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Short Communication

Mass food challenges in a vacant COVID-19 step-down facility: reflections on the management of anaphylaxis

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A popular western misconception dating back to at least the time of President John F Kennedy is that one of the Chinese characters in the word "crisis" means opportunity. The manuscript "Management of anaphylaxis in children undergoing oral food challenges in an adapted COVID-19 field hospital" [1] detailed a highly successful attempt to not only mitigate the effects of the crisis for elective care brought by the COVID-19 pandemic but to seek to maximize the opportunity by better utilization and redeployment of staff allowing the team to reduce pre-pandemic waiting lists by 57%. This project required significant engagement among many different relevant stakeholders and showed the potential for large-scale day procedure reorganization, not just for paediatric allergy services but also for other initiatives such as mass vaccination or developmental screening clinics. The primary contribution of this study was to demonstrate that oral food challenges (OFCs) could be carried out in an improvised field hospital environment. While this required significant planning, it showed that altered nursing and staffing ratios could be operationalized safely. Here we discuss the planning undertaken before during and after this project with an emphasis on how each issue relates to the literature and the clinician with a particular emphasis on anaphylaxis.

The first consideration was to ensure the safe management of potential anaphylaxis in a field hospital. With OFCs the risk of anaphylaxis is inherent in the process so contingency planning for this was required. Anaphylaxis is a severe potentially life threatening systemic hypersensitivity reaction characterized by the rapidity of onset with life threatening airway, breathing and circulatory problems often but not always associated with mucosal and skin changes. Prompt recognition and treatments are the principles of care. While in the OFC setting the allergen is obvious, up to 20% of cases in the community the elicitor cannot be identified [2]. The presence of a dedicated onsite anaesthetist experienced in paediatric airway management along with a fully equipped onsite resuscitation bay was deemed an absolute requirement by the planning team.

The first line treatment for any signs of a severe reaction is intramuscular (IM) adrenaline though a significant percentage (between 8% to as high as 20% in the community) will require a second administration of IM adrenaline [3-6]. One systematic review demonstrated 26% of emergency department presentations requiring a second dose [7]. This approximated the observed rate of second dose IM adrenaline in the field hospital experience at 28% of anaphylaxis cases (or 1.5% of all OFCs). Protocols were prepared, in accordance with the prevailing guidelines [2,8-11] with multiple simulations prior to launch. The planning team decided that in the event of a second dose of adrenaline being administered, the child would be then transferred to a paediatric hospital for further care. This contrasts with ED data where approximately 20% of patients requiring a second dose of adrenaline were discharged [7] following stabilization. None of the admitted patients in the OFC cohort required airway intervention or PICU admission and all were discharged the following day. This experience and the lack of adverse outcomes may help inform future initiatives.

International research has documented increased rates and severity of anaphylaxis in the community with increased rates of hospital attendance [12-17]. This included increased rates of PICU admission and has been observed in multiple environments while fatal food anaphylaxis

has fortunately remained largely static [16,18]. As a result of these observations and the fact that food remains the chief allergen responsible for anaphylaxis in children, the demand for OFC will most likely rise in the future. Therefore the field hospital experience should serve as a guide to the introduction of high volume challenge provision, even within the constraints of COVID-19 or another pandemic. The underlying reasons for the increase in severity and rates of anaphylaxis are unclear but chief risk factors for mortality have been identified in the paediatric cohort: delay to administration of adrenaline, poorly controlled asthma, nut allergy, adolescence and pre-existing cardiac and respiratory conditions [18-20]. As a result of the increasing burden of disease but relative stability in fatality figures the paradigm within allergy has changed from one of avoidance to more of a multidisciplinary model that seeks to improve overall quality of life for the child and their family. The role of education, appropriate adrenaline auto-injector provision and appropriate re-introduction of foods will have an on-going importance. The increased availability of peanut immunotherapy will have a positive impact on families over time.

The first line treatment of severe allergic reaction is well established as IM adrenaline [21]. With regard to IM adrenaline it should be noted that its administration supplements endogenous adrenaline. This fact explains why many cases of anaphylaxis may indeed be self limiting [22]. Nevertheless, there is no reliable biomarker or sign to determine which patients' symptoms will self-resolve and which will develop into life-threatening symptoms. Therefore as the adverse effects from IM adrenaline administration are usually minimal, we recommend if in doubt to give IM adrenaline in any case of suspected anaphylaxis. A 2007 Cochrane systematic review on the role of anti-histamines showed no clinical trials of sufficient quality existed, this paucity of evidence remains [23]. This lack of evidence has resulted in anti histamines use being largely removed from anaphylaxis guidelines [2,8,24-26]. Glucocorticoids are commonly used for the theoretical benefit of preventing a delayed biphasic reaction however their use has little to no evidence [11,27]. Nevertheless, glucocorticoid use remains common with 52% of those requiring adrenaline in the field hospital cohort also given oral corticosteroids. Bronchodilators may be given to treat wheeze however none of these treatments are alternatives to adrenaline. There is an on-going need for well-designed clinical trials to more fully assess each of these second line treatments. A key aim for allergy specialist is educating primary and even secondary health care providers on the primacy of adrenaline for anaphylaxis and to ensure that all other treatments are at best second line and in no way to be considered an alternative to adrenaline.

The decision to treat with IM adrenaline is a function of the severity of reaction. In the field hospital project 2 allergists or general pediatricians with a special interest in allergy were present each day covering the 3*6 bedded pods. In the community or home setting there may not be such experience to rely upon for guiding the decision to treat, as a result parents are often reluctant or unsure when to administer adrenaline. In the absence of controlled trials, the risk benefit payoff favors treating with adrenaline if there are concerns about a severe reaction. An ongoing body of research is dedicated to determining an evidence based severity grading system in order to facilitate accurate communication between patients and health care professionals and teams [26]. Within this body of research it is clear that a true consensus with regard to severity is lacking, for instance gastrointestinal symptoms are a common occurrence in food allergy whereas in venom allergy these same symptoms are an indication of systemic reaction [26]. Severity grading schemes may therefore be based on different triggers leading to a proliferation of scoring systems that may be difficult for the non specialist to apply and potentially warrants the provision of clinical decision support tools [26,28,29]. One recent study surveyed practicing pediatricians, providing 8 clinical scenarios with questions on whether the case constituted anaphylaxis and if adrenaline was warranted. This showed a high level of discrepancy with the highest consensus case only having 86% agreement, with most cases closer to 50% [30]. This discordance is common even within the allergy community with just one in 10 cases having a 90%+ agreement in another similarly designed study [31]. This highlights the on-going need for research dedicated towards homogenization of approaches towards anaphylaxis recognition and management, as the clinician a patient meets should not be a determining factor in management [32].

The emergence of food allergen immunotherapy (AIT) most commonly oral immunotherapy (OIT) for IgE mediated food allergies represents great opportunity along with practical challenges within the allergy field. OIT consists of daily ingestion of the particular allergen starting below the patients documented tolerated dose threshold. Doses would then be slowly increased with the aim to increase tolerance towards that specific allergen. This underlines the paradigm shift from the historic approach of avoidance with the OFC being to determine if tolerance has spontaneously developed. A diagnosis of IgE mediated allergy is necessary before AIT may be considered [33]. Guidelines have been drafted including by the EAACI on the approach to AIT [33]. AIT is a resource intensive process and requires many times the resources required for OFC. Contraindications would include risk factors for fatal anaphylaxis such as poorly controlled asthma. Eosinophilic esophagitis is a contra-indication due to the risk of the OIT exacerbating these symptoms. Consideration needs to be given to the likely spontaneous resolution of allergy in younger children, notably with cow's milk, egg, wheat and soy allergy. The current focus of practice is on AIT for peanut allergy and persistent cows milk or hen egg allergies [34]. In two recent trials OIT was superior than sublingual immunotherapy (SLIT) when measured by threshold dose, in that children could tolerate a higher dose [35,36]. OIT is associated with higher risk of adverse effects, thus increasing the need for appropriate staffing and organization. Doses administered successfully in the clinical environment may then be administered at home with parental understanding on the signs of anaphylaxis and knowledge on appropriate self-management. The effect of this approach is to drastically increase the number of visits to the day ward/clinical environment relative to a once only OFC. The field hospital experience indicates that large scale OIT may be viable and in turn reducing the burden of disease.

By a wide range of metrics the project was a success. Quantitatively, the increased numbers of completed OFCs showed this. Qualitatively, this was indicated by the high rates of family satisfaction, 83% rated the overall experience as excellent with 12% more deeming it above average. This is not to say however that this approach is suitable for all. Many allergic children will have special requirements that are not optimally catered for in this model, for example those <2 years of age or those with extreme anxiety potentially requiring play therapy or children with autism spectrum disorder who may find such an environment distressing. Patients in these and other cohorts that are at greater risk of severe reaction such as those with poorly controlled asthma would be best

accommodated with the traditional in hospital model.

This project was commenced in response to the opportunity afforded by unused step down capacity created in response to the COVID-19 pandemic. The extra limitations and demands placed on clinical services have led to the need for improvisation and the development of new well-designed models of care. The take home messages are numerous. This represented the collation of different clinical processes in a short space of time with adjustments made including the reallocation of general nurses with adequate senior allergy nurse specialist supervision. Trainee doctors and students were redeployed to this center also and adapted like other team members. Historically allergy departments, like many others, operated in relative isolation with minimal interaction with services such as clinical engineering, clinical risk, infection control and anesthesiology. With this project early and intense engagement was required with all stakeholders. In a 6-week period 474 OFCs were delivered, the separate contributing units would normally only deliver 900 cumulatively in 46 weeks. In Silicon Valley parlance, this is a truly disruptive approach that challenges the existing models of care. The inclusion of specialist trainees as well as medical students in this high volume model lends itself towards greater training opportunities where OFCs can be very often few and far between. An AAAAI report indicated that 56% of allergy fellows surveyed had the opportunity to perform 10 or less OFCs with 29% having performed none at all [37]. Implementation of this model would provide unparalleled experience to the trainee allergist in a safe environment where even the most severe anaphylaxis can be detected quickly and managed promptly.

The COVID-19 crisis has forced numerous changes to patient care. The pandemic crisis and the ensuing cancellation of elective care provided us with this unique opportunity to redesign food challenges for children. Crisis is the Latin form of the Greek "krisis ", often used by Galen and Hippocrates, meaning decision or a turning point in disease. This pandemic may well be a turning point in how we conceptualize the provision of elective clinical care in the future.

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