Meeting Abstracts

Abstract #1

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS): Interest of Skin Tests.

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Rationale

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a severe adverse drug reaction. The main management of DRESS syndrome is the discontinuation of culprit drug. The identification of this drug can be challenging as many patients take multiple medications concomitantly. The aim of this study is to evaluate the usefulness of skin tests in identifying of causative drugs of DRESS syndrome.

Methods

We carried a retrospective study including all DRESS cases notified to the Department of Clinical Pharmacology at the University Hospital of Monastir between 2004 and 2022.The DRESS diagnosis was defined using RegiSCAR scoring. Six weeks after DRESS resolution, the skin tests were performed according to the ENDA recommendations

Results

We included **116** patients (50H/61F) with a median age of 54 years (from 4 to 86 years).The median time between starting medication and symptoms onset was 22 days. The most commonly affected organ was the liver. Skin tests to highly suspected drugs were performed in 99 patients (85 %) and were positive in 40 (40 %) of them. Carbamazepine was the drug most associated with positive patch tests (17/19 cases) followed by cefotaxime with positive intradermal tests (11/17cases). No positivity was detected neither with allopurinol (25 cases) nor with sulfasalazine (10 cases). No systemic reaction has occurred during skin tests.

Conclusion

Skin tests constitute a safe and useful tool in identifying the culprit drug in DRESS syndrome mainly for antiepileptic and antibiotic drugs. Further prospective studies still required to evaluate sensitivity and specificity of these tests in DRESS syndrome.

Abstract #2

The Value of Skin Tests In Exploring Co-Sensitization During DRESS Syndrome: A Case Series

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Rationale

Recurrence of drug hypersensitivity to chemically and pharmacologically unrelated drugs in patients with a history of DRESS syndrome known as '"neo-sensitization", is resulting from the administration of drugs during the immunological depression occurring in the initial DRESS episode. Neosensitisation is rarely described in the literature and can be proven thanks to skin tests which can be of valuable help to not only identify the causative drug but also to explore neosensitisation

Methods

We retrospectively analysed all cases of DRESS notified to the Department of Clinical Pharmacology at the University Hospital of Monastir over an 18-year period (2004-2022), using RegiSCAR diagnostic criteria.

Results

From 119 probable and definite DRESS cases according to RegiSCAR; 11 were retained in this study. The mean age of the patients was 45.1 ± 22.5 years (range: 3 - 73). The average latency period was 22.9 ± 8.5 days (range: 3-33). The commonest culprit drugs were anticonculsvant drugs (N=6) including carbamazepine: N=4 and lamotrigine: N=2, followed by allopurinol in 4 patients and cefotaxime in one patient. Generalised morbilliform exanthema in 10 patients. Facial edema, fever, and cervical adenopathy were seen in seven, eight and six cases, respectively. Eosinophilia was present in 10 patients with mean (±SD) value of 2857 ± 730 cells/µl. Liver was the commonest internal organ involved in night patients and kidney in four patients. Exploring sensitisation to newly, introduced drugs during DRESS let to positive intradermal tests in 10 cases for amoxicillin and one case for teicoplanine and paracetamol each.

Conclusions

Skin tests can be of valuable help to not only identify the causative drug but also to explore neosensitisation to newly applied drugs during dress syndrome leading to the recurrence of drug hypersensitivity.

Abstract #3

The Role of IFN-y ELISpot Testing in Drug Causality Assessment for Cotrimoxazole-Associated DRESS in an HIV Infected Population

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Rationale
Cotrimoxazole is a critical drug in the management of HIV. It prevents opportunistic infections, significantly reducing morbidity and mortality**.** However, it has been identified as a common cause of severe cutaneous adverse reactions (SCAR) such as DRESS syndrome. A challenge in treatment of this vulnerable population lies in the prompt identification and removal of the causative drug often amidst the context of polypharmacy. Through a review of cases within the IMARI-SA registry and biorepository we aimed to describe cotrimoxazole-associated DRESS and explore in-vitro IFNγ ELISpot as a diagnostic tool.

Methods
RegiSCAR DRESS phenotyping and Naranjo drug causality scoring was applied to all suspected cotrimoxazole-associated DRESS cases. IFNγ ELISpot was done on PBMC's with TMP/SMX and 4-NIT as targets.

Results
Twenty-five suspected cotrimoxazole-associated DRESS patients were identified (Naranjo>4). 15 DRESS patients validated so far as definite:4 (26.7%), probable:8 (53.3%) and possible: 3(20%) were selected. Majority were female (66.7%) and 80% had a TB diagnosis. Median CD4 count was 86 and mean age was 37 years. In 3(15%) cotrimoxazole was the highest scoring drug while in 12(80%) it was cotrimoxazole and other drugs. ELISpots were done on all validated cases. 4(26.7%) had positive ELISpot results (>50 SFU/million) to cotrimoxazole and/or its metabolite. 2(13.3%),4(26.7%),1(6.7%) had positive results to TMP/SMX 50/250 µg/ml, 4-NIT- 10 µg/ml, and 4-NIT-100 µg/ml respectively.

Conclusion

We present preliminary findings, which need investigation with an increased sample size. In view of the low ELISpot sensitivity, there is need for optimization and to explore other in vivo and /invitro drug diagnostic tools.

Abstract #4

Novel Technologies to Define the Immunogenomics and Immunopathogenesis of Severe Cutaneous Adverse Reactions

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Rationale

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) is a Severe Cutaneous Adverse Reaction (SCAR) mediated by interactions between human leukocyte antigens (HLA) and T-cells following the introduction of small drug molecules. SCAR are historically understudied due to low incidence of disease, difficulty obtaining patient samples, and a lack of laboratory methods to study disease pathogenesis. Additionally, low specificity yielded by patch and intradermal testing implicates the need for effective *in vitro* systems to determine culprit drugs.

Methods

The Phillips Lab is dedicated to implementing novel technologies in efforts to investigate individual cases of SCAR while contributing to the overall knowledge of the field. Here, we highlight four laboratory techniques that allow for the study of immunogenomics and immunopathogenesis of SCAR. Each case begins with HLA profiling and the identification of dominant T-cell receptors (TCRs) using single cell technology. These sequences can be used to create patient-specific cell lines for *in vitro* functional assays. Some cases of SCAR may not be caused by introduction of drug alone, but rather involve interactions with endogenous peptides which can be identified using T-Scan technology. Further study of disease pathogenesis includes the use of multiplex cytokine assays which will allow for identification of potential biomarkers of disease progression.

Results

Taken together, these technologies fulfill a critical need in identifying additional risk factors and biomarkers associated with SCAR.

Conclusions
The development and implementation of additional laboratory techniques can be utilized to employ new strategies for prevention and earlier diagnosis as well as promote targeted treatments in clinical settings.

Abstract #5

Sequential Drug Challenge Reactions to FLTB drugs in the context of DRESS in an HIV/TB Coinfected Population

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Rationale
First Line anti-Tuberculosis Drug (FLTD) associated DRESS in an HIV/TB co-infected population poses a complex diagnostic and therapeutic challenge. Sequential drug challenge (SDC) of FLTDs aims to provide an efficient way of identifying offending drug/s and avoiding unnecessary exclusions.

Methods
We aimed to describe clinical outcomes of SDC reactions in FLTD-associated DRESS in an HIV/TB co-infected population through a record review January 2019 – September 2022 at Groote Schuur Hospital (Cape Town, South Africa).

Results
21 cases of REGISCAR-validated DRESS (9 Probable and 12 Definite) experienced treatment excluding positive FLTD SDC reactions. Almost half were female(48%) with a median age of 34 years(IQR28-44). Antiretroviral(ART) and cotrimoxazole use at time of DRESS were 62% and 43% respectively. The median CD4 cell count was 112 cells/uL(IQR58-170). The median latency of DRESS from FLTD initiation was 18 days(IQR10-26) and the median time from DRESS to SDC was 28 days(IQR19-42). The median time to reaction from SDC was 36 hours(IQR12-110). Most common reaction symptoms were itching, rash, fever and facial oedema. Five cases additionally experienced non-treatment limiting reactions to FLTD or non-FLTDs on SDC. Multiple reactions to FLTD occurred in five cases; 80% were on ART with a median CD4 cell count of 58 cells/uL. This compares to the single reactor group where 46% were on ART (p=0.225) with a median CD4 count of 112cells/uL (p=0.1388).

Conclusions

Significant heterogeneity exists in timing, severity and number of treatment-limiting SDC reactions. Further work is needed to understand the biological basis of the heterogeneity of SDC reactions and why certain persons react to >1 FLTD.

Abstract #6

Vancomycin Drug Reaction With Eosinophilia And Systemic Symptoms Is Strongly Associated With HLA-A*32:01 In An Electronic Health Record-Based Study

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Rationale

Vancomycin is the most common cause of antibiotic-associated drug reaction with eosinophilia and systemic symptoms (DRESS), associated with a mortality rate of 10% and development of autoimmune diseases as long-term sequelae. We aimed to reproduce the association of HLA-A*32:01 and vancomycin DRESS and perform a genome-wide association study (GWAS) compared to a large electronic health-record (EHR) based cohort of vancomycin tolerant controls.

Methods

Vancomycin DRESS cases were identified prospectively from two academic centers (Vanderbilt University Medical Center [VUMC] and Austin Health) and evaluated for age, sex, and HLA-A*32:01. Vancomycin tolerant controls were identified using Synthetic Derivative, VUMC's de-identified EHR linked to a DNA biobank, BioVU. Controls were defined as adults, age >= 18 years, receipt of >= 10 days of vancomycin, and available MEGA^{EX} genotype array data. HLA alleles from MEGA^{EX} were imputed using SNP2HLA.

Results

Overall, 69 cases of vancomycin DRESS were identified with a median age of 55 years, 60% female and 72.5% HLA-A*32:01 positive. For vancomycin tolerant controls, 3,443 cases were

identified with a median age of 63 years, 74% female, and 5.7% HLA-A*32:01 positive. Carriage of HLA-A*32:01 was significantly associated with the development of vancomycin DRESS (p<.00001). In multivariable logistic regression, adjusting for age and sex, HLA-A*32:01 carriage was associated with an aOR, 44.2 (95% CI 23.6, 74.8), p=<2e-16. GWAS showed the most prominent signal to be within the MHC with other genes identified.

Conclusions

Vancomycin DRESS is strongly associated with HLA-A*32:01in patients exposed to prolonged vancomycin therapy when compared to vancomycin tolerant controls from a large EHR cohort.

Abstract#7

Assessment Of Lymphadenopathy In Patients With Drug Reaction And Eosinophilia (DRESS): A Comparative, Descriptive Study (EM)

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Rationale

Lymphadenopathy (LN) is part of RegiSCAR validation criteria of drug reaction with eosinophilia and systemic symptoms (DRESS), but HIV and TB co-infection are known to impact LN at different stages of the disease. This study aims to describe the prevalence of LN in DRESS and characterize quality, size, and distribution of lymph nodes in a high HIV/TB burden setting.

Methods

Twenty-five acute DRESS cases admitted to a tertiary centre in Cape Town, South Africa over a 26-month period were prospectively enrolled and systematically examined for LN. Hospitalised non-DRESS HIV/TB co-infected patients were used as controls.

Results

Fourteen of the 25 cases (56%) were HIV-infected, with a median (IQR) CD4 count of 254 (66-478) cells/mm^3 and 7/14 were TB co-infected. LN in 2 ≥ anatomical sites occurred in 18/25 (72%)

and in all seven with HIV/TB co-infection. In contrast, only 2/5xx/xx ((40%)) of hospitalised non-DRESS HIV/TB co-infected control patients had LN. Cervical LN in 17/25 (68%) was commonest, followed by axillary and inguinal. Cervical lymph nodes ranged between 1- 2cm in size. Amongst the 8/25 (32%) that followed up, LN had regressed in all within 6 weeks post cessation of offending drug and initiation of TB treatment. There was no correlation with CD4 cell count and LN.

Conclusion

Lymphadenopathy is a common feature of acute DRESS even amongst HIV and TB-co-infected patients with advanced immunosuppression.

Abstract #8

In-vivo and ex-vivo Have Long-Term Durability in Antibiotic-Associated Drug Reaction with Eosinophilia and Systemic Symptoms

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Rationale

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a presumed T cell-mediated drug hypersensitivities. The durability of T-cell immune responses to implicated drug over extended periods of time as well as *in vivo* (e.g., intradermal skin testing [IDT]) and *ex vivo* (e.g. Enzyme linked ImmunoSpot [ELISPOT] assay) tests remain ill defined. We sought to examine the durability of immunological responses over time in a cohort of antibiotic-associated DRESS.

Methods

We recruited 11 patients from two multicentre Australian prospective cohort studies with: phenotypic RegiSCAR scores of ≥ 4; ≥ 12 months from DRESS; and prior confirmed positive IDT or ELISpot assay. Following informed consent, we preformed ELISpot analysis and repeated IDT to known positive drugs.

Results

The median age was 54 and median REGIScar was 5. The median latency from DRESS onset to first performed testing was 109 days (IQR=229, Range 66-2782) and to secondary repeat testing was 1297 days (IQR=3182, Range 551-3692). The most common presumed causal drugs were vancomycin (n=7, 63%) and penicillins (n=3, 27%). Ten patients (90.9%) had positive IDT to initial and repeat testing. Nine patients (82%) had positive initial ELISpot and seven (63.6%) of these had positive repeat testing.

Conclusions

In vivo and *ex vivo* immune responses are durable over extended periods in patients with high phenotypic scores for DRESS - suggesting an increased utility of *in vivo* and *ex vivo* diagnostics in the post-acute period and that rechallenge remains unwise due likely persistent immune memory.

Abstract #9

T Cell Phenotype of Patients with DRESS Show Signs of Chronic Activation Even After Disease Resolution

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Background

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a severe multi-organ drug hypersensitivity reaction (DHR) involving T cells. DRESS patients are at risk of subsequent drug exposure leading to further DHR, resulting in a multiple drug hypersensitivity syndrome (MDH). This project aims to characterize DRESS patients with and without MDH to recognize which patients are at risk of further DHR.

Methods
In this prospective multicentre explorative study, we investigated the clinical picture, the T cell activation phenotype after DHR resolution and *in vitro* cytokine release of patients' leukocytes to tested drugs (cyto-LTT). Four groups were investigated: 8 DRESS without MDH (mono-DRESS), 13 DRESS with MDH (DRESS/MDH), 5 maculopapular exanthema and 5 healthy controls (HC).

Results
DRESS culprit drugs belonged to β-lactam antibiotics (12/21), non-β-lactam antibiotics (7/21) and antiepileptic drugs (3/21). All subjects were sensitized in cyto-LTT, while 14/21 were sensitized in patch test. DRESS patients' T cells show signs of chronic activation even during homeostasis compared to HC, with increased CD69 and PD-1 but reduced CD38 and OX-40. Based on T cell activation markers, DRESS/MDH is indistinct from mono-DRESS. Cyto-LTT with culprit drugs revealed a dominance of IL-5 release, with 10X more cytokines produced by MDH/DRESS patients' leukocytes.

Conclusions
DRESS patients' T cells remain chronically activated after DHR resolution. DRESS with or without MDH are likely the same phenotype, with increased drug exposure increasing the risk for MDH.

Abstract #10

The Immunological Profile of the Skin in DRESS Reactions to First-line Tuberculosis Drugs in HIV-infected Patients.

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Rationale
A greater incidence of severe cutaneous adverse drug reaction (SCAR) such as Drug Reaction with Eosinophilia Systemic Symptoms (DRESS) occur in HIV-infected patients. We sought to characterize the immunohistological phenotype of the skin in DRESS to first-line TB (FLTB) drugs in HIV infected cases, with a hypothesis that a possible depletion of T-regulatory cells (TREGS) and expansion of effector cells may contribute to DRESS in the context of HIV.

Methods
HIV cases with distinct DRESS phenotypes (probable or definite) and confirmed reactions to either one or many FLTB drugs were chosen (n=15). These cases were matched against controls of HIV-uninfected patients who develop DRESS (n=5). Immunohistochemistry assays were carried out with the following antibodies: CD3, CD4, CD8, CD45RO and FOXP3. Positive cells were normalized to the number of CD3+ cells present.

Results
Infiltrated immunoreactive T cells in DRESS were mainly found in the dermis. Dermal and epidermal CD4+ T-cells (and CD4+/CD8+ ratios) were lower in HIV-infected versus uninfected DRESS; $P < 0.001$ and $P = 0.004$, respectively. In contrast, dermal CD4+FOXP3+ TREGS were non-significantly increased in HIV-infected versus uninfected DRESS; median (IQR) CD4+FOXP3+ TREGS: [10 (0 - 26) cells/mm^2 versus 6 (3 - 14) cells/mm^2 versus, $p = 0.56$]. No significant differences in the number of dermal or epidermal T cell infiltrates were observed in HIV-infected DRESS patients clinically reacting to more than one FLTB drug (n=3) compared to single drug reactors (n=10).

Conclusions
CD4+ T-cells were decreased in HIV-infected DRESS, in line with known HIV pathology. While inter-individual variation was high, dermal Tregs were in fact increased in HIV-infected DRESS, and this requires further research to understand their role and possible impact on lower SCAR mortality amongst HIV-infected patients.

Abstract #11

DRESS Patients with Cytopenia Have Increased Length Of Hospital Stay: A Retrospective Cohort Study

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Rationale
Hematologic abnormalities are a well-documented feature in patients with drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome, but the relationship between these abnormalities and clinical outcomes is not known.

Methods
We performed a retrospective cohort study to examine demographics and outcome variables among DRESS patients with and without cytopenia. 65 patients were stratified into cytopenia groups based on blood cell counts at DRESS diagnosis.

Results
Average lengths of stay (days) for patients with thrombocytopenia (7.07), anemia (9.68), and leukopenia (10.83) were higher than those with normal counts (5.32). This effect was amplified in patients with leukopenia/thrombocytopenia (12.33), pancytopenia (15.5), and leukopenia/anemia (16.67). 20 (83%) of the 24 patients rehospitalized after discharge had cytopenia, with anemia accounting for most cases (N = 14). All five patients who died within a year of discharge had cytopenia. Significant differences were observed between patients with any cytopenia (N = 46) and patients with normal counts (N = 19) for age (54.5 vs. 47.0 years, p = 0.029) and length of hospital stay (7.0 vs. 4.0 days, p = 0.040), respectively.

Conclusions
Patients with DRESS syndrome and cytopenia are older and have longer hospital stays and higher death rates. The multiple cytopenia stratifications used in this study represent a unique way of examining DRESS patient features and highlights anemic patients as a potential high-risk group. Our data emphasize the importance of close blood count observation in DRESS patients and suggest a relationship between the presence of cytopenia upon diagnosis and worse clinical outcomes.

Abstract #12

Drug Reaction with Eosinophilia And Systemic Symptoms: A Systematic Review Of Current Literature

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Rationale
Drug reaction with eosinophilia and systemic symptoms (DRESS) is a life-threatening drug reaction; recognising the diversity of its clinical presentations, commonly implicated drugs and management modalities can aid in diagnosis and reduce morbidity and mortality.

Methods
In accordance with PRISMA guidelines, we reviewed all articles relating to DRESS between 1979-2021 in Pubmed, Medline and Embase.Only publications with an assigned RegiSCAR score of four or greater were included (indicating 'probable' or 'definite' diagnosis). If there was no assigned score in the publication, the authors assigned a score based on previous published methods. The main outcomes included implicated drugs, patient demographics, clinical manifestations, treatment and sequelae for each included publication.

Results
A total of 1124 publications were screened and 131 met the inclusion criteria, amounting to 151 cases of DRESS. Antibiotics and anticonvulsants were the most common implicated drug class. Cutaneous manifestations occurred in 99% of cases and the median onset was 24 days. Common features were fever, eosinophilia, lymphadenopathy and liver involvement.
Systemic corticosteroids were the mainstay of treatment. 13 cases (8.6%) resulted in mortality .

Conclusions
DRESS diagnosis is challenging due to the diverse clinical features and delayed onset.
However, this diagnosis should be considered in the presence of a cutaneous eruption, fever, eosinophilia, liver involvement and lymphadenopathy. The class of implicated drug may influence outcome, as allopurinol was associated with 23% of cases that resulted in death (3 cases). Given potential DRESS complications and mortality, it is importantly that DRESS is recognised early so that any suspect drugs are ceased promptly.

Abstract #13

Therapeutic Management And Outcomes Of Drug Reaction With Eosinophilia And Systemic Symptoms (DRESS) Syndrome

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Rationale
Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a potentially life-threatening drug reaction commonly treated with systemic corticosteroids. The goal of this study is to describe short and long-term outcomes for patients treated with topical versus systemic therapy at their initial hospitalization.

Methods
Patients diagnosed with DRESS by the inpatient dermatology service from 11/2012 through 1/2020 were identified. Cases with RegiSCAR≥4, or RegiSCAR=3 plus strong clinical suspicion for DRESS were included. Patients with DRESS greater than 6 weeks or those completing systemic therapy prior to consultation were excluded.

Results
80 patients were included. In addition to the discontinuation of causative drugs, 26 patients received systemic therapy and 52 initially received topical corticosteroids only. 22/52

subsequently required systemic therapy while 30/52 patients were successfully treated with topical alone. Indications for systemic therapy included hepatitis, severe cutaneous features, persistent fever, and rash progression. For patients initially receiving topical only versus those receiving systemic therapy, there was no statistically significant difference ($p<0.05$) in time from consultation to hospital discharge (8.3 versus 6.2 days), cutaneous flares, DRESS-related readmissions, and long-term sequelae. However, within the initial topical-only group, patients ultimately requiring systemic therapy had the longest time to discharge (14.3 versus 7.1 days).

Conclusions

While systemic therapy may not be necessary for all cases, a delay in systemic therapy may prolong time until discharge for some patients that initially receive topical treatment only. Further research is needed to evaluate markers of severity to better guide management decisions and to assess the frequency of treatment-related adverse events.

Abstract #14

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) Sequelae

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Rationale

While many may fully recover from drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome, some have persistent morbidity. We aimed to characterize sequelae and quality of life (QOL) associated with DRESS survivorship.

Methods

DRESS cases from Mass General Brigham were identified utilizing informatics methods and manually confirmed. We characterized sequelae of DRESS in an electronic questionnaire

including healthcare utilization and the Drug Hypersensitivity QOL Questionnaire (DrHy-Q), which was bidirectionally translated and adapted for content and face validity.

Results
40 participants (μ age 54 [SD 17.4], 63% female, 88% White, 5% Black, 5% Asian) had DRESS syndrome μ 5.6 (SD 3.4) years prior to questionnaire completion. Regular visits or hospitalizations after DRESS were reported for problems related to: skin (n=26, 65%), infections (n=10, 25%), heart/blood vessels (n=8, 20%), breathing/lungs (n=7, 18%), kidneys (n=7, 18%), thyroid (n=7, 18%), digestive/gastrointestinal (n=6, 15%), and liver (n=5, 13%). Skin problems included pruritus (n=16, 40%), drug rashes (n=14, 35%), dry skin (n=13, 33%), hives (n=9, 23%), and flushing (n=8, 20%). Many DRESS survivors reported fear of being given a drug to which they are allergic (83%). In addition, they expressed fear (63%) and anxiety (50%) because of their problem with medications, and worry in context of taking a new drug even if not the one that caused DRESS (58%).

Conclusions
DRESS survivors report longitudinal health problems across diverse organ systems. Skin problems were common, including drug rashes in over one-third. DrHy-Q responses indicate DRESS has substantial QOL impact. More detailed sequelae studies can inform DRESS follow-up care recommendations.

Abstract #15

Health-Related Quality of Life in Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) Survivors

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Rationale
Drug reaction with eosinophilia and systemic symptoms (DRESS) can result in significant morbidity for patients, but health-related quality of life (QOL) after DRESS is not well

characterized. We aimed to characterize health concepts for DRESS survivors utilizing the RAND 36-Item Health Survey 1.0 (SF-36).

Methods
DRESS cases from Mass General Brigham were identified utilizing informatics methods and manually confirmed. Participants consented to an electronic survey that included the RAND 36-Item Health Survey 1.0 (SF-36). Greater SF-36 scores indicate better health-related QOL, ranging 0-100. We compared mean SF-36 scores for DRESS participants to the general historic population from RAND sample using t tests. Data were analyzed using SAS (v9.4).

Results
40 participants (μ age 54 [SD 17.4], 63% female, 88% White, 5% Black, 5% Asian) had DRESS syndrome μ 5.6 (SD 3.4) years prior to completing the electronic questionnaire. Compared to population norms, DRESS survivors scored lower in physical functioning (66.50 vs 70.61, p=0.002), energy/fatigue (44.50 vs 52.15, p=0.03), social functioning (67.50 vs 78.77, p=0.006), pain (60.19 vs 70.77, p=0.009), and general health (49.00 vs 56.99, p=0.02). Health change (51.92 vs 59.14, p=0.05) and emotional well-being (66.30 vs 70.38, p=0.25) were also somewhat lower for DRESS survivors. Role limitations due to physical (61.46 vs 52.97, p=0.19) and emotional (67.08 vs 65.78, p=0.84) functioning were comparable.

Conclusions
DRESS survivors a mean of 5.6 years following DRESS reported lower QOL than population norms across many health-related domains. Future work must assess active interventions following DRESS, optimize clinical and supportive care, and improve QOL in this population.

Abstract #16

Outcomes And Long-Term Sequelae Of Drug Reaction With Eosinophilia And Systemic Symptoms (DRESS) In The Pediatric Population: A Systematic Review

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Rationale
In adults, the mortality rate of DRESS is estimated to be between 2 and 10%, and various autoimmune sequelae have been reported. Understanding the diverse clinical outcomes of pediatric DRESS is needed to inform guidelines for effective management and follow-up of these patients.

Methods
We conducted a systematic review of currently available articles on DRESS. Of 10,391 articles identified, a full-text review was conducted for 2,156 articles. 597 cases of pediatric DRESS were assessed, amongst which 200 have been analyzed thus far.

Results
We included 200 pediatric cases (mean age 9.4 years) in the analysis (see abstract St George-Hyslop et al.). After withdrawal of the culprit drug (100%), management strategies included systemic corticosteroids (80.5%), intravenous immunoglobulins (14%), and cyclosporine (0.5%), all either alone or in combination. Supportive therapy alone was reported in 12%. A flare-up of disease symptoms occurred in 13.5% of cases, usually associated with corticosteroid tapering over a median follow-up of 4 months (IQR = 1.5 – 9 months). Long-term sequelae were reported in 8% of patients, most commonly autoimmune thyroid disease (4%), alopecia areata (2.5%), and diabetes (2%). The mortality rate was 5.5%.

Conclusions
Although most children with DRESS recover, the mortality rate in the pediatric population is similar to adults. A significant number of pediatric patients develop long-term autoimmune sequelae, most commonly within the 1st year after resolution of DRESS. Structured follow-up and monitoring for sequelae in DRESS survivors are important to improve outcomes in pediatric patients.

Abstract #17

The DRESS Spectrum Of Severity: A Cohort Of Patients With mini-DRESS Syndrome

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Rationale
DRESS is well described in the literature, although many MPE present with symptoms/signs that resemble DRESS without meeting formal diagnostic criteria. This study describes a population of

patients that reported a reaction consistent with mini-DRESS or severe-MPE, defined as an extensive cutaneous exanthem with more than 50% of body surface area and a RegiSCAR score of 2 to 3 (possible DRESS).

Methods
Patients with antibiotic-associated hypersensitivity reactions, including delayed reactions such as DRESS and MPE, were prospectively recruited from Melbourne, Australia (03/2017- 09/2022). The RegiSCAR score was calculated, and *in vivo* testing (patch (PT) or delayed intradermal testing (IDT)) was performed on the implicated and alternative drug(s).

Results
1,102/2,175 reported a delayed reaction. Among these, 44 patients (57 allergy labels) had a recorded RegiSCAR of 2 or 3. The median age was 56.5 (44;64), with 50% (22) males and 95% Caucasians. The age-adjusted CCI was 4 (1,5), with 25 (57%) immunocompromised. The majority of the patients (32) reported a recent reaction (< 1 year; mean latency between the reaction and skin testing 152 days), 16/57 (28%) had a biopsy, 49/57 (86%) were hospitalized, and 38/57 (66%) received treatment. Penicillins (amoxicillin and amoxicillin/clavulanic acid [N=13/57], piperacillin/tazobactam [N=8/57]), were considered culprit in 53% (30) of patients, cephalosporins in 11% (6) and vancomycin in 6 (11%). Concurrent antibiotics were taken in 32/57 (56%) cases. Skin testing was performed in 40 patients (IDT – 35 [88%] and PT – 11 [28%]). Delayed IDT was positive in 21 (52%), with amoxicillin/ampicillin and penicillin G both identified in 14 patients, followed by piperacillin/tazobactam (N=8), flucloxacillin (N=6) and vancomycin (N=5).

Conclusions
We describe a cohort of patients diagnosed with "mini-DRESS" associated with beta-lactams and confirmed by delayed IDT. For this mild phenotype, beta-lactams predominate, with > 50% having confirmatory positive *in vivo* diagnostic approaches.

Abbreviations
CCI, Charlson comorbidity index; DRESS, drug reaction with eosinophilia and systemic symptoms; MPE, maculopapular exanthema.

Abstract #18

Differences in Laboratory Peak Days amongst Various DRESS Drug Triggers

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Rationale
Drug reaction with eosinophilia and systemic symptoms (DRESS) is a severe cutaneous drug eruption with a long latency period that may be confused with low risk morbilliform eruptions. Laboratory tests and internal organ involvement may provide insight into proper diagnosis, as recent reports have shown that liver abnormalities may appear before the onset of skin eruptions. (1) However, it is unknown whether laboratory values vary in peaks based on different triggers.

Methods
Patients were grouped into four groups based on causative medication (vancomycin only, Non-Vancomycin Antibiotics, Non-antibiotics, and Vancomycin and another antibiotic (Mixed)). Simple linear regression models were constructed with a response variable of the number of days it takes for each lab test (eosinophils, creatinine, ALT, AST) to reach their peaks.

Results
Among the lab values, only AST displayed significant differences in the number of days it takes to reach its peak. Compared to patients receiving only vancomycin (3.83 days), patients receiving mixed antibiotic vancomycin (0.33 days, β coefficient, -2.44 [95%CI, -4.54 to -0.35]; P= 0.024), and non vancomycin antibiotics (1.22 days, β coefficient, -1.14 [95%CI, -1.90 to -0.39]; P= 0.004) were associated with earlier AST peak days.

Conclusions
AST abnormalities in vancomycin-associated DRESS may be delayed compared to other triggers. Physicians need to be aware of this potential delay and monitor for delayed-onset liver injury in these patients.

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Abstract #19

An Informatics Roadmap to Facilitate DRESS Epidemiology and Pharmacogenomics Studies

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Rationale
Drug reaction with eosinophilia and systemic symptoms (DRESS) is a severe drug reaction with great diversity in presentation, making it difficult to identify cases. Utilizing informatics methods, we aimed to identify, validate, and recruit a DRESS patient cohort for epidemiology and pharmacogenomics studies.

Methods
DRESS cases were identified using informatics methods (including natural language processing [NLP] and machine learning [ML]), leveraging structured and free-text electronic health records (EHRs) of five decades (1980-2022) at Mass General Brigham, Boston, MA. We then validated cases via chart review and collected data using REDCap to facilitate epidemiology studies. Eligible patients who met inclusion criteria were recruited for sequalae and quality of life (QOL) surveys and pharmacogenomic studies.

Results
After chart review, 366 patients were validated with definite or probable DRESS. Most of the cohorts were female (n=214, 58.5%). Mean and standard deviation of age were 52.4 and 19.0, respectively. White (n=248, 67.8%) was the most common race, followed by black (n=38, 10.4%) and Asian (n=37, 10.1%). We further contacted 214 eligible patients with antibiotic DRESS, of whom 92 (43.0%) were interested in participating in the studies. As of October 7, 2022, 44 patients have completed a sequelae and QOL survey, 33 have returned saliva samples for genetic testing, and 20 have participated in qualitative interviews on their experience and symptoms during and after DRESS.

Conclusions
Our experience exemplifies a collaborative study led by a multidisciplinary research team who developed an informatics roadmap that can utilize large-scale EHR data for phenotyping and facilitating subsequent epidemiology and pharmacogenomics studies.

Abstract #20

Differences in Face-to-Face Time Spent with a Physician Among Patients With DRESS Syndrome Based on Race and Ethnicity

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Rationale
Race and ethnicity are important factors in understanding disease etiology, however, there is limited knowledge on how these differences affect the presentation of DRESS syndrome.[1,2] A 2021 study suggests that time spent receiving care may relate to severity of illnesses.[3] We thus aimed to evaluate the association between a patient's race and time spent receiving care for symptoms of DRESS syndrome.

Methods
We performed a cross-sectional analysis of data from the National Ambulatory Medical Care Survey from 2010 through 2016.[4] We identified all patients with DRESS syndrome using ICD-9 code 693, and ICD-10 code L27.0. A simple linear regression model was constructed to evaluate the association between patient race and visit duration for treatment of DRESS symptoms.

Results
A weighted estimate of 4,339,420 (95% CI, 2,665,844 – 6,012,997) patient visits for DRESS syndrome was identified. Compared to White patients who had a mean visit duration of 33.71 minutes, Black patients had a mean duration of 46.36 minutes (β coefficient, 0.3189 [95%CI, 0.3181 to 0.3196]; P< 0.0001), and Asian patients had a mean duration of 22.99 minutes (β coefficient, -0.3827 [95%CI, −0.3831 to −0.3823]; P< 0.0001).

Conclusions
Our findings provide evidence that time spent receiving care for symptoms of DRESS syndrome differs significantly among racial and ethnic groups. Further research is needed to assess whether differences in duration of visits are linked to severity of DRESS syndrome symptoms. These findings highlight a need for further research to identify potential racial predilections to the development and clinical course of DRESS syndrome.

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Abstract #21

Drug Rash With Eosinophilia And Systemic Symptoms (DRESS) Associated With An Arthritis: An Unusual Case

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Rationale
Although rare, DRESS syndrome is a life-threatening adverse drug reaction which could lead to multiorgan failure. The most frequently affected organs are liver, kidney and lung..We describe a case of DRESS with unusual organ involvement.

Case
A 50 year-old man, with no medical history, developed a diffuse skin rash with facial edema, on day 32 of metronidazole and cefotaxime and day 8 of teicoplanin administration, for lung abscess All antibiotics were discontinued. One day later, he complained of bilateral coxalgia, fever and loss of motion that affects his walking. Ultrasound of the hips joints revealed a bilateral articular effusion. Laboratory findings revealed eosinophilia and hepatic cytolysis. A DRESS associated with bilateral reactive osteoarthritis was retained (RegiSCAR score 7). One week after antibiotics discontinuation, the patient has completely recovered. Intradermal tests to cefotaxime and metronidazole were carried out and were positive to cefotaxime. Teicoplanin was re-administered without recurrence of symptoms.

Conclusion
We reported unusual case with atypical presentation of DRESS, highlighting the clinical heterogeneity of this entity. An early diagnosis and withdrawal of the incriminated drug could improve the prognosis of organ involvement.

Abstract #22

Identification of Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) Syndrome in Electronic Health Records

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Rationale
Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a rare and severe drug hypersensitivity reaction associated with substantial morbidity and mortality. Studying how DRESS syndrome has been documented in the electronic health records (EHR) will enable more efficient case identification that supports patient enrollment for epidemiological and pharmacogenetic studies and drug safety.

Methods
We applied rule-based informatics approaches to identify DRESS cases from Mass General Brigham between January 1, 1980 and June 19, 2020 via multiple (semi-)structured EHR components, including problem list, medical history, allergy list and encounter billing/diagnosis. Identified cases were manually confirmed by chart review. We assessed the prevalence, positive predictive value (PPV), and sensitivity of each EHR component for DRESS case identification.

Results
310 possible DRESS cases were reviewed, of which 240 (77.4%) had confirmed DRESS syndrome. The prevalence and PPV varied among EHR components: allergy list 206/245 (77.7%) problem list 94/104 (90.4%), encounter billing/diagnosis 93/102 (91.2%), and medical history 30/33 (90.9%). Sensitivities were 85.8%, 39.2%, 38.6%, and 12.5% respectively.

Conclusions
An EHR component alone is not sufficient to identify all DRESS cases and documentation quality varies. Although most of cases were only mentioned in allergy list, allergy documentation still requires improvement to support case finding and safe medication prescription.

Abstract #23

Identifying Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) Syndrome Cases Using Natural Language Processing from Clinical Notes

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Rationale
Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a severe reaction with high morbidity and mortality. Missed documentation of DRESS syndrome in structured electronic health record (EHR) fields can hinder its prompt recognition and safe medication prescription. We aimed to develop machine learning (ML) models to identify missed cases from free-text notes.

Methods
This study was conducted at Massachusetts General Brigham, Boston MA. We first created a labeled dataset by searching structured EHR fields (e.g., allergy list) for possible DRESS cases and reviewed their charts to confirm if DRESS syndrome was occurred. We then created another dataset by searching clinical notes using DRESS-related keywords. Multiple ML models (e.g., support vector machine [SVM] and XGBoost) were developed and validated for classifying DRESS syndrome using the two datasets. Predictors were n-grams generated from clinical notes documented between 1980 and 2022. The models were assessed in terms of AUC, F1 score, and precision at top 50 probable cases.

Results
The first dataset contains 315 cases, of which 216 (61.5 %) are positive cases. The SVM model achieved the best performance with an AUC of 0.89 and F1 score of 0.84. Applying the best performed model (SVM) to the second dataset, 217 (10.0%) out of 2161 cases were predicted as positive. Among the top 50 probable cases, 31 (62.0%) were true positive and 9 (18.0%) were possible.

Conclusions
Our study showed that ML model can identify additional DRESS cases merely mentioned in clinical notes and accelerate case recognition and drug safety.

Abstract #24

Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) Syndrome in the Immune Mediated Adverse Reaction of Southern Africa (IMARI-SA) Registry and Biorepository

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Rationale
DRESS is a severe cutaneous adverse drug reaction associated with significant morbidity, prolonged hospitalisation, and treatment complexity. DRESS is the commonest SCAR phenotype amongst HIV-infected patients.

Method
We aim to describe patients admitted with a diagnosis of DRESS Syndrome in two tertiary dermatology services in South Africa and prospective part of the IMARI-SA registry/biorepository, including patients admitted between 18 January 2019 and 25 October 2021.

Results
During this 34-month period, 96 patients were admitted with a provisional DRESS diagnosis. REGISCAR validation has occurred for 68(49%) with 28/68 (41%), 19/68(28%), and 21/68(31%) definite, probable, and possible DRESS respectively.
Of the 68 validated DRESS cases, 42(62%) were female with a median (IQR) age of 38 (30-47) years. Three quarters - 49(75%) were PLHIV with median (IQR) CD4 cell count of 141 (66-330) cells/mm3. Of HIV-infected DRESS, 44(65%) had TB and 33(67%) were on ART, and 23(47%) cotrimoxazole. First-line anti-TB drugs were suspected offending agents in 43/68(63%), cotrimoxazole 23/68(43%), and anticonvulsants 9/68(13%). 7(10%) cases had more than one drug suspected. Overall DRESS severity include median(IQR) BSA of 55% (30-70), with 37(54%) cases with ALT >2ULN. The median (IQR) length of hospitalisation was 22 (11-47) days with 12 (9%) deaths. Sequential drug rechallenge confirmed the offending FLTD in 31(46%).

Conclusion
In high HIV/TB burden settings, DRESS occurs most commonly due to FLTB drugs and cotrimoxazole. High proportions of severe immunocompromise, co-morbid disease, polypharmacy and limited treatment options make this a particularly vulnerable population with diagnostic and management complexities.

Abstract #25

Severe Cutaneous Adverse Reactions following Vaccination: A Systematic Review

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Rationale
Increasing cases of vaccine-related severe cutaneous adverse reactions (SCARs) are reported in the literature.

Methods
This was a systematic review on case reports, case series, observational studies, and post-market surveillance of SCARs following vaccination. Data on demographic information, classes of vaccination, past medical history and medications, and types, manifestations, management, and prognosis of SCARs, including drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalized exanthematous pustulosis (AGEP), Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), and generalized bullous fixed drug eruptions (GBFDE), were extracted.

Results
In the present systematic review on vaccine-related SCARs, a total of 1,788 cases of SCARs were identified from 7 cohort studies or post-market surveillance, 2 case-control studies, 2 case series, and 59 case reports. The varicella vaccine (n=247), measles-mumps-rubella vaccine (MMR) (n=241), and pneumococcal vaccine (n=239) contributed to most of the reported cases of SCARs induced by vaccines other than COVID-19 vaccines. Within cases of SCARs associated with COVID-19 vaccines (n=32), 16 cases (50%) received mRNA vaccines. AGEP and DRESS were more frequently reported with mRNA vaccines (31.25% and 25%, respectively) compared to viral vector vaccines (30% and 10%) and inactivated virus vaccines (0% and 16.67%). No SCAR has been reported for protein-based vaccines. Patients who developed SJS/TEN to COVID-19 vaccines were older than those with AGEP (56.8±18.6 vs 37.2±15.8, p=0.016).

Conclusions
Vaccine-associated SCARs consisted of a high proportion of AGEP and DRESS. Suspected culprits for DRESS included varicella vaccine, MMR, pneumococcal vaccine, and COVID-19 vaccines particularly mRNA, viral vector, and inactivated virus vaccines.

Abstract #26

Characterizing DRESS in Pediatric Patients: Major Associated Drugs and Clinical Presentations - A Systematic Review

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Rationale
Data on DRESS in pediatric populations is limited. A better understanding of the clinical presentation may facilitate earlier diagnosis and support the development of prospective studies.

Methods
We conducted a systematic review of DRESS. Of 10,391 articles screened, there were 294 articles involving 597 pediatric DRESS patients, of which 200 cases have been analyzed thus far. To explore if the clinical course of DRESS varies between children of different ages, we stratified our dataset into 3 cohorts: ages ≤ 5 years (n = 54), ages 6–10 years (n = 49), and ages 11-17 years (n = 97).

Results
DRESS was most commonly reported in patients aged 11-17, and many patients had an underlying seizure disorder (49%). Carbamazepine was the most frequently implicated drug, (21% of cases). The liver was the most impacted organ (87%), with manifestations including hepatitis and hepatomegaly. Hepatomegaly occurred in fewer patients over 11y (31% vs. ~50% for the two other cohorts), while renal failure and lower level of consciousness were more common in patients under 5y (7% vs. ~3% and 13% vs. ~3%).

Conclusions
Seizure disorders and the use of anti-epileptics were common in this pediatric population with DRESS. We detected a previously unrecognized trend of a lower level of consciousness amongst younger children, and variations in organ involvement between age categories. Prospective studies are required to further understand age-specific features of DRESS. Raising awareness of the diverse manifestations in DRESS across different ages would help improve early recognition and thus outcomes.

Abstract #27

Pediatric DRESS –Challenges in Management and Prognosis

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Rationale
Pediatric Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) is an emergent reaction to medications with a recurrence rate of up to 25% of cases and estimated mortality of lower than 10%.

Methods
This is a case regarding an 11-year-old Caucasian male with a history of recurrent pseudomonal otitis and mastoidectomy was diagnosed with DRESS Syndrome at the age of 9 due to cefepime and/or meropenem. He was started on systemic steroids. Over time, he has been diagnosed with iatrogenic adrenal insufficiency, osteopenia, obesity, migraines, severe narcolepsy with cataplexy, and Postural Tachycardia syndrome.
It has been exceptionally difficult to wean him from prednisone (30mg) with over 8 relapses in 2 years. After his 3rd relapse, he started mycophenolate mofetil (MMF) as a steroid sparing agent. Upon his 6th relapse secondary to a precipitous taper, IVIG was initiated and resolved his symptoms. He began maintenance IVIG every four weeks and tolerated a slow prednisone taper. He has tested negative multiple times for viral etiology.

Results
Currently, the patient is on a stable regimen of 18.5mg of prednisone with a taper of 0.5mg every other week, IVIG every 4 weeks, and MMF with frequent monitoring.

Conclusions
This case adds to the literature of pediatric DRESS. There have been reports of autoimmune polyglandular syndrome in patients treated with pulsed dose steroids and IVIG in the initial acute phase. Though our patient did not receive IVIG acutely, we wonder if patients who are predisposed to autoimmune conditions develop DRESS or if DRESS causes clinical expression of autoimmunity.

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Abstract #28

A Shorter Time to DRESS – Redefining Beta-Lactam Associated Drug Reaction With Eosinophilia And Systemic Symptoms

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Rationale
Drug reaction with eosinophilia and systemic symptoms (DRESS) is a severe cutaneous adverse reaction (SCAR) that can occur with exposure to many medications, including antibiotics. Traditional teaching suggests delayed symptom onset of 2 to 6 weeks following medication exposure, however, recent studies report shorter latency with antibiotic-associated DRESS. The aim of this study was to determine latency of confirmed beta-lactam DRESS in comparison to other antibiotic groups.

Methods
We utilized two prospective multicenter cohorts of antibiotic allergy tested patients to identify those with antibiotic-associated DRESS. Patients with beta-lactam or vancomycin-associated DRESS who had RegiSCAR score of >2 and with positive testing to implicated antibiotic (skin testing and/or Enzyme-linked immunosorbent spot (ELISpot)) were included. Those with vancomycin DRESS were also confirmed to be HLA-A*32:01 positive. We used linear regression for latency comparison.

Results
Twelve patients had confirmed beta-lactam DRESS and 17 patients had confirmed vancomycin-associated DRESS. Median latency with beta-lactam DRESS was 4.5 days, while median latency for vancomycin DRESS was 16 days; median latency of beta-lactam DRESS was 60% shorter compared to vancomycin DRESS (p=0.007) . The majority of patients (83%) with beta-lactam DRESS had latency less than 14 days (p=0.02).

Conclusions

Although our study is limited to small cohort, our findings of this rare disease suggest significantly shorter latency with beta-lactam associated DRESS than previously thought while vancomycin DRESS remained greater than 14 days. Early recognition of DRESS is essential to avoid disease progression, and awareness of shorter latency with specific antibiotic classes is crucial to diagnosis recognition.

Abstract #29

Duvelisib as a Novel Cause of DRESS Syndrome

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Rationale

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a rare drug-induced reaction that can be life-threatening. Duvelisib, an oral phosphatidylinositol-3 kinase inhibitor, is a medication recently approved to treat specific lymphoma and leukemia. We report a novel case of DRESS syndrome secondary to Duvelisib.

Methods

We describe the case of an individual with a past medical history of anaplastic large cell lymphoma treated with oral Duvelisib monotherapy. The diagnosis of DRESS syndrome was suggested per RegiSCAR criteria.

Results

The patient presented with fever and a diffuse erythematous pruritic eruption involving her arms, trunk, legs, and face. The onset of symptoms occurred 55 days after initiation of Duvelisib. Lab results were significant for increased peripheral blood eosinophilia and elevated liver transaminases. RegiSCAR score was five, suggesting a probable case of DRESS syndrome. Our patient's cutaneous and systemic systems resolved after a prompt removal of the offending agent and initiation of systemic steroids.

Conclusions

Severe cutaneous adverse reactions are listed as a boxed warning for Duvelisib; however, this is the first report to document DRESS syndrome secondary to Duvelisib in the literature. Our report attempts to increase awareness of the association between DRESS syndrome and Duvelisib to aid in early detection and prompt management.

Abstract #30

Ethambutol-induced Hypersensitivity Relapse Followed by DRESS Induced by Isoniazid: A Multiple Drug Allergy or Drug-related Relapse?

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Rationale

DRESS (Drug Rash Eosinophilia and Systemic Symptoms) induced by antituberculosis drugs (ATD) is frequently reported in literature. However, due to the concomitant multi-drug regimen, identification of the offending drug remains challenging.

Methods

We report a case of hypersensitivity relapse to ethambutol after isoniazid-induced DRESS in patients treated with first-line ATD.

Results

A 42-year-old female, treated with isoniazid, rifampicin, pyrazinamide and ethambutol for multifocal tuberculosis, developed, forty days later, hyperthermia, facial edema, cervical lymphadenopathy and generalized exanthema. Biological test results revealed eosinophilia, atypical lymphocytes, thrombocytopenia and liver injury. DRESS was suspected, and four antituberculosis drugs were withdrawn. As patch tests for the four ATD showed negative results, we decided to reintroduce pyrazinamide, ethambutol and rifampicin separately with a three-day interval. Pyrazinamide and rifampicin were tolerated by the patient. However, six hours after receiving ethambutol, she developed fever and generalized rash, with no biological abnormalities, which resolved two days later. Since ethambutol was claimed to be the culprit drug, isoniazid was added, and 10 hours later, the patient developed fever, facial edema, generalized rash, eosinophilia and liver injury. This clinical and biological pattern resolved two weeks later. Nevertheless, a

desensitization of EMB was performed, in our case, with success. However, the patient was unable to tolerate isoniazid desensitization

Conclusions

Based on the Naranjo algorithm it is probable that the systemic reaction was due to INH. This is an original case report describing an hypersensitivity (HS) to chemically unrelated drugs (INH/EMB). it's can be explained by either an initially INH- induced DRESS with HS relapse with ethambutol or a multiple drug reaction usually described with concomitant administration of ATD. This situation should be considered by the clinicians who should try to reintroduce the elicitor drug of HS relapse to optimize tuberculosis treatment.

Abstract #31

Drug Reaction With Eosinophilia And Systemic Symptoms (Dress) Syndrome To Iodinated Contrast Media

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Rationale

Delayed hypersensitivity reactions (DHRs) to intravenous low-osmolality contrast media (CM) have been described in the literature. In this study, we describe two cases of drug reaction with eosinophilia and systemic symptoms (DRESS) secondary to CM and the role of *in vivo* and *ex vivo* diagnostic tools for these patients.

Methods

Patients with CM-associated DRESS were recruited from Austin Health, Melbourne, Australia. *In vivo* testing (nonirritant intradermal testing (IDT)) was performed with the implicated (radiology confirmed and Naranjo scores ≥5) and available alternative CM (iohexol, iodixanol, iopromide

and ioversol) at 1:10 and 1:1 concentration. The concentrations were confirmed non-irritant following testing on five healthy controls. Interferon-□ enzyme-linked ImmunoSpot assay (IFN-□ ELISpot) was performed with the patient's peripheral blood mononuclear cells stimulated with the relevant ICM concentrations.

Results
Patient 1 was a 86 year old female known for HTN, AF and CKD with a CCI of 5. Before her DRESS RegiSCAR 5, she had presented two non-severe MPE to the same CM, iohexol. Patient 2 was a 34-male known for acute promyelocytic leukemia, type 2 diabetes mellitus, and bipolar disorder with a CCI of 3. This patient presented a RegiSCAR 6 DRESS where antibiotics and iohexol were considered culprits. In this context, the patient was subsequently re-exposed to iohexol and presented with a severe MPE. Both patients had a positive delayed IDT to the culprit ICM but also to iodixanol, iopromide and ioversol (latency testing patient 1 – 177 days and patient 2 – 65 days). In this context, no challenge to CM was performed. Patient 2 also had a positive delayed IDT to piperacillin/tazobactam and clavulanic acid, consistent with the multiple drug hypersensitivity syndrome described by WJ Pichler. The IFN-□ ELISpot was performed for both patients across a range of concentrations with inconsistent results.

Conclusions
In this exploratory study, including two well-phenotyped DRESS patients, we demonstrate, via *in vivo*, the implication of a T-cell delayed hypersensitivity to CM with a broad cross-reactivity pattern.

Abbreviations: AF, atrial fibrillation; CCI, Charlson Comorbidity Index; CKD, chronic kidney disease; HTN, hypertension

Abstract #32

Drug Rash With Eosinophilia And Systemic Symptoms To Anti-Tuberculosis Therapy: Retrospective Review Of Inpatients At An Academic Medical Center In The United States

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Rationale
Drug reaction with eosinophilia and systemic symptoms (DRESS) presents potential challenges when associated with antimicrobials for infections such as tuberculosis (TB).

Methods
We searched the UCSF dermatology inpatient log from 2009-2021, yielding 133 unique episodes of DRESS, including 67 (50.3%) attributed to antibiotics as first / equally likely culprit with 5 (3.5%) specifically to anti-TB treatment.

Results
Median patient age was 82; 80% were male. Rifampin was a likely culprit in 4 cases, isoniazid in 2, and ethambutol in 1; 3 cases involved 2 equally likely culprits (exclusively anti-TB agents in all 3). All 5 patients had morbilliform eruption and systemic DRESS manifestations: hepatic involvement in 5, fevers in 4, renal involvement in 1, pulmonary involvement in 1, and lymphadenopathy in 1. Four patients had new peripheral eosinophilia; 1 patient was on steroids for TB meningitis with possible blunting. Putative culprits were stopped in all 5 cases, with 1-3 antimicrobial discontinuations per patient. Four patients required prednisone, and 1 was treated with culprit agent withdrawal alone. Steroid duration ranged 3-56 weeks (mean 27.8). In 2 cases, TB impacted choice of steroid regimen (lower dose / accelerated taper); however, there was no mention of TB exacerbation with steroids for any of the 5 patients.

Conclusions
While this study was conducted in a TB non-endemic area, anti-TB treatment was implicated in 7.5% of cases of anti-microbial induced DRESS, highlighting the importance of these regimens in inducing such hypersensitivity in the US. While limited by small population size, TB exacerbation by systemic steroids was not reported.

Abstract #33

Oblique Earlobe Crease as a Novel Physical Examination Finding in Drug Reaction with Eosinophilia and Systemic Symptoms

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Rationale

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is associated with facial swelling, but this edema can be challenging to identify. This study evaluates the utility of a novel physical examination finding, the oblique earlobe crease, to support the diagnosis of DRESS.

Methods

This is a retrospective case-control study in which dermatologists evaluated for the presence of an oblique earlobe crease in patients diagnosed with DRESS syndrome compared to unmatched controls with morbilliform drug reactions, Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis (SJS/TEN), or acute generalized exanthematous pustulosis (AGEP).

Results

When comparing DRESS vs. all eruptions (low-risk morbilliform, SJS/TEN, and AGEP), the presence of an oblique earlobe crease had a sensitivity of 81% (CI 64-93%), specificity of 71% (CI 57-83%), and positive predictive value (PPV) of 68% (57-78%) for diagnosis of DRESS ($\chi 2$, $p<.0001$, AUC =.617).

Conclusions

The presence of an oblique earlobe crease on physical examination is a moderately sensitive and specific non-invasive indicator for the potential diagnosis of DRESS syndrome when compared to other SCARs and low-risk morbilliform eruptions. The presence of an oblique earlobe crease in a patient with a suspected drug eruption is a strong indication to proceed with additional laboratory testing to complete a validated DRESS scoring assessment given that the prevalence of bilateral diagonal earlobe creases in the general population has been reported to be only 2.7%.

The earlobe crease can be used as a proxy for facial edema, and therefore warrants consideration for incorporation into DRESS assessment systems.

End of Meeting Abstracts