## Contents

- Reviews & Comments .................................................................................................................. 4
- Disease Management And Clinical Features .................................................................................. 4
- Epidemiology ................................................................................................................................... 4
- Comorbidities ................................................................................................................................. 4
- Quality of life (QoL) ....................................................................................................................... 5
- Vitiligo triggers ............................................................................................................................... 5
- Case reports .................................................................................................................................... 5
- Understanding mechanisms of vitiligo pathogenesis ..................................................................... 5
- Genetic studies ............................................................................................................................... 6
- Candidate biomarkers .................................................................................................................... 7
- Mechanisms of treatments .............................................................................................................. 7
- Methodological advancements ........................................................................................................ 7
- Novel treatment modalities ............................................................................................................. 7
- Clinical studies and trials ............................................................................................................... 8
- Reviewed and prepared by: ............................................................................................................ 9
• The Vitiligo Noticability Scale, a novel tool to measure vitiligo treatment efficiency, beats routinely used percentage of depigmented skin in reflecting both patient- and clinician-reported global treatment success.

• Genetic variation might predict efficiency of phototherapy for vitiligo

• Wnt signaling pathway and miR-25 microRNA emerge as novel possible targets in vitiligo treatment

This is a review of research results in the vitiligo field which were indexed in the PubMed database (www.ncbi.nlm.nih.gov/pubmed) for the period from July 2015 till September 2015. Abstracts of papers were retrieved from the PubMed database using the search term "vitiligo" with a filter set up to retrieve records with creation date between July 01, 2015 and September 30, 2015. Retrieved records were manually checked for a relevance to and significance for the field of vitiligo research. Fifty three records were found to be relevant and of interest, and were included in this quarterly overview.
Reviews & Comments


Disease Management And Clinical Features

Batchelor et al. [PubMed] evaluated a novel patient-reported vitiligo treatment outcome measurement tool, the Vitiligo Noticability Scale (VNS). In this pilot study, authors found significant correlation of VNS with both patient- and clinician-reported global treatment success. Importantly, routinely used percentage of repigmentation showed weaker association. Thus VNS emerges as a better and more consistent indicator of treatment success, which should be further validated in large-scale studies.

Epidemiology

Based on analysis of 100 Indian male patients with nonvenereal genital dermatoses, Saraswat et al. [PubMed] identified vitiligo as the most frequently encountered one (18%) among 15 others conditions presented.

Comorbidities

Hammoud et al. [PubMed] conducted a meta-analysis of studies aiming to assess a risk of melanoma and non-melanoma skin cancer in vitiligo patients. Authors’ results confirmed that vitiligo patients have lower risk of skin cancer development, with possible reasons for this phenomenon being discussed.

Saylam Kurtipek et al. [PubMed] after analysis of 108 Turkish vitiligo patients found lower that previously reported rate of thyroid dysfunction, thus arguing the need for routine examination of vitiligo patients (at least in Turkish population) without clinical history for thyroid abnormalities. On the contrary, Yazdanpanah et al. [PubMed] confirmed high prevalence of thyroid disease in a group of Iranian vitiligo patients, with no difference found for patients with active or stable disease.

Results of Karadag et al. [PubMed] obtained for 61 vitiligo patients, suggest eye involvement, with vitiligo patients possibly being more prone to dry eye syndrome,
although larger studies are needed to confirm this. In line with this, Dogam et al. reported indeed apparent association between vitiligo and dry eye syndrome.

Quality of life (QoL)

Eleftheriadou developed a novel vitiligo burden questionnaire, which might facilitate development of consensus vitiligo treatment outcome measurement.

Boza et al. conducted translation, cross-cultural adaptation and validation of vitiligo-specific health-related QoL questionnaire (VitiQol) into Brazilian Portuguese thus enabling conduction of QoL studies among Brazilian vitiligo patients using this specific evaluation tool.

Vitiligo triggers

Wu et al. analyzed permanent hair dyes as vitiligo trigger.

Case reports

AlJasser et al. analysed series of cases comprising from 127 vitiligo patients treated by NB-UVB, for photolichenoid papule complications. This type of complication has been observed with the frequency 3.1%, it was reversible upon phototherapy withdrawal and was associated with longer treatment duration and higher cumulative dose. Based on this observation, authors warrant prompt recognition and management of this complication of phototherapy in vitiligo patients.

Byun et al. reported a case of successful childhood vitiligo treatment by He-Ne laser and topical tacrolimus, supporting efficiency of this type of vitiligo treatment reported earlier.

Gaurkar et al. reported a unique case of sequential development of several autoimmune disorders including vitiligo in HIV-seropositive patient.

Zhou et al. reported the first case of discoid lupus erythematosus complicated with vitiligo and hyperthyroidism.

Understanding mechanisms of vitiligo pathogenesis

Wang et al. investigated biological effect of protective genetic variant of aryl hydrocarbon receptor (AHR) gene variant and found that it confers increased transcriptional activity which correlates with increased production of regulatory T-cell cytokines, thus further extending knowledge about possible molecular pathomechanisms of vitiligo and providing a mechanistical link between genetic susceptibility to vitiligo and its impact on cellular and molecular processes.

Findings of Adly et al. on lowered glia-derived neurotrophic factor (GDNF) expression by vitiligo lesional keratinocytes suggest possible role of GDNF in vitiligo pathogenesis and prompt future studies in this direction.

Regazzetti et al. found that Wnt signaling pathway has specific alterations in vitiligo skin, namely, oxidative stress results in its down-regulation in both melanocytes and
keratinocytes, and Wnt signaling agonist induced repigmentation in depigmented vitiligo skin ex vivo. In summary, these findings point on Wnt agonists as a novel class of compounds potentially useful for vitiligo treatment.

Shi et al. found that oxidative stress results in induction of miR-25 microRNA in both keratinocytes and melanocytes which is responsible, besides direct promotion of oxidative stress-driven melanocyte destruction, for lowered production of key melanogenic factors, SCF and bFGF, by keratinocytes. These findings enlighten miR-25 microRNA as a potential target in vitiligo.

Wang et al. investigated possible role of Rnaset2 protein in vitiligo pathogenesis following previously identified genetic link between RNASET2 and vitiligo. The authors found that stress conditions induce Rnaset2 production by melanocytes and keratinocytes with suppressive effect on melanocyte outgrowth and migration, thus providing possible link from genetic susceptibility to pathomechanism of vitiligo. Involvement of RNASET2 gene in vitiligo might also be realized through the role of the Rnaset2 in regulation of antioxidant tone and response to oxidative stress as demonstrated by Caputa et al.

Machado do Nascimento et al. based on genetic and biochemical evidences, suggested that BCHE gene and its expression product, butyrylcholinesterase, are involved in vitiligo pathogenesis.

Al-Shobaili & Rasheed presented results of their study showing that oxidation of tyrosinase by reactive oxygen species might stimulate development of autoimmune reaction in vitiligo, thus providing yet another mechanism of melanocytic auto-antigen formation in vitiligo and additional role of oxidative stress as vitiligo trigger.

Genetic studies

Kemp reported association of ERCC1 gene single-nucleotide polymorphism with NB-UVB phototherapy efficiency in vitiligo patients.

Results of case-controlled (281 cases) study of Schunter et al. suggest association of FoxD3 transcription factor gene polymorphism with vitiligo and with thyroid immunoregulation as judged by association with elevated anti-Tg and anti-TPO antibody presence.

Results of meta-analysis conducted by Wu and co-authors suggest that -308 nt G/A polymorphism of tumor necrosis factor-α gene is not linked to vitiligo. At the same time, Lee & Bae concluded that it might be a risk factor in Middle Eastern population.

Rashed et al. reported association of ACE gene insertion/deletion polymorphism with vitiligo based on analysis of small (74 and 75 subjects) comparison groups, which replicates previous results obtained for Egypt vitiligo patients. In addition, an association has been observed with higher VIDA score and interleukin-6 level. The discrepancy between several other reports on the lack of ACE polymorphism association with vitiligo might be reasoned by ethnic divergence of genetic susceptibility to vitiligo, while effects of small sizes of study cohorts and case-controlled study design cannot be excluded.
Candidate biomarkers

Edgunlu et al. assessed serum level of TNF-related apoptosis-inducing ligand (TRIAL) and its receptor DR4 gene polymorphism in vitiligo patients. While no genetic association has been revealed, vitiligo patients had higher level of TRIAL. However the elevation was minor, and its significance in vitiligo pathogenesis remains unclear.

Abdellatif et al. investigated serum level of GM-CSF in vitiligo patients and healthy controls (40 subjects in each group) and found that vitiligo patients have 2-fold higher GM-CSF level. This finding is in line with previous report of Tu et al. and further suggest that GM-CSF might be one of the determinants in autoimmune pathogenesis of vitiligo.

Along with possible role in vitiligo pathogenesis, Shi et al. observed correlation between microRNA miR-25 serum level and disease activity.

Mechanisms of treatments

Ning et al. demonstrated that epigallocatechin-3-gallate (EGCG), a major constituent of green tea with potent anti-oxidant and anti-inflammatory activities, inhibit interferon-γ-induced activation of JAK2 protein kinase, a recently emerged promising target in vitiligo.

Lu et al. found that bilobalide, a main terpenoid constitutive of Ginkgo biloba extract, which was previously reported to be useful in vitiligo management, can attenuate hydrogen peroxide-induced melanocyte death, induce intrinsic cellular anti-oxidant defense system and reduce Hsp70 release, thus potentially (based on previously uncovered role of Hsp70 in vitiligo pathogenesis) suppressing autoimmune response against melanocytes.

Methodological advancements

Results of Gupta & Devendra demonstrated that microskin grafting is simple and efficient technique to treat genital vitiligo.

Sheth et al. reported development and initial validation of an automated computer-based image analysis program to objectively determine depigmentation area within a lesion. Development of software of this type would improve evaluation of treatment outcome, especially during clinical trials.

Novel treatment modalities

Garg et al. reported a development of novel ethosome-based hydrogel for improved skin delivery of methoxsalen. The developed delivery vehicle was characterized by enhanced percutaneous penetration of the drug with lowered phototoxicity and erythema observed in preclinical model.
Clinical studies and trials

Silpa-Archa et al. [PubMed] compared different methods of recipient site preparation and dressing compositions in melanocyte-keratinocyte transplantation. Authors concluded that broadly used dermabrasion is time- and labor-consuming while laser-assisted dermabrision, besides being costly, might increase risk of depigmentation. This experimental study was topped by a review on the topic by Al-Haldidi and co-authors [PubMed].

Abdel Latif & Ibrahim [PubMed] reported results of a left-right comparative study of 308 nm eximer light versus combination of topical steroids and vitamin D3 analogues on a group of 44 patients with localized and stable non-segmental vitiligo. Authors concluded that while the former treatment modality resulted in earlier onset of repigmentation, both treatments were efficient with no statistically significant difference at the end-point.

Park et al. [PubMed] unexpectedly found that combination of excimer laser phototherapy with topical tacrolimus, while being superior over either of the monotherapy at the beginning, likely does not provide better final (after 6 months) outcome than monotherapy.

Ashique & Kaliyadan [PubMed] presented results of retrospective analysis of 30 stable vitiligo patients who underwent suction blister epidermal grafting, with the conclusion on better efficiency on lips and face compared to proximities, and on small compared to large patches. Authors observed high efficiency of the method, with 50% rate of excellent response.

Bagherani [PubMed] reported results of 308 nm excimer light phototherapy alone or in combination with topical khellin and/or tacrolimus in vitiligo treatment.

Singh et al. [PubMed] reported results of comparative studies of oral minipulse corticosteroid and low-dose methotrexate in active vitiligo treatment and found equal efficiency of these two treatments in ceasing vitiligo progression, thus offering an alternative treatment for patients with contradictions for corticosteroid use.

Bao et al. [PubMed] in a single-lesion comparative study found that blister roof grafting, cultured melanocyte and non-cultured cell suspension transplantations are equally efficient in vitiligo treatment, with blister roof grafting giving faster repigmentation onset followed by cultured melanocyte and non-cultured cell suspension transplantation.

Leone & Paro Vidolin [PubMed] compared efficiency of excimer laser phototherapy combined with topical antioxidant cream or placebo in a left-right comparative study, with the finding on earlier repigmentation onset when antioxidant cream was used. However study cohort consisted from only 10 patients so the results should be considered as preliminary.

In line with several previous reports, Vachiramon and co-authors [PubMed] reported that addition of laser-assisted skin ablation to combination of NB-UVB and topical steroids in some cases might improve efficiency of treatment of resistant vitiligo lesions.

Singh & Nasir [PubMed] revealed that reservoir effect of clobetasol propionate and fluticasone propionate after their application on depigmented skin lasts for 5 days, so based on this data, reduction of frequency of topical steroid application for vitiligo treatment can be considered.
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