilation perfusion mismatch and desaturation [34]. Some evidence from the last decade has suggested that desaturation could be a valuable marker of aspiration.

One study administered a water swallow test with oxygen saturation being measured for 2 minutes afterwards [35]. Stroke patients (n=49) were compared to 2 control groups divided into younger (n=55) and older age groups (n=66). Relevant to the mechanisms of PSP, subjects with impaired consciousness and pneumonia were excluded. The average desaturation was significantly higher in the stroke group (2.9%) compared to the controls (0.8-0.9%). The fall in desaturation was significantly associated with SALT (speech & language therapist) determination of aspiration status. This lends evidence to the fact that desaturation is a useful marker of aspiration and should be used in conjunction with clinical SALT assessment to predict aspiration pneumonia.

Notably one of the control groups, being age- and sex- matched subjects (n=66; 28 men, mean age of 71 years), did not show desaturation patterns like the acute stroke patients. This observation increases evidence for consistent hypoxia in clinically aspirating stroke patients. Notably, as SALT assessors on detecting aspiration undertook the appropriate measures to prevent pneumonia, desaturation did not correlate with pneumonia retrospectively. It is reasonable to assume that without intervention, those identified with aspiration would have been at increased risk of developing pneumonia.

The accuracy of bedside measures was compared to that of fibre-optic endoscopy in a
separate prospective study [36]. Oxygenation was measured prior to, and immediately after, a water swallow test (WST) using oximetry. Uniquely the study aimed to identify silent aspirators, who are often missed by bedside techniques [12]. Patients at risk of aspiration were identified either with clinical signs e.g. cough or a desaturation > 2%. Results showed that pulse oximetry had a sensitivity of 77% and a specificity of 83% whereas the WST had a sensitivity of 85% and a specificity of 75%. But the combination of these measures, termed the 'bedside aspiration test' caused the sensitivity to climb to 100% with a specificity of 71%. This reflects a highly sensitive screening tool.

Additionally, the correlation with pneumonia was investigated retrospectively. Detecting aspiration via fibre-optic endoscopy had a positive association with the development of pneumonia (relative risk =1.24) unlike bedside measures. This finding is biased by the fact that dietary interventions after identifying aspiration were not investigated and controlled for. This may have masked the effect of the bedside aspiration correlating with pneumonia risk.

Contrastingly, there is much research disputing the true utility of pulse oximetry in aspiration risk. For example, swallow-related desaturation has also been shown to be a normal physiological phenomenon in the geriatric population [37]. Desaturation rates of 2% and 4% were found in 52% and 14%, respectively, of normal patients without dysphagia. This also indicates that desaturation is multi-factorial and difficult to robustly correlate with aspiration risk.

Bedside measures are renowned for their low sensitivity (50%; [38]) in detecting aspiration – partly due to patients without obvious clinical signs, known as silent aspirators. Nonetheless, aspiration detected by videofluoroscopy has been associated with up to a 7 fold increase in PSP [39] although detection of aspiration is neither a necessary nor sufficient condition to develop PSP. A recent trial with blinded assessors compared the accuracy of pulse oximetry, bedside assessment and videofluoroscopy in predicting unsafe swallows [40]. Previously quoted criteria for desaturation thresholds for identifying aspiration risk are generally between 2-4% [41]. This trial employed less stringent criteria of 2-5% to improve predictive ability. Despite this, it was found that desaturation was not significantly associated with detecting aspiration risk. In fact, pulse oximetry and bedside assessment, either used alone or in combination, did not show significant predictive value when compared to videofluoroscopy. Notably, lack of compliance led to high rates of non-inclusion and mild to moderate strokes. Other patients whom may have had a more severe stroke, bearing risk factors identified earlier such as reduced consciousness, would have been no doubt at a greater risk for aspiration and missed by this study. This suggests that desaturation may be a more viable indicator of aspiration risk in clinically severe stroke specifically.

Finally, a recent systematic review evaluated methods for identifying dysphagia [42]. Three studies employing desaturation > 2% to detect dysphagia found sensitivity ranging from 56% to 87% with specificity ranging from 39% to 97%. A combination of a water swallow test and desaturation improved sensitivity to 73-98% and yielded a specificity of 63-76% and was therefore concluded as the “best method to screen for dysphagia”. Notably, the ranges in these psychometric properties were hugely variable between studies. The conclusions that can be drawn from the systematic review are extremely limited given that data was only reliable from 2 of the included studies with potentially vast underestimation of dysphagia rates.

Conclusions

Post-stroke pneumonia adversely affects patient outcomes. Evidence shows that patients do worse acutely, in terms of mortality and institutionalisation and worse chronically, in terms of functional outcome. The major mechanism is typically dysphagia leading to aspiration. Other risk
factors may be conveniently divided into pre-stroke factors such as older age and COPD and post-stroke factors such as cognitive impairment and cognitive impairment. Stroke lesions may also predict the development of pneumonia. Lesion size, cerebro-basilar as well as multihemispheric lesions have been shown to be potent neuroanatomical predictors of PSP.

The clinical significance of PSP signals the need to intervene. Hence, the academic debate regarding the value of antibiotic prophylaxis. Current guidelines are driven by evidence suggesting that prompt treatment of PSP adequately reduces negative outcomes. This does little to formally warrant prophylactic intervention. The most recent meta-analysis concluded that prophylaxis caused a 15% reduction in pneumonia but didn't impact patient mortality. A NNT of 7 was generated highlighting the potential for development of prophylaxis. However, a lack of concordance pneumonia definitions, primary outcome measures and NIHSS inclusion criteria rationalise the need for further evaluation. These would benefit from secondary outcome measures including functional outcomes of patients.

Developing an effective screening tool for those truly at risk from PSP could improve the outcome of antibiotic prophylaxis trials. These could include the defined risk factors for PSP as well as a practical and repeatable test for aspiration. One such method is pulse oximetry with a desaturation > 2% indicating aspiration risk. Trials are inconclusive with older evidence suggesting a reasonable predictive value of combined desaturation and water swallow test. Newer evidence suggests that bedside measures are simply not sensitive enough to compete with specialised tests including video-fluoroscopy and fibre-optic endoscopy. Future longitudinal cohort studies need to verify whether a true correlation between desaturation and subsequent pneumonia exists.

In summary, there is a lack of high quality evidence to cogently argue the introduction of antibiotic prophylaxis. This signals the need for further investigation and Cochrane evaluation. Identifying risk factors and suggesting an easily repeatable test like pulse oximetry could herald the development of a psychometrically validated screening tool for the development of PSP. This would likely advance evidence in favour of antibiotic prophylaxis in select groups of patients.

References
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