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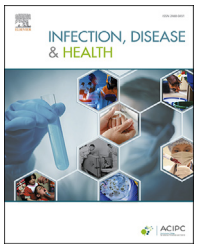

Discussion paper

What can the early infection preventing pioneers teach infection prevention and control teams today?

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Abstract *Background:* Puerperal fever and erysipelas were common Streptococcal infections of the 18th and 19th centuries which caused extensive nosocomial outbreaks. With dramatic clinical presentations and high-mortality, physicians struggled to understand and prevent them. Three infection prevention and control (IPC) pioneers (Gordon, Holmes and Semmelweis) in the pre-antibiotic and pre-epidemiology era made significant discoveries. Although much has been written of their breakthroughs, this has been selective and at times misinterpreted.
Methods: The primary sources of the three IPC pioneers (1 translation) were reviewed to present 3 narratives of their discoveries. An interpretation of the pioneers' discoveries in the current context is provided.
Results: The IPC pioneers' achievements are much wider than acknowledged in extant hand hygiene guidance — in relation to the role of indirect contact transmission (environment and equipment), e.g. Semmelweis considered the primary measure to prevent infection to be the avoidance of contamination — not hand hygiene.
Conclusions: The pioneers provided strong evidence of both direct and indirect transmission to significant 18th –19th century infections. They make a strong case for environment and equipment decontamination and cleanliness alongside decontaminating hands.

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Highlights The 3 most prominent Infection Prevention and Control Pioneers (Gordon, Holmes and Semmelweis), works have been reviewed:

- Gordon produced a line list of patients with puerperal fever. The list enabled for the first time Gordon to assert that puerperal fever was associated with specific physicians. Alas for Gordon, the most common person involved with cases, was himself.
- Holmes investigated cases of puerperal fever also noting clustering of cases associated with specific physicians. 4-Years before Semmelweis was appointed he recommended that doctors and midwives who deliver babies should not also do post-mortem examinations.
- Semmelweis — published 12 years after his discoveries. In that book he asserted that the most important means to prevent infection was to avoid contamination — not *per se* hand hygiene.
- Holmes and Semmelweis, both believed that transmission occurred via directly hands and indirectly via fomites.
- Current hand hygiene guidance has downplayed the full extent of the pioneers' discoveries and their conclusions.

Introduction

The streptococcal diseases, puerperal fever and erysipelas were once prevalent and, in the pre-antibiotic era, untreatable. Erysipelas presented anywhere on the body but most commonly on the face and legs [1]. Puerperal fever was a severe clinical infection presenting in the first 7 days post-delivery. Before a fully formed germ theory or the science of epidemiology, three Infection Prevention and Control (IPC) pioneers (Gordon 1795 [2], Holmes 1843 [3], Semmelweis 1861 [4]) sought to understand and prevent these diseases. Both diseases occurred sporadically and as nosocomial or community outbreaks. These IPC pioneers collected data, developed hypotheses, and experimented. In a reassessment of their historical breakthroughs, it became evident that their discoveries have, at times, been misinterpreted and this misinterpretation still impacts the focus of IPC today. Thus the reason for this paper was the discovery that renowned hand hygiene guidelines from the World Health Organization [5], and the Centers for Disease Control [6], provide a historical context that omits or de-emphasises the indirect routes of transmission as discovered by these IPC pioneers. These extant guidelines omit that both Semmelweis and Holmes considered indirect transmission a significant issue, and that both concluded the primary control measure to prevent infection was the avoidance of contamination — not hand hygiene [3,4]. Thus, arguments are made for acknowledging the IPC pioneers' wider achievements. Finally, the IPC pioneers' work merits retelling to provide insight on the discoveries that changed opinions, practices, and saved lives. The first pioneer is Alexander Gordon of Aberdeen.

Dr. Alexander Gordon 1752—1799 (published 1795)

Gordon was the first to present evidence to describe the infectious nature of puerperal fever (PF) and its transmission. In a 123-page treatise, Gordon detailed non-hospital clusters which began in Aberdeen in December 1789 and lasted 27 months [2a]. This was 66 years before Semmelweis's book was published. Gordon's key finding was the association of the disease with specific clinicians. Gordon stated he could foretell who would be affected based on who had attended the birth [2b]. He asserted he had "*evident proofs*" of the infectious nature of PF and its means of transmission stating "*every person who has been with a patient in the Puerperal Fever became charged with an atmosphere of infection which was communicated to every pregnant woman who happened to come within its sphere*" [2c].

To evidence this assertion, Gordon presented a table of 77 consecutive cases of whom 64% died [2d]. This table lists by name and address those women who were treated by Gordon for PF, and the names of the midwives/physicians who had delivered them. The data were presented as a case study. The information on women who were delivered by these clinicians but remained well were omitted. There are 21 physicians/midwives in the table (includes 1 indecipherable and 1 anonymous). Gordon delivered the most cases 16 (20.8%) which he acknowledged [2e]. There were 15 clusters of 2 or 3 cases which appeared consecutively for 8 physicians/midwives (Gordon had the most 5 clusters). However, Gordon's "*evident proofs*" appear insufficient as 7 (9%) of cases were delivered by a midwife who experienced just one case. A further 5 people had 2 or 3 cases separated by a considerable time period; however, *Streptococcus pyogenes* is known to colonise people and cause secondary cases with a time between cases of several months [7].

Gordon described the disease in painful-to-read details, as well as the pathological features from which he asserted its inflammatory character. Gordon considered that once transmitted, due to the injuries of labour, the contagion gained access and caused infection. He correctly recognises the similarities between PF and erysipelas. Of note, a nosocomial outbreak of erysipelas was happening alongside the PF clusters. Although they both arrived and ended at the same time, further connection was unmentioned [2f]. Gordon's error was focusing on a cure which was wrong (suggesting extensive bleeding of the patient). His chapter on prevention is the weakest. Gordon states "*I must speak with great uncertainty because in its matter I have not*

experience for my guide" [2g]. He refers the reader to another and recommends only that patients' apparel, and bedclothes were burnt or thoroughly purified and those in attendance ablute and get their clothes fumigated before being re-worn [2h].

Gordon provided strong evidence of the infectious nature of PF and its association with individual clinicians. The theory is however incomplete, as where 21 clinicians first acquired their 'atmosphere' before they transferred it is unexplained. Gordon's data were included in what can be considered a systematic review 1840s style by Holmes entitled the *Contagiousness of Puerperal Fever* [3].

Oliver Wendall Holmes Sr. (1809—1894) (published 1843)

Holmes, unlike Gordon and Semmelweis, was not an obstetrician and never cared for patients with PF. As part of a group of doctors he founded the Boston Society for Medical Improvement. In 1842, the society heard several reports of patients dying with PF and of a doctor who had died of a similar disease after sustaining a wound during a post-mortem (PM) on a patient with PF. Holmes resolved to investigate [8]. The result was a lecture to the society which was subsequently published in 28 pages [3]. It is challenging to evaluate the findings presented by Holmes as some references were incomplete, some were anecdotes and others personal experiences presented at meetings. All were written as a narrative. Holmes's evidence was tabulated (data not presented) and summarised as follows:

There are 16 anecdotes, i.e. a doctor reporting events he had second-hand knowledge of that support the assertion PF was associated with specific clinicians and not all [3]. In these anecdotes there was one case of a clinician performing a PM on a PF case prior to a cluster (2 cases) in patients who were subsequently delivered. There are just 2 suggestions of a possible indirect mode of transmission involving clothes and bed linen. The first is an anecdote of a 'nurse' who washed the linen of a fatal PF case who subsequently went on to deliver 2 women who became cases [3a]. There is another anecdote of a doctor attending a PM on a PF case, who without changing his clothes went on to deliver 3 women who subsequently acquired PF [3a].

There are 4 first-hand reports of single cases, whose physician/midwife had attended a PM of a PF case prior to attending these patients. There are also 15 first-hand reports of clusters involving between 2 and 43 cases (excludes Gordon's 77 cases). Of these, 13 mention a PM on a PF case preceding the onset of the cluster [3]. And 3 reportedly arose after the involved clinician cared for a patient with erysipelas or 'infection'[3].

The potential for contamination was great and illustrated by comments such as "… *carried the pelvic viscera in his pocket to the classroom … unable to wash hands he went without further ablution …*" [3b], "… *the contagion might have been carried on the gloves he had worn upon the previous case*" [3c].

From his findings in the literature and the anecdotes, Holmes goes further than merely stating that PF is contagious, but specifically, that it is carried to patients by attending clinicians. Holmes became convinced that the discharges from PF patients were highly infectious [3d]. Furthermore, Holmes proposes there was strong evidence sufficient to suggest that "*most fatal series of PF have been produced by an infection originating in the matter of effluvia of erysipelas*" [3e]. For prevention, Holmes provided 8 control measures. The first was that physicians who were preparing to attend midwifery should never take any active part in the PM of a PF case [3f]. If they do, they were advised to thoroughly ablute and change every article of clothes. These same precautions apply to the PM of erysipelas cases. Further controls, including abstinence from midwifery, apply to those clinicians who experienced cases. The final control measures relate to monitoring nurses and other assistants to prevent them from becoming a source [3f]. There is no recommendation regarding instruments and gloves (which were reportedly going from case to case) without decontamination.

Holmes began his treatise with a distressing image to help disbelievers understand why not all cases led to outbreaks: "*Children that walk in calico before open fires are not always burned to death*" [3g]. He ends by addressing those who still failed to believe in the contagious nature of the disease: "*whatever indulgence may be* granted *to those have here-tofore been ignorant of so much misery, the time has come … the practitioner … should give way to his paramount obligations to society*" [3f].

Holmes was charting the epidemiology of community cases of PF associated with some and not all clinicians. Holmes limits comment on nosocomial outbreaks other than to use derogatory terms to acknowledge the transmission therein: "*Impure lying-in hospitals*", "*pestilence of the Maternité*" [3h], "… *the murderous poison of hospitals*" [3i]. However, Holmes considered the evidence sufficiently strong to conclude and publish 4 years prior to Semmelweis's appointment that those in attendance at PMs of PF cases should not deliver women. This very thing was happening on an industrial scale in the Vienna Hospital.

Ignaz Semmelweis (1818—1865) (published 1861)

At the time of Semmelweis's appointment, it was known that the medical first clinic had an infection rate three times higher than the second clinic where midwives worked [4a]. This had been investigated but the variation in mortality remained unexplained [4b]. Two events led to the development of Semmelweis's theory. The first was the death of his friend from infection that developed from a PM injury, in which Semmelweis noted pathological similarities to those women who died of PF [4c]. The second was noting that in the 4 months prior to his appointment, when PMs went largely unassisted by medical students, there was a fall in the PF mortality rate [4d]. From these observations, he concluded that cadaverous material was being taken from the PM room to women in labour [4e]. Unaware of the work

of Holmes, Semmelweis considered that introducing a disinfectant hand hygiene regimen on entry to the labour suite would remove the cadaverous material from hands and prevent PF [4f]. Within 2 months of appointment this disinfection hand hygiene regimen, his first quality improvement (QI) initiative, began. There followed 3 months of the lowest mortality rates [4g]. However, two small outbreaks were attributed to contact with patients who were admitted and already infected [4h]. His second QI initiative was to extend the disinfectant hand hygiene regimen to include after contact with infected patients. These patients were also to be isolated [4h]. The third QI initiative was introduced when he recognised that contamination was also arising from "*everything that can come into contact with the genitals*" [4i]. Semmelweis provided a list of the fomites which carry cadaverous material "*the many items,* e.g. *sponges, instruments, washbowls, that are used for both the ill and the healthy, linen and bed equipment that is not always kept clean …*" [4j]. Thus, Semmelweis introduced the disinfection of instruments and advocated for better and cleaner hospitals. He also advocated the removal of items that could not be disinfected. Eight consecutive months of the lowest mortality rates followed [4k].

Semmelweis wrote of medical students failing to comply with his instructions — which he strongly reinforced [4l]. Others have attributed the failure to comply with his regimen to it being 'imposed' upon them [5]. However, this solution (chloride of lime) was a disinfectant that is today considered unsafe to use on skin [9]. It was to be used after soap and water washing for "*as long as is necessary to make the hands slippery*" [4m]. Thus compliance was likely affected from its harmful and unpleasant effects on skin.

In error, Semmelweis stated that "*With the exception of internal obstetrical examinations, an individual can carry out every possible medical examination with contaminated hands without the slightest danger*" [4n]. Semmelweis got the diagnosis right and proved the concept but the agent to remove the cadaverous material was harmful. His contract went unrenewed and he left in March 1849, by which time the data (presumably due to non-compliance) was at pre-intervention — non-outbreak levels. For all he is remembered for hand hygiene, his independent discovery of direct and indirect transmission and the need to disinfect instruments and keep the environment clean are rarely mentioned or attributed elsewhere.

Semmelweis concluded - as Holmes had before - that the most important means to prevent PF was to avoid people becoming contaminated, i.e., those who attend PMs should not also deliver babies [4o].

Discussion

This paper on the IPC pioneers' discoveries aimed to present a more inclusive summary of their achievements and to show that hand hygiene guidelines have been selective in presenting the 'historical perspective'. Gordon was the first to identify that the disease PF was the result of infection. Gordon's data came from a 27-month long outbreak involving 77 cases [2]. Holmes' data came from published reports, personal experiences and anecdotes [3]. Thus the identification that specific clinicians, and or specific procedures (prior PMs on PF or erysipelas cases), was easier to identify for Gordon and Holmes. In contrast, the Vienna Hospital where Semmelweis worked had over 90 cases in the first 2 months of 1846 and multiple people attended each case [4].

These works suggest that the contact modes of transmission were involved possibly exacerbated by airborne dissemination from patients and colonised midwives/physicians [2-4.]. Direct contact transmission involves two people, the source and the susceptible individual with no-one and nothing else involved [10]. Gordon identified that cases were connected to specific clinicians (including himself) [2]. Gordon considered that once 'affected', specific clinicians could transfer the infection to consecutive patients for some time thereafter. As the time between cases reported by Gordon and Holmes [2,3] was sometimes days and weeks, transmission from a single failure of decontaminating hands post contact with a case cannot explain all transmission. Although extremely rare today, this direct person-to-person transmission from a colonised HCW still results in outbreaks [11]. The airborne dispersal from colonised 'cloud HCWs' can arise when there is increased activity and friction with clothing [11]. Thus Gordon's claim that transmission was from clinicians being charged with 'an atmosphere of infection' [2c] appears apt. Holmes and Semmelweis's [3,4] descriptions of physicians going from the PM room to the delivery room without further or minimal ablution suggests that direct transmission via hands was occurring and playing a significant role. Additionally, only minimal hand decontamination could have been achieved by hands washed in a basin of water poured from a jug. However, given the descriptions of practice, the indirect route (from person-to-person involving someone or something else (fomites)) [10] must also have been significant.

Holmes and Semmelweis both recognised that the contagion is first acquired from contact with infectious materials from those, alive or dead, who suffered from PF or erysipelas [3,4]. In hospitals, the level of this contamination must have been overwhelming as so many patients died of PF and their dissected organs were handled by people wearing the same clothes when they subsequently examined women in labour. Of note, all three IPC pioneers considered that transmission involved more than hands [2—4]. Holmes stated it was carried by clinicians, but never specified hands (there was much discussion of clothes and other fomites). Semmelweis, alongside hand disinfection, introduced instrument disinfection and the banning of items in contact with the genitals that could not be disinfected. The descriptions of contaminated fomites, e.g. instruments, gloves and sponges being shared between patients suggests that indirect contact was a common mode of transmission [As an aside, and apparently unknown to Semmelweis, Holmes writes that his Vienna Hospital had previously identified 'sponges' as a contaminated fomite which transmits infection] [3j].

Thus direct transmission (person-to-person via touch) and indirect (person-to-person via another person or contaminated fomites) both played a role in the occurrence of outbreaks and incidences of cross-infection of both PF and erysipelas. That PF and erysipelas are today extremely rare is testament to improved practices and hygiene (hand, environment and equipment). It is still difficult to evaluate the size of the direct vs. indirect transmission routes. Although it is possible to see when hand hygiene is, and is not done, it is more difficult to detect when indirect

transmission occurs [12]. For example, one cannot see when pathogens dispersed by air land on people or surfaces or when items visibly clean but microbially contaminated are used. Effective hand hygiene is extremely important to prevent transmission from the hands of HCWs, but it does not negate the need for environment and equipment decontamination to prevent transmission. As always in IPC there are a plurality of risks and a plurality of actions needed to negate transmission.

For prevention Gordon offers little apart from recommending the opinions of others [2g]. However Holmes, went for an elimination strategy. To prevent the clinicians becoming contaminated Holmes recommended they should cease performing PMs on both erysipelas and PF cases and the care of women in labour [3f]. Semmelweis initially went for a strategy of hand hygiene (an administrative control which is considered less effective) [13]. However, when challenged by non-compliance and after identifying the risk from contaminated instruments, Semmelweis advocated the prevention of contamination as the primary measure. He appealed to governments to proclaim laws preventing those who deliver babies from activities likely to contaminate their hands. [4o]. That Semmelweis is considered merely the *father of hand hygiene* [5], and not the first person to recognise the importance of environment and equipment contamination and the instigator of instrument disinfection is baffling — particularly as he got the intervention (an unsafe-for-skin disinfectant) wrong.

The pioneers became strong advocates for their important discoveries. Gordon exaggerated the evidence in suggesting he had "evident proofs" [2c]. Holmes considered anyone who disagreed with him to be ill-informed [3]. Although Holmes cites evidence to support his theory and control measures, there is an absence of any critique of the citations [3]. For Semmelweis, the question remains, why as the only difference between the medical first and midwifery second clinic was the attendance at PMs, did he not stop the students' attendance as an initial control measure? The IPC pioneers' writings show that even those who made the greatest advances in infection prevention, left much to be discovered. This again highlights that quality improvement is a continuous journey and never a destination. The lessons for patient safety today are clear: aim to understand and improve, produce and analyse data, accept mistakes will be made, look to the evidence of others with an open mind and publish your work.

The final note - it is best to read seminal works first-hand - for both accuracy and recreation.

Conclusions

Three IPC pioneers provided strong evidence of both direct and indirect transmission to significant 18th and 19th century infections. They make a strong case for environment and equipment decontamination and cleanliness alongside decontaminating hands.

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Ethics

No ethical referral was required for this historical analysis.

Limitations

One source was a translation and thus there could have been some errors therein that could not be identified.

Declaration of competing interest

None to report.

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