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RATIONALIZING PHOTOTHERAPY SERVICES DURING THE COVID-19 PANDEMIC: STRATEGIES AND IMPACTS ON PATIENT ACCESS AND OUTCOMES

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Background: Public health directives throughout COVID-19 have significantly constrained phototherapy services. At our centre, phototherapy was unavailable from March-June 2020, and then resumed at 50% capacity.

Objectives: We will assess the impacts of COVID-19 on patient outcomes and the efficiency of rationalization strategies utilized to optimize service delivery.

Methods: To objectively prioritize patients, nursing staff were trained to assess disease severity using a validated Investigator Global Assessment and Body surface area (IGAxBSA) scoring tool. Dermatology Life Quality Index (DLQI) questionnaires were completed by patients. Patients were treated using phototherapy regimens incorporating curtailed treatment frequencies (once or twice a week) over 10-week cycles, with higher incremental dosing (up to 20%).

Results: A total of 657 patients were undergoing phototherapy prior to clinic closure. Proportion of contacted patients declining phototherapy following re-opening was 31% (n=142). Baseline assessment of patients with psoriasis (n=192) and eczema (n=71), revealed median IGAxBSA scores of 20 (psoriasis) and 24 (eczema). Capacity modelling revealed a 75% cumulative percentile of IGAxBSA scoring distribution as the most optimal threshold for choosing treatment frequency. Based on this, patients had twice weekly treatment if IGAxBSA scores were ≥ 30 (psoriasis) and ≥ 40 (eczema). DLQI ≥ 21 (extremely large effect on quality of life) qualified for twice weekly treatment regardless of disease severity. Preliminary analysis on efficacy after ten weeks showed median IGAxBSA scores of 9 (psoriasis; n=129) (55% median improvement) and 16 (eczema; n=40) (33% median improvement).

Preliminary Conclusions: Our ongoing review will provide unique insights into the efficacy of objective service rationalization strategies.

Category: Early experiments with well-defined objectives/hypotheses

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BIASING OF ACTIVATED PROTEIN C FUNCTION TO ACCELERATE CUTANEOUS WOUND HEALING

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The serine protease activated protein C (APC) possesses dual functions as a vital anticoagulant and a cytoprotectant. In human pilot studies, topical and subcutaneous injection of APC has been shown to accelerate healing of cutaneous ulcers in poorly managed diabetes, pyoderma gangrenosum and chronic pressure sores. The regenerative functions of APC are attributed to its anti-inflammatory, anti-apoptotic and stabilization of epithelium. These cytoprotective effects are thought to be mediated by cleavage of protease-activated receptor 1 (PAR-1) expressed on differential cell types throughout the integument. Recombinant engineering of APC variants within the autolysis loop that possess no anticoagulant activity but preserved PAR-1 signaling are just entering larger clinical trials. Work from our lab has isolated a new physiologic pathway that biases APC activity towards PAR-1 signaling. Cleavage assays with N-terminal sequencing analysis and functional biochemical assays show that the enzyme plasmin proteolyzes APC within the autolysis loop and impairs anticoagulant function with no effect on PAR-1 signaling. Our findings parallel findings with engineered APC variants and implicate an alteration in APC activity with modulation of the autolysis loop. Plasmin has been shown to play an important regulatory role in wound healing by inducing keratinocyte migration and remodeling of the extracellular matrix. We believe that the functional modulation of APC by plasmin plays an important regulatory role in wound healing. Further dissecting this pathway may provide novel and exciting insights into the management of chronic wounds. This will ultimately further our understanding to develop new applications to accelerate the wound healing process.

Category: Early experiments with well-defined objectives/hypotheses

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RISK FACTORS FOR SKIN CANCER IN BC

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Background and Objectives: Risk prediction models can potentially aid in screening high risk patients. Most skin cancer prediction models are based on populations with high skin cancer incidences such as in Australia and therefore may not be generalizable to other populations. Also, previous studies have not adequately assessed clinical risk factors in their models. We aim to develop skin cancer risk prediction models incorporating clinical histories that are directly applicable to the North American population.

Methods: This is a case-control study from patients at the Skin Care Centre in Vancouver. Risk factor data (demographics, environmental exposures, medical history, phenotypic features, and sun exposure) is collected and used to develop skin cancer risk prediction models via logistic regression modeling.

Preliminary Results: A total of 299 patients have been recruited. 160 patients had ≥ 1 skin cancers, which include melanoma = 37, basal cell carcinoma (BCC) = 119, and squamous cell carcinoma (SCC) = 45, and 139 controls. Univariate regressions showed significant odds ratios to be: 6.91 (1.97-26.1), 5.21 (2.37-12.0), and 2.11 (1.03-4.26) for >20 adult sunburns, few freckles, and some/many nevi respectively for melanoma; 8.69 (2.68-39.3), 7.17 (4.06-13.3), 3.92 (1.60-10.1), and 3.43 (1.94-6.21) for many lentigines, history of actinic keratoses, >20 childhood sunburns, and age 71+ respectively for BCC; and 9.66 (3.64-33.5), 4.95 (2.17-13.4), and 3.51 (1.24-9.89) for age 71+, history of actinic keratoses, and 11-20 adult sunburns respectively for SCC.

Preliminary Conclusions: Univariate regression modeling demonstrates there are characteristics that will allow risk prediction models to identify high-risk skin cancer patients.

Category: Early experiments with well-defined objectives/hypotheses

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TOPICAL APPLICATION OF A NOVEL POWDERED SCAFFOLD FOR RAPID TREATMENT OF SKIN INJURIES

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Introduction: Limitations to skin-substitutes include antigenicity, poor wound integration, and precarious mechanical properties. To address these, our group previously developed an *in situ*-forming nutritional scaffold proven to accelerate wound repair. Due to its gel-like properties, this scaffold is optimized for cavernous wounds and requires a time-consuming reconstitution process. This study investigated whether a powdered form of this scaffold could accelerate healing of superficial wounds, thus broadening the range of applications while providing a ready-to-use product.

Materials and Methods: Splinted full-thickness wounds were generated on the backs of 12 mice and treated with either powder, the original gel scaffold, or no treatment (NT). Efficacy of the powder scaffold was assessed through comparison of clinical wound measurements and histological assessments.

Results: Powder application promoted wound epithelialization at days 7 ($p < 0.05$) and 14 ($p < 0.01$) compared to NT. Powder treated wounds were completely healed 20% faster than untreated wounds. Although no significant difference in wound epidermal thickness (ET) or dermal cellularity were found between treatments, both the ET and dermal cellularity in the tissue adjacent to the wounded tissue were significantly decreased ($p < 0.05$) compared to NT.

Conclusion: These results suggest that this powder scaffold may outperform standard wound dressing protocols and the native gel scaffold by accelerating wound closure while displaying fewer signs of aberrant healing. Through a rapid *in situ*-reconstitution that conforms to wound topography, this powdered scaffold may improve upon current models by providing a ready-to-use product that accelerates healing of superficial wounds.

Category: Applied/Functional Experiment

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ALLERGIC CONTACT DERMATITIS CAUSED BY TOPICAL MEDICAMENTS

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Topical medicaments are an increasingly frequent cause of allergic contact dermatitis (ACD), with the relative contribution of specific allergens constantly evolving due to the introduction of new products and shifts in their usage. Geographic variability is also seen due to the regional availability of certain products. Our objective was to characterize local trends in ACD to topical medicaments. A retrospective chart review was performed for patients patch tested at St. Paul's Hospital in Vancouver, BC between November 2016 and June 2019. Data from the North American Contact Dermatitis Group from 2015-2016 and Ottawa Patch Test Clinic from 2000-2010 were also reviewed. We focused on 12 allergens found in topical medicaments, including 3 antibiotics, 6 corticosteroids, 2 anesthetics and propylene glycol. Topical antibiotics remain the most common cause of medicament-induced ACD, making up 50.7% of the positive results in our study, with bacitracin being the most frequent. Lidocaine and benzocaine were the 3rd and 7th most common allergens, respectively. Propylene glycol was the 4th most common allergen, seen in 13.3% of patients testing positive to at least one of the 12 allergens, and in 1.8% of all patch-tested patients. For the 12 allergens under study, corticosteroids made up 18.3% of the positive reactions, with the most common being tixocortol pivalate (8.4%) and budesonide (5.6%). Cosensitization rates (number of cases positive to more than one allergen) were highest for the antibiotics: neomycin (22.9%), bacitracin (20%) and polymyxin B (18.6%).

Category: Pilot/Exploratory experiments

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VIEWING THE MICROSCOPIC SKIN WOUND HEALING RESPONSES TO PRECISE SELECTIVE PHOTOTHERMOLYSIS USING NON-INVASIVE MULTIMODALITY MICROSCOPY AND IMAGING GUIDED MICRO-RAMAN SPECTROSCOPY

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Background and Objective: The ability to restore tissue architecture and function after an injury is critical to health maintenance. Previous studies established that skin repair system involves specific and simultaneous processes for epithelial regeneration and dermal modification. In this study, we will investigate the specific events occurring during skin wound healing after highly targeted micro-injury.

Materials and Methods: A tightly focused ultrafast laser beam will be directed to flexural forearm skin to generate separate micro-thermal injuries in the epidermis and dermis, respectively. The treatment power will be set at 400 mW and the exposure time 2 s. Then a multimodality microscope which incorporates two photon fluorescence (TPF) signal, second harmonic generation (SHG), and confocal reflectance microscopy (RCM) is used to monitor cellular morphological changes and tissue architectural modifications. Imaging guided Micro-Raman Spectroscopy will be used to detect biochemical changes. The measurements will be taken at 7 time points, including: immediately after, 3hrs, 1 and 3 days, 1, 2, and 4 weeks after laser treatment.

Preliminary Results: The TPF signal of the treated area appears to be significantly increased immediately after the laser micro-injury. The fluorescence was still high at 1 week following treatment with gradual decrease in the intensity afterwards. No obvious collagen remodeling and dermal structural changes was recorded during the first week after treatment. Starting from 1 day following the laser treatment, small enhanced TPF points can be observed possibly due to the recruitment of inflammatory cells to the damage site.

Category: Pilot/Exploratory experiments

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HERPETIFORM STREPTOCOCCAL SKIN INFECTION IN CHILDREN: A REPORT OF 2 CASES

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Background: Acute skin and associated skin structure infections (SSSIs) are extremely common in children and can have a wide range of presentations from impetigo to necrotizing fasciitis. Specimens for cultures are often not taken and, even if an infection is suspected, antibiotic coverage is often empiric. Misdiagnosis of superficial skin infections and lack of recognition of bacterial superinfection can lead to delays in treatment and various sequelae can result if these SSSIs are left untreated.

Case descriptions: We report the cases of 2 patients who presented to an academic emergency department with herpetiform skin lesions and were subsequently referred to paediatric dermatology for further management. Due to the herpetiform appearance of the lesions, eczema herpeticum was considered in one case and dermatitis herpetiformis was considered in the other. Both were found to have Group A *streptococcus* skin infections and were appropriately treated.

Conclusion: These cases highlight the importance of performing swabs for bacterial culture to properly identify streptococcal infections when crusted herpetiform lesions are present. Proper treatment is important to prevent complications of streptococcal infections including rheumatic fever and post-streptococcal glomerulonephritis.

Category: Pilot/Exploratory experiments

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INTERFOLLICULAR DISTANCE: A NOVEL METRIC FOR ASSESSMENT OF HAIR FOLLICLE DISTRIBUTION ON THE SCALP

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Average hair density and hair diameter are two quantitative parameters that are often measured serially by trichometry in patients presenting to specialized hair disorder clinics. Both parameters contribute to the global appearance of hair loss on the scalp. However, neither parameter directly takes into account the spacing between follicular units. As such, follicular units that are clustered in very close proximity to one another, and those that are at notable distances from one another, could result in the appearance of focal or diffuse hair loss due to increased distance. We have devised a technique to compute the mean distance between all hair follicles in a trichoscopy image. In this proof of concept study, we have assessed this metric in various trichoscopy images that were acquired from patients with varying hair disorders. This metric has also been computed for various simulated scenarios to demonstrate how it can complement measurements of hair diameter and hair density. Finally, we have devised a mathematical model to yield the most ideal distribution of follicular units in a trichoscopy image. This model provides uniform spacing between follicular units in order to minimize the appearance of focal or diffuse hair loss. This metric may be able to supplement hair density and hair diameter measurements in the diagnosis of androgenetic alopecia. Furthermore, its use could be implemented in hair transplantation clinics to aid in hair follicle placement planning.

Category: Pilot/Exploratory experiments

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PROPYLENE GLYCOL: A COMMON INGREDIENT IN TOPICAL CORTICOSTEROIDS AND ITS ROLE IN ALLERGIC CONTACT DERMATITIS

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Background: Functioning as a solvent, humectant, emulsion stabilizer, preservative or antimicrobial, propylene glycol is a commonly used ingredient in cosmetics, personal care products, foods, and medications, including many topical corticosteroids. In sensitized individuals, it causes allergic contact dermatitis. Thus, the use of topical corticosteroids with this ingredient will complicate the treatment course of steroid-responsive conditions in sensitized individuals.

Objectives: To identify all topical corticosteroid products currently available in Canada that are propylene glycol free.

Methods: Using product monographs, with confirmation via product labels, and/or direct communications with manufacturers, we identified all propylene glycol-free topical corticosteroids preparations available in Canada in 2021.

Results: Out of 106 topical corticosteroid products made by various manufacturers, 24 products without propylene glycol were identified. We have created a practical clinical resource for practitioners to identify suitable topical corticosteroid treatment options for individuals with contact allergy to propylene glycol.

Category: Pilot/Exploratory experiments

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TERT PROMOTER MUTATIONS IN AMBIGUOUS MELANOCYTIC LESIONS

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Background: While the majority of melanomas can be distinguished from melanocytic nevi histologically, a subset of lesions are difficult to classify. An adverse outcome (recurrence, regional or systemic metastasis) occurs in 1-4% of these ambiguous melanocytic proliferations (AMPs). Recurrent TERT promoter mutations are reported in up to 65% of primary cutaneous melanomas but are rare in melanocytic nevi. Four hotspot mutations that create new transcription factor binding sites are predominant. Recent studies suggest that TERT promoter mutation status distinguishes melanoma from benign nevi with an accuracy approaching the current melanoma FISH assay. However, the predictive value in AMPs has not been established.

Objectives: The aim of this study is to determine whether TERT promoter mutations correlate with aggressive behavior in AMPs.

Methods: Cases meeting inclusion criteria of an AMP with >5 years of clinical follow-up are being identified by database search that includes hospitals across British Columbia. Histologic diagnosis and presence of sufficient residual tumor tissue are confirmed prior to DNA extraction and mutational analysis. Associations between mutation status and clinicopathologic features are determined by statistical analysis.

Preliminary Results: Ongoing chart review thus far returned 12 cases of AMPs with adverse outcome. DNA was extracted from three cases and yielded sufficient material for molecular analysis. A TERT promoter hotspot mutation c.228C>T was detected in one of the AMP samples.

Overall, these studies will help to determine the potential of TERT promoter mutation testing as a rapid and cost effective molecular tool for the diagnosis of ambiguous and unpredictable melanocytic proliferations.

Category: Early experiments with well-defined objectives/hypotheses

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**UNIVERSITY OF BRITISH COLUMBIA RURAL AND REMOTE DERMATOLOGY –
DESCRIBING CONSULT CHARACTERISTICS AND PATIENT DEMOGRAPHICS FROM MAY
TO DECEMBER 2020**

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We present preliminary results from a trial of telemedicine for small communities defined by the Rural Subsidiary Agreement (February 2020). The model had three components: telemedicine, working relationships, and education. Telemedicine between consulting dermatologists and referring family physicians were conducted by phone, text, teleconference, and email. Patient charts were held by a central Electronic Medical Record system (MedAccess). Privacy and confidentiality standards conformed to British Columbia (BC) legislation for “public bodies” (Freedom of Information and Protection of Privacy Act) with some exceptions allowed by a BC Public Health Order, which can be amended in the future. Data presented here are from May to December 2020. We highlight month-to-month call volume, billing data, patient population, most common diagnoses, Global Positioning System (GPS) location analysis (including distance to the nearest dermatologist), and referring provider method of contact. We will also present some early findings from telephone interviews with referring providers (about 50 to date). The evaluation of the latter two components, working relationships and education, will be later investigated.

Category: Early experiments with well-defined objectives/hypotheses

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AN OPTICAL INSTRUMENT FOR IMAGING-GUIDED BIOCHEMICAL ANALYSIS OF MICROSCOPIC SKIN TISSUE STRUCTURES *IN VIVO*

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Raman spectroscopy is an optical modality that captures highly specific spectral fingerprints of molecules thereby allowing their identification. It has been used for noninvasive skin cancer diagnosis, skin hydration analysis, barrier function assessment, drug penetration monitoring, and other skin related studies. Among various *in vivo* investigations, there are limited studies correlating microscopic tissue morphology of skin with corresponding Raman spectra, which would be helpful for detecting and analyzing the biochemical components that underlie *in vivo* cutaneous structures. To study this correlation confidently, two challenges must be addressed. First, the structure needs to be located and measured at the same time. Secondly, the Raman spectra acquired should cover the whole structure instead of a point to be representative. We are aiming to develop a confocal Raman spectroscopy (CRS) system for measuring histologic regions of interest with any shape under the visual guidance of reflectance confocal microscopy (RCM). This system integrates an RCM with a CRS measurement module. The RCM is used to optically section the skin and acquires skin tissue morphology data in real-time; specific tissue structures in any shape (e.g. point, line, curve, circle) can be selected and the corresponding Raman spectra measured simultaneously. The system's single field of view will cover 300 μm x 300 μm . The spatial resolution for the imaging and Raman measurement module will be 1.5 μm and 4 μm . The penetration depth will be 200 μm . The system will be tested for skin capillary blood analysis and skin cell type differentiation.

Category: Early experiments with well-defined objectives/hypotheses

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CRISABOROLE 2% OINTMENT VS CLOBETASOL 0.05% OINTMENT FOR TREATMENT OF PEDIATRIC CHRONIC HAND DERMATITIS

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In clinical practice, dermatologists have noted a favourable response treating pediatric chronic hand dermatitis using crisaborole 2% ointment. Chronic hand dermatitis often necessitates treatment with high potency topical steroids, which long-term may be associated with various adverse side effects. We plan to examine the efficacy of crisaborole 2% ointment compared to clobetasol propionate 0.05% ointment for the treatment of pediatric chronic hand dermatitis. A prospective controlled single blinded clinical study design will be used to compare crisaborole to clobetasol, whereby patients will apply clobetasol propionate 0.05% ointment BID to one hand and crisaborole 2% ointment BID to the other hand, for a total of 3 months. The patient will be assessed at the first visit by the dermatologist with the "Hand Eczema Extent Score" and the "Investigator Global Assessment" evaluations. Every month thereafter for 3 months the patient will be reassessed with the same evaluations. After 3 months, we will compare the changes in the scores at baseline to 1- 2- and 3- months post-initiation of treatment to determine if there is a statistically significant difference in the two treatment arms. The two treatment arms will be compared using a two-sample T-test. We hope this clinical study will provide more objective data to confirm or refute the clinical observation that crisaborole 2% ointment may be as effective as clobetasol propionate 0.05% in treating pediatric chronic hand dermatitis.

Category: Early experiments with well-defined objectives/hypotheses

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COMPARING THE BRITISH COLUMBIA CANCER REGISTRY TO HEALTH ADMINISTRATIVE CLAIMS-BASED ALGORITHMS FOR ASCERTAINING KERATINOCYTE CARCINOMA

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Keratinocyte carcinomas (KCs), comprising basal or squamous cell carcinomas, are the most common human malignancy in North America. The BC Cancer Registry coded and recorded all pathologically confirmed KC cases between 1970 and 1994 and then again in 2003. We aim to compare methods of KC ascertainment using previously validated health insurance claims-based algorithms to the BC Cancer Registry data, in the study period of the years January 1, 1992 to December 31, 1993, and January 1, 2002 to December 31, 2003. The Medical Services Plan and the BC Cancer Registry databases will be accessed within the Population Data BC system to identify KCs and this will be compared to the number of cases ascertained via claims-based algorithms. Ascertainment performance will be calculated (sensitivity, specificity, positive predictive value, negative predictive value). From these ascertainment approaches, we will derive descriptive statistics for skin cancer incidence. We hypothesize that MSP claims will be a reasonable surrogate for the "gold standard" (histopathological confirmation) in identifying KCs. PopData and claims-based algorithms can be used to assess healthcare burden of KCs in future epidemiologic studies.

Category: Early experiments with well-defined objectives/hypotheses

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IS VITAMIN D ASSOCIATED WITH CONGENITAL ICHTHYOSIS? A LITERATURE REVIEW FOR GUIDANCE IN MANAGEMENT

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Background: Congenital ichthyoses are a group of conditions that exhibit an impaired epidermal barrier due to mutations and are characterized by extensive scaling, hyperkeratosis and abnormal desquamation. Vitamin D deficiency is not uncommon in congenital ichthyoses, however, there is a paucity of knowledge within the literature on whether vitamin D supplementation or treatment can help manage the cutaneous manifestations of congenital ichthyoses. Current management strategies are limited and varying in success.

Objective: This review aims to scope the current state of knowledge on the clinical impact of vitamin D supplementation or treatment in individuals with congenital ichthyoses and to assess how vitamin D can be integrated in the management armamentarium for individuals with congenital ichthyoses.

Results: 7 published reports were included and reported on 19 patients with congenital ichthyosis. A large proportion of reported cases of congenital ichthyosis were also co-morbid with rickets requiring vitamin D₃ supplementation. With vitamin D₃ administration at high-dose or supplemental-dose, many cases reported clinical cutaneous improvement.

Conclusion: Checking vitamin D levels in patients with congenital ichthyoses may reveal a vitamin D deficiency. Vitamin D₃ supplementation may not only improve biochemical homeostasis, but also, may improve cutaneous manifestations of congenital ichthyoses. High-dose vitamin D₃ may be more effective than supplementation dose vitamin D in providing cutaneous benefit in individuals with congenital ichthyoses. Vitamin D₃ is a safe option for vitamin D₃ deficient patients with congenital ichthyosis and may be a useful adjunct therapeutic option to current management strategies.

Category: Pilot/Exploratory experiments

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MANAGEMENT OF PEDIATRIC STEVENS-JOHNSON SYNDROME AND TOXIC EPIDERMAL NECROLYSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Treatment of Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN) in children is challenging because of insufficient evidence to support one adjuvant treatment over another. We conducted a systematic review to summarize causes and disease associations of pediatric SJS, SJS-TEN overlap, and TEN (SJS/TEN) and quantify adjuvant treatment effects on mortality and healing time. The Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, Cochrane Database of Systematic Reviews, and the Database of Abstracts of Reviews of Effects were searched through February 2018. All studies with at least one patient up to 18 years old diagnosed with SJS/TEN reporting at least one outcome of interest were included. Two reviewers assessed studies' eligibility, risk of bias and performed data extraction according to PRISMA and MOOSE guidelines. A robust standard errors model was used for data synthesis. The primary outcome is mortality associated with SJS/TEN for each treatment group. Secondary outcomes include healing time assessed by surrogate measures (time to arrest of blistering progression, time to re-epithelialization, and length of hospital stay), disease-specific mortality, and sequelae. A total of 199 of 7587 screened studies met inclusion criteria. The most common causative agents were antibiotics (34%) and anticonvulsants (31%). The most common comorbid diseases were seizure-related disorders (31%) and infections (17%). There were 79 reported deaths (4.9%) demonstrating that mortality from SJS/TEN is low in children. Primary and secondary outcome measures stratified by treatment group are to be calculated to determine their effect on morbidity and mortality, if any, and results are to follow.

Category: Systematic review