Sri Lakshmi Narayana Institute of Medical Sciences

Date-20-10-2017

From
Dr. K. Harsha Vardhan
Professor and Head,
Department of Dermatology,
Sri Lakshmi Narayana Institute of Medical Sciences
Bharath Institute of Higher Education and Research,
Chennai.

To
The Dean
Sri Lakshmi Narayana Institute of Medical Sciences
Bharath Institute of Higher Education and Research,
Chennai.

Sub: Permission to conduct value-added course: Acne vulgaris

Dear Sir,

With reference to the subject mentioned above, the department proposes to conduct a value-added course titled: **Acne vulgaris** on 20-11-2017. We solicit your kind permission for the same.

Kind Regards

Dr. K. Harsha Vardhan

FOR THE USE OF DEANS OFFICE

Names of Committee members for evaluating the course:

The Dean: Dr. Jayalakshmi

The HOD: Dr. K. Harsha Vardhan

The Expert: Dr. A. Buvanaratchagan
The committee has discussed about the course and is approved.

Dr. A. BUVANARATCHAGAN, MD.,
Reg. No. 27110
Asst. Professor, Dermatology
Sri Lakshmi Narayana Institute of Medical Sciences
Oosudu, Agaram, Puducherry - 605502

PROFESSOR & HEAD
DEPT. OF DERMATOLOGY
SRI LAKSHMI NARAYANA INSTITUTE OF
MEDICAL SCIENCES
OSUDU, PUDUCHERRY

Dr. G. JAYALAKSHMI, BSC., MBBS., DTCD., M.D.,
DEAN
Sri Lakshmi Narayana Institute of Medical Sciences
Osudu, Agaram, Kodiyakkam Post,
Villianur Commune, Puducherry - 605502.

Subject Expert

HOD

OFFICE OF THE DEAN
Sri Lakshmi Narayana Institute of Medical Sciences
OSUDU, AGARAM VILLAGE, VILLIANUR COMMUNE, KUDAPAKKAM POST,
PUDUCHERRY - 605 502.
[Recognised by Medical Council of India, Ministry of Health letter No. U/12012/249/2005-ME (P -II) dt. 11/07/2011]
[Affliated to Bharath University, Chennai - TN]

Circular

27.10.2017

Sub: Organising Value-added Course: Acne Vulgaris (Nov 2017 to Feb 2018)

With reference to the above mentioned subject, it is to bring to your notice that Sri Lakshmi Narayana Institute of Medical Sciences, **Bharath Institute of Higher Education and Research** is organizing **"Acne Vulgaris"**. The course content is enclosed below."

The hard copy of the application should be sent to the institution by registered/ speed post only so as to reach on or before 13-11-2017. Applications received after the mentioned date shall not be entertained under any circumstances.

Dr. G. JAYALAKSHMI, BSC., MBBS., DTCD., M.D.,
DEAN
Sri Lakshmi Narayana Institute of Medical Sciences
Osudu, Agaram, Kudapakkam Post,
Villianur Commune, Puducherry - 605502.

DEAN

Encl: Copy of Course content

COURSE PROPOSAL

Course Title: Acne vulgaris

Course Objective: to review the pathogenesis and current treatment modalities of acne to second year mbbs students

Course Outcome: Completed

Course Audience: second year mbbs students

Course Coordinator: Dr. K. Harsha Vardhan

Course Faculties with Qualification and Designation:

1. **Dr. K. Harsha Vardhan**
   Professor, Department of dermatology
2. **Dr. Buvanaratchagan**
   Associate professor, Dept of Dermatology

Course Curriculum/Topics with schedule (Min of 30 hours)

SlNo	Date	Topic	Time	Hours	Lecture taken by
1	20-11-17	Introduction to acne	5 to 7 pm	2 hours	Dr.K.HarshaVardhan
2	24-11-17	Skin microbiome	4 :30 to 6:30 pm	2 hours	Dr. Buvanaratchagan
3	28-11-17	Predisposing factors	5 to 7 pm	2 hours	Dr. K. Harsha Vardhan
4	4-12-17	Pathogenesis	4:30 to 6 30 pm	2 hours	Dr. Buvanaratchagan
5	8-12-17	Complications	4 to 6 pm	2 hours	Dr. K. Harsha Vardhan
6	12-12-17	General measures in management	4 :30 to 6:30 pm	2 hours	Dr. Buvanaratchagan
7	18-12-17	Grading of acne	5 to 7 pm	2 hours	Dr. K. Harsha Vardhan
8	25-12-17	Topical therapy	4 to 6 pm	2 hours	Dr. Buvanaratchagan
9	29-12-17	Systemic therapy	4 :30 to 6:30 pm	2 hours	Dr. K. Harsha Vardhan
10	2-1-18	Daily care for acne	5 to 7 pm	2 hours	Dr. K. Harsha Vardhan
11	5-1-18	How to choose products in acne prone skin	4 to 6 pm	2 hours	Dr. Buvanaratchagan
12	9-1-18	Caution in comedogenic skin	4 :30 to 6:30 pm	2 hours	Dr. K. Harsha Vardhan
13	15-1-18	Case discussion: different scenarios	5 to 7 pm	2 hours	Dr. Buvanaratchagan
14	19-1-18	Future modalities of treatment	4 to 6 pm	2 hours	Dr. K. Harsha Vardhan
15	24-1-18	Q&A, mcq	5 to 7 pm	2 hours	Dr. Buvanaratchagan
			Total Hours	30	

REFERENCE BOOKS: 1. Rooks Textbook of dermatology
2. Fitzpatrick's dermatology in general medicine

ABSTRACT-VALUE ADDED COURSE

1. Name of the programme & code

Acne vulgaris and DR06

2. Duration & Period

30 hrs & Nov 2017 to Feb 2018

3. Information Brochure and Course Content of Value Added Courses

Enclosed as Annexure- I

4. List of students enrolled

Enclosed as Annexure- II

5. Assessment procedures:

Multiple choice questions- *Enclosed as Annexure- III*

6. Course Feed Back

Enclosed as Annexure- IV

7. No. of times offered during the same

Nov 2017 to Feb 2018

8. Year of discontinuation: 2018

9. Summary report of each program year-wise

Value Added Course- Nov 2017 to Feb 2018					
Sl. No	**Course Code**	**Course Name**	**Resource Persons**	**Target Students**	**Strength & Year**
1	DR06	Acne vulgaris	Dr. Buvanaratchagan	2nd yr MBBS	15 (Nov 2017– feb 18)

10. Certificate model

Enclosed as Annexure- V

Dr. Buvanaratchagan — **RESOURCE PERSON**

Dr. K. Harsha Vardhan — **COORDINATOR**

ABSTRACT-VALUE ADDED COURSE

1. Name of the programme & code

Acne vulgaris and DR06

2. Duration & Period

30 hrs & Nov 2017 to Feb 2018

3. Information Brochure and Course Content of Value Added Courses

Enclosed as Annexure- I

4. List of students enrolled

Enclosed as Annexure- II

5. Assessment procedures:

Multiple choice questions- *Enclosed as Annexure- III*

6. Course Feed Back

Enclosed as Annexure- IV

7. No. of times offered during the same

Nov 2017 to Feb 2018

8. Year of discontinuation: 2018

9. Summary report of each program year-wise

Value Added Course- Nov 2017 to Feb 2018

Sl. No	Course Code	Course Name	Resource Persons	Target Students	Strength & Year
1	DR06	Acne vulgaris	Dr. Buvanaratchagan	2nd yr MBBS	15 (Nov 2017-feb 18)

10. Certificate model

Enclosed as Annexure- V

Dr. Buvanaratchagan

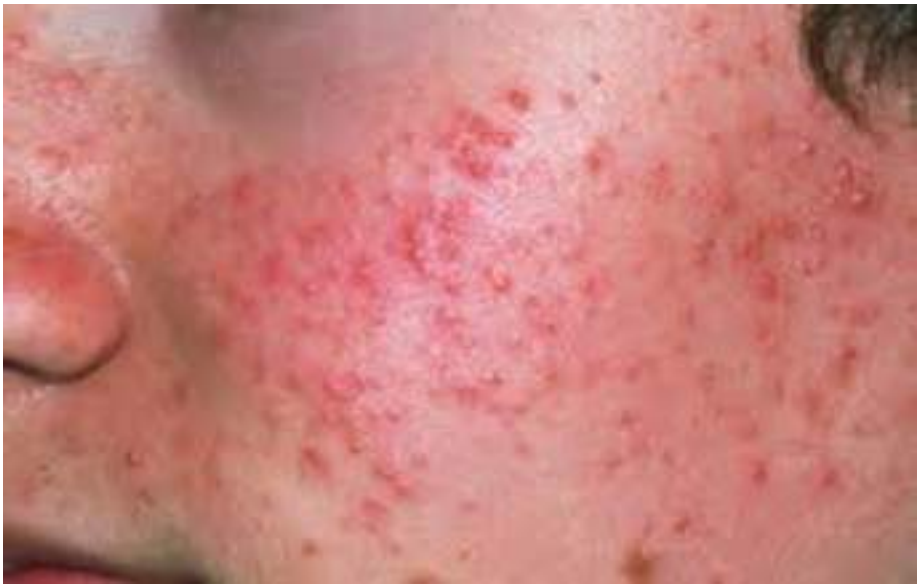
RESOURCE PERSON

Dr. K. Harsha Vardhini

COORDINATOR

ANNEXURE 1

ACNE VULGARIS-AN OVERVIEW



PARTICIPANT HANDBOOK

COURSE DETAILS

Particulars	***Description***
Course Title	*Acne vulgaris – An overview*
Course Code	*DR06*
Objective	1. *To learn about the clinical features* 2. *To learn about the diagnosis* 3. *To learn about the treatment*
Further learning opportunities	*Recent advances in management*
Key Competencies	*To make a diagnosis and provide adequate treatment*
Target Student	*2nd MBBS Students*
Duration	*30hrs Nov 2017 to Feb 2018*
Theory Session	*10hrs*
Practical Session	*20hrs*
Assessment Procedure	*Multiple choice questions*

Introduction

Acne vulgaris (commonly called acne) is a common, chronic skin disease that arises in the hair follicle and often involves inflammation. Approximately 85% of adolescents and young adults are affected by the disease,[1] while moderate and severe acne accounts for 15–20% of cases.[2] Based on the data from the Global Burden of Disease study in 2013, acne accounted for 0.29% of all skin conditions, which contributed 1.79% to the global burden of disease. Acne ranks second among the most common dermatological conditions after dermatitis.[3]

Four factors have been thought to contribute to acne: hyper-secretion of sebum, abnormal proliferation and differentiation of keratinocytes in the hair follicle, bacterial colonization, and host inflammatory response.[4] Among these factors, the skin commensal Propionibacterium acnes is thought to trigger an inflammatory response and lead to subclinical and inflammatory acne lesions.[5]

Skin is colonized by hundreds of microorganisms, which occupy different cutaneous environmental niches and form various communities.[6] When the normal flora is disturbed or the host immune defence is weakened, opportunistic microorganisms may trigger or aggravate certain skin diseases.[7] The relationship between skin microorganisms and acne has long been implicated but not fully elucidated. With the rise of the microbiome field in recent years, new findings from studies of the skin microbiome have provided improved understanding of the role of skin microorganisms in health and acne.[8–12]

Antibiotics have been an effective and widely used treatment for acne in the past four decades. However, worldwide increase of antibiotic resistance due to frequent and long-term use of antibiotics raises significant concern regarding how the commensal skin microbiome and its protective role for the skin are affected. A better understanding of the relationship among acne, the skin microbiome, and antibiotic treatment may provide new insight on the treatment of the disease while restoring a healthy microbiome.

THE SKIN MICROBIOME AND ACNE

The skin is the largest organ in the body, with an average area in adults of 1.8–2 m2. If considering hair follicles, sweat gland ducts, and other skin appendages, the body surface area can reach up to 30 m2 according to Meisel et al. Various heterogenous communities of microorganisms, including bacteria, viruses, fungi, and mites, occupy different skin environmental niches and appendages.[6,14]

Bacteria are the most dominant and best studied members of the skin microbiome. More than 40 bacterial genera have been identified on human skin, mainly belonging to four phyla: Actinobacteria, Firmicutes, Proteobacteria, and Bacteroidetes.[8–10] The proportions of these bacteria in each community vary depending on individuals, body sites, as well as skin micro-environments.[9,11,15] Propionibacteria, Staphylococcus and Corynebacteria, and Gram-negative bacteria are predominant in the sebaceous area, moist skin, and dry skin, respectively. Skin bacteria are not only diverse in taxonomy, but also vary in quantities. Culture based methods suggest that the total colony-forming units per cm2 skin varies from 3.7 × 104to 1.2 × 106.[16] It has been estimated that 106 aerobic bacteria are present per cm2 of moist skin, whereas less than 102 aerobic bacteria and up to 106anaerobes are present per cm2 of dry skin.[17] The balance of the skin microbiome and its interaction with the host affect the states of skin health and disease.

Propionibacterium Acnes and Acne

P. acnes was first observed by Unna[18] in 1896 and later isolated by Sabouraud[19] from acne lesions in 1897, which led to speculation regarding its involvement in acne pathogenesis. P. acnes was initially named Bacillus acnes, which was then changed to Corynebacterium acnes as it is morphologically similar

to Corynebacteria. The name was changed again in the 1940s to P. acnes due to its production of propionic acid.[20] With the identification of distinct phylogenetic groups based on multi-locus sequence typing (MLST) and whole-genome sequencing, it was proposed in 2015 to name the three major types as three subspecies known as P. acnes subsp. acnes, P. acnes subsp. defendens, and P. acnes subsp. elongatum.[21] In 2016, a new genus, Cutibacterium, was proposed for cutaneous propionibacteria[22] and, as such, P. acnes was renamed again to Cutibacterium acnes, although the name P. acnes continues to be used in the field in an effort to reduce the confusion between Cutibacterium and Corynebacterium.[23]

In the pilosebaceous unit, where acne arises, P. acnes is the most prevalent and abundant species, accounting for ~ 90% of the microbiome.[10,12] The scalp and facial skin harbour the highest density of P. acnes (~ 105–106/cm2), followed by the upper limbs and torso, and the lower limbs have the lowest density of P. acnes (~ 102/cm2).[24] The abundance of P. acnes also varies with age. It is low on the skin of children before puberty, but gradually increases with age, starting from adolescence to adulthood, and then decreases in older persons of age above 50 years.[24–26]

Several mechanisms of acne pathogenesis involving P. acnes have been proposed, including changes in sebaceous gland activity, comedone formation, and host inflammation.

- Increasing sebum secretion: the colony-forming units of P. acnes in the pilosebaceous unit are correlated with the total amount and composition of the lipids on the skin. The secreted sebum is used by P. acnes as metabolic substrates to promote its growth.[24,27]P. acnes further enhances sebum secretion by increasing the activity of diacylglycerol acyltransferase, and exacerbates pre-existing androgen-related seborrhoea.[28]

- Promoting comedone formation: P. acnes breaks down triglycerides secreted from sebaceous glands and releases free fatty acids. Porphyrins secreted by P. acnes are catalytic factors for the oxidation of squalene, a main component of sebum. Free fatty acids and oxidized squalene promote comedogenesis.[29] Comedones form due to retention of hyper-proliferating keratinocytes/corneocytes in the follicular duct. Studies have shown that P. acnes not only forms a biofilm to increase keratinocyte adhesion,[30,31] but also activates the insulin-like growth factor 1 (IGF-1)/IGF-1 receptor signaling pathway to up-regulate filaggrin expression. The up-regulation of filaggrin expression leads to increased levels of integrin-α3, -6 s, and -vβ6, and thereby affects keratinocyte proliferation and differentiation[32,33] and comedone formation.

- Inducing/aggravating inflammation: upon binding to Toll-like receptor (TLR)-2 and -4 on the surface of keratinocytes, P. acnes induces monocytes and other cells to produce interleukin (IL)-1α, IL1-β, IL-6, IL-8, IL-12, tumour necrosis factor (TNF)-α, interferon, chemotactic factors, β-defensin, and other cytokines and polypeptides, thereby triggering and/or aggravating inflammatory responses.[34–37]P. acnes also activates the classical and alternative complement pathways to form C3a and C5a, which increase the vascular permeability and the involvement of chemotactic leukocytes in inflammatory responses.[38,39] Furthermore, P. acnes stimulates sebocytes and promotes the conversion of naïve T cells into T helper (Th) 17 cells by secreting transforming growth factor-β, IL-1β, and IL-6. P. acnes can

also activate the NLRP3 inflammasome to induce the release of IL-1β, IL-8, and TNF-α from sebocytes.[40] P. acnes produces lipases, proteases, hyaluronidases, and phosphatases, and induces multiple cells to produce matrix metalloproteinases, thus directly impairing hair follicles, sebaceous glands, and dermal extracellular matrix, and ultimately aggravating inflammation.[41–43]

While a causal role of P. acnes in acne pathogenesis remains to be proven, P. acnes is also considered an important commensal for skin health. It releases free fatty acids through triglyceride hydrolysis to maintain low skin pH and inhibits the colonization of pathogenic bacteria, such as Staphylococcus aureus and Streptococcus.[44–46]P. acnes typing and genome sequencing efforts suggest that P. acnes can function as a commensal or an opportunistic pathogen depending on the strains and the disease.[10,47,48]P. acnes was previously classified into two types, I and II, based on serum lectin response, cell wall sugar content, and susceptibility to phages.[49] Later, an additional phylotype, type III, was defined.[50] Within type I, P. acnes can be further separated into clades IA1, IA2, IB, and IC based on the Belfast MLST scheme[51] or I-1a, I-1b, and I-2 based on the Aarhus MLST scheme.[52] With the whole-genome sequencing effort of a large number of P. acnes isolates,[48] higher resolution of the phylogeny became available. Based on the single nucleotide polymorphisms (SNPs) identified throughout the core genome regions, P. acnes can be classified into phylogenetic clades IA-1, IA-2, IB-1, IB-2, IB-3, IC, II, and III.[10,48]Table 1summarizes the corresponding nomenclatures of the phylogenetic clades based on the whole-genome sequences and different MLST schemes.[48,51,52] Additionally, based on the 16S ribosomal RNA (rRNA) sequences, P. acnes can be classified into multiple ribotypes (RTs) with RTs 1–10 being the most common RTs found in the population.[10] These classifications are useful in understanding the associations between P. acnes strains and disease or healthy skin (Table 1). Strains from clades IA-2, (mainly RT4 and RT5), IB-1 (RT8), and IC (RT5) are strongly associated with acne. Type II strains, including RT2 and RT6, are associated with healthy non-acne skin. Strains from clades IA-1, IB-2, and IB-3 have been found in both healthy individuals and acne patients.[10,48,53] Type III strains are rarely found on the facial skin, but are abundant on the back and have been linked to the skin condition progressive macular hypomelanosis.[54,55]

Recent studies of P. acnes and the skin microbiome have shed new light on the strain-level differences in the roles of P. acnes in health and acne. Fitz-Gibbon et al.[10] revealed that certain P. acnes strains were enriched in acne patients, while some other strains were mostly found in healthy individuals. Tomida et al.[48] further compared the genomes of P. acnes strains isolated from healthy individuals and patients with acne, and identified that the non-core genomic regions of P. acnes strains associated with acne contain extra virulence-related genes when compared with other strains. Johnson et al.[56]showed that acne-associated strains produce more porphyrins, which are a group of pro-inflammatory molecules inducing inflammation in keratinocytes and aggravating tissue damage by producing reactive oxygen species. Kang et al.[57] further demonstrated that vitamin B12 supplementation alters the

transcriptional activities and increases porphyrin production in acne-associated P. acnes strains, while health-associated P. acnes strains do not respond to vitamin B12 supplementation. Furthermore, several recent studies have shown that acne-associated P. acnes strains induce significant inflammatory responses in keratinocytes, sebocytes, and peripheral blood mononuclear cells, while health-associated strains do not.[58–61] These studies suggest that different strains of P. acnes may play different roles in skin health and acne pathogenesis.

Multiple other skin bacteria colonize the external surface of the skin, some of which may play a role in maintaining skin health or exacerbating diseases. Staphylococcus epidermidis, Staphylococcus hominis, and other coagulase negative staphylococcal species can be found on the skin of healthy and acne individuals.[62] In acne skin, the relative abundance of S. epidermidis increases at the expense of P. acnes.[49] Several studies suggest that P. acnes can be inhibited by S. epidermidis. Wang et al.[63]showed that S. epidermidis strains could produce succinic acid, which has anti-P. acnes activity. The study by Christensen et al.[64] suggested that S. epidermidis possesses a functional ESAT-6 (early secreted antigenic target of 6 kDa) secretion system, which could inhibit P. acnes growth through polymorphic toxins that are antibacterial. Additionally, it was shown that S. epidermidis secretes staphylococcal lipoteichoic acid, which could reduce P. acnes-associated inflammation by inducing expression of miR-143 and inhibiting TLR-2 expression in keratinocytes.[65] These studies suggest that Staphylococci, especially S. epidermidis, may protect skin against acne. However, this hypothesis requires further examination.

Malassezia and Acne

Malassezia has been thought to induce acne.[66]Malassezia is the most abundant fungal organism on the skin, co-existing with P. acnes and other bacterial species. In a study by Hu et al.,[67] acne lesions were significantly reduced after administration of antifungal drugs. The authors suggested that Malassezia, not P. acnes, was potentially the cause of refractory acne.[67]The findings from several other studies are in support of this hypothesis. Song et al.[68] and Numata et al.[69] reported that Malassezia restricta and Malassezia globosa can be isolated from young acne patients. Akaza et al.[70] showed that the lipase activity of Malassezia is ~ 100 times higher than that of P. acnes. Malassezia can also hydrolyze triglycerides in the sebum to produce free fatty acids, which may affect the abnormal keratinization of hair follicular ducts, chemotize polymorphonuclear neutrophils,[71,72] and promote secretion of pro-inflammatory cytokines from keratinocytes and monocytes.[73,74] The role of Malassezia in acne pathogenesis remains to be further investigated.

ANTIBIOTICS IN ACNE TREATMENT

Bacterial factors and inflammation are both thought to contribute to acne pathogenesis. Although acne is not a typical infectious disease, the use of antibiotics has been the mainstay in acne treatment for over 40 years. Topical antibiotics are largely used for their bactericidal effects against P. acnes. Oral antibiotics have anti-inflammatory effects in addition to antimicrobial effects, which target both P. acnes and host immune response.[4,75,76]

Based on several treatment guidelines and expert consensus documents, macrolides, clindamycin, and tetracyclines are recommended as the first-line therapy in the acute inflammatory phase of acne.[77–82] Erythromycin, clarithromycin, roxithromycin, and azithromycin are macrolides. Clindamycin belongs to lincosamides. Tetracyclines for acne treatment mainly include tetracycline, doxycycline, and minocycline. The effects of macrolides, clindamycin, and tetracyclines on the skin microbiome, including the target bacterium P. acnes and other non-target bacteria, and the associated issue of antibiotic resistance are discussed in Sects. 3.1–3.3. Several other antibiotics, such as trimethoprim–sulfamethoxazole, levofloxacin, rifampin, dapsone, and metronidazole, may also be used in acne treatment. However, current data on the effects of these antibiotics are limited in scope and quality. Additional studies are needed to address multiple knowledge gaps regarding these antibiotics.

Influence of Antibiotic use on P. acnes

Effect of Macrolides and Clindamycin.

Erythromycin and clindamycin have been widely used in the last 40 years in acne treatment, and are still frequently prescribed by physicians. Long-term use of oral macrolides for acne treatment facilitates the increase of macrolide-resistant P. acnes strains.[83] In recent years, increasing levels of resistance of P. acnes to macrolides and clindamycin have been reported in several regions of the world.[83] In some countries, the resistance of P. acnes to erythromycin is over 50%,[83,84] and the resistance to azithromycin reaches 82–100%.[85,86]Similarly, the resistance of P. acnes to clindamycin increased from 4% in 1999 to 90.4% in 2016.[85,87] There was a high proportion (52%) of acne patients who carried at least one P. acnes strain resistant to clindamycin.[88] When topical clindamycin was administered for 16 weeks for acne treatment, the amount of resistant P. acnes was increased by 16 times from the baseline.[89]After antibiotic treatment is ended, tolerant P. acnes strains may remain on the skin for a considerably long period of time, and the presence of resistant P. acnes strains manifests as a re-occurrence of acne.[4] Furthermore, when patients are treated again with antibiotics, the efficacy of such drugs is reduced or voided.[4,90]

Different P. acnes strains exhibit a varying degree of antibiotic resistance. Based on multiple recent studies of P. acnes isolates collected from different geographic areas including Italy, Sweden, UK, Australia, USA,[10,47,51,91]Denmark,[88] and Greece,[92] RT4 and RT5 strains, which are mostly clonal complex 3 (CC3) strains and some CC18 strains based on MLST,[51,88]accounted for 85–95% of the antibiotic-resistant strains.[47,51,91,92] The underlying molecular mechanisms for resistance include point mutations G2057A, A2058G, and A2059G in the domain V of 23S rRNA, as well as the presence of erm(X) gene.[92–96] It is common that resistance to erythromycin correlates with resistance to clindamycin.[93] Cross-resistance to erythromycin and clindamycin of P. acnes isolates from acne patients varies from 11.6 to 100%, as reported in different studies.[51,97–100]

To reduce the emergence of antibiotic resistance, it is currently recommended that topical antibiotics be used in combination with benzoyl peroxide (BPO) or retinoid in acne treatment.[83] Studies have shown that combining clindamycin with BPO or retinoid for topical application not only significantly reduced the total number of P. acnes on the skin, but also lowered antibiotic resistance of P. acnes to erythromycin and clindamycin.[101]

Effect of Tetracyclines.

Tetracyclines are another class of antibiotics frequently used for treating moderate to severe acne. Although this group of antibiotics is still largely active against the majority of P. acnes isolates, antibiotic resistance is rising and needs the attention of the medical field. The rate of resistance to tetracycline differed from 2 to 30% in studies from different geographic regions in recent years.[86,97,99,101] In parallel, resistance to doxycycline among isolated P. acnes strains varied between 2 and 44.2%.[85,86,97,101] The combined resistance to tetracycline and doxycycline ranged from 1.2 to 100% in different groups of patients.[99,102] In contrast to this high resistance rate to tetracycline and doxycycline, a lower resistance rate to minocycline (< 2%) was observed in Europe, Latin America, Northern America, and parts of Asia. This makes minocycline the most effective agent in the tetracycline class for acne treatment.[85,92,97] The resistance mechanism against tetracyclines is a G1058C mutation in P. acnes16S rRNA gene.[96] Additionally, an amino acid substitution in the ribosomal S10 protein contributes to reduced doxycycline susceptibility.[103]

Influence of Antibiotic Use on Other Skin Bacteria

Effect of Macrolides and Clindamycin.

The use of macrolides and clindamycin in acne treatment results in resistance in other skin bacteria in addition to P. acnes. At least 30% of S. epidermidis isolates from acne patients were resistant to erythromycin, roxithromycin, and clindamycin.[104]Harkaway et al.[105] reported that after 12-week treatment with topical erythromycin alone, erythromycin-tolerant S. epidermidis became predominant on the skin surface, and the relative abundance of S. aureus at nostrils rose from 15 to 40%. Similarly, Mills et al.[106] reported that in acne treatment with topical erythromycin, the proportion of patients with erythromycin-tolerant staphylococci on the face was 87% at baseline, and increased to 98% at week 12 of treatment. Furthermore, the proportion of patients with resistant staphylococci was only slightly reduced 12 weeks after drug withdrawal. The average density of tolerant bacteria at non-treated sites, such as the back, increased at the end of the treatment. Transmission of such bacteria to different sites may cause serious consequences.[106] Like macrolides, clindamycin exerts selection pressure on both P. acnes and staphylococci. The study by Nakase et al.,[95] which analyzed the correlation of antimicrobial resistance between P. acnes and S. epidermidis, reported that clindamycin-resistant S. epidermidis strains were isolated from more than 80% of the patients who also carried clindamycin-resistant P. acnes.

Effect of Tetracyclines.

There are few established data on the effect of tetracyclines on the skin bacteria besides P. acnes. Doxycycline 40 mg modified release has been used for the treatment of inflammatory lesions in moderate and severe acne. Limited evidence suggested that this dose showed no effect on the normal skin flora as well as the rate of antibiotic resistance while being effective in reducing acne lesions.[76,107]

Lymecyclin and sarecycline are new members of tetracyclines in acne therapy. A recent study based on 16S rRNA sequencing demonstrated that at 6 weeks after lymecyclin treatment, the relative abundance of Propionibacterium on the cheeks of patients decreased, but the relative abundances of Streptococcus, Staphylococcus, Micrococcus, and Corynebacterium increased. Changes in this microbial community after drug withdrawal were not investigated.[108] Sarecycline (two phase III clinical trials completed in 2017) has a narrow antibacterial spectrum relative to other tetracyclines. It might have less selective pressure on enteric Gram-negative bacteria, but there are no data available on its influence on the skin microbiome.[109]

Applications of Antibiotics in Acne Treatment

The growing prevalence of antibiotic resistance in P. acnes and other skin commensal bacteria is becoming increasingly alarming. For mild-to-moderate acne, topical antibiotic monotherapy is not recommended. Topical retinoid, BPO, or a combination therapy (topical retinoid + BPO, topical antibiotic + BPO, topical retinoid + topical antibiotic + BPO) is recommended.[110] For moderate-to-severe acne, the recommended first-line treatment is oral antibiotics combined with BPO and/or a topical retinoid. Oral antibiotic monotherapy is not recommended.[111] To reduce antibiotic-resistant microorganisms on the skin, as alternative treatments, BPO can be used for at least 5–7 days between antibiotic courses.[5] Oral contraceptives or anti-androgens may be another alternative for some female patients. To obtain better clinical efficacy and reduce antibiotic resistance, information on past exposure to macrolides or clindamycin should suggest avoidance of prescription of these antibiotics. Given that some acne patients are colonized by antibiotic-resistant P. acnes strains, Sinnott et al.[112]recommended that swabbing, culturing, and testing for resistant strains may be one way to help avoid long-term use of ineffective antibiotics.

The recommended minimum course of acne treatment with oral antibiotics is 6–8 weeks. Oral antibiotics may continue to be used after taking effect, but should not be used for longer than 12 weeks.[83,113] However, it is reported that in practice, 17.5% of antibiotic treatment courses last ≥ 6 months and 7% of the treatments last over 9 months, with an average treatment time of 125–129 days.[114,115] The long-term use of antibiotics may significantly alter the skin microbiome and increase drug resistance. Future longitudinal studies of long-term use of antibiotics may shed light on its effect on the composition and dynamics of the microbiome.[83]

CONCLUSION

Although the pathogenesis mechanisms of acne have not yet been fully elucidated, it is recognized that P. acnes and inflammatory response play important roles in the development of the disease. The use of bactericidal and anti-inflammatory antibiotics remains an important strategy for treating acne. Thus, rational selection of antibiotics according to the classification of P. acnes strains and corresponding drug susceptibility is preferred. However, this recommendation has not yet gained sufficient attention in clinical practice.

Given the rapid emergence of antibiotic resistance on the global scale and considering the effects of antibiotic use on the human microbiome, alternative clinical practice to antibiotic prescription in treating microbe-related diseases has become critical. A recently published study suggested a potential vaccination approach against acne by targeting Christie–Atkins–Munch–Petersen (CAMP) factor as an antigen.[116] Meanwhile, other studies showed promise in microbiome-based therapies, which may shift the balance among the microbial members, influence the function of immune cells, and prevent diseases while restoring a healthy microbiome.[117–119] In one such study, Nakatsuji et al.[119] showed that reintroduction of coagulase-negative Staphylococcus (CoNS) strains, which produce antimicrobial peptides, to patients with atopic dermatitis decreased S. aureus colonization on the skin. The study demonstrated how commensal skin bacteria can defend against pathogens and suggested that correcting microbiome dysbiosis may potentially be used to treat or improve certain conditions. Future studies on how to effectively reduce the load of pathogenic microorganisms and inflammation while preserving the balance of the commensal microflora may lead to potential new therapies.

ANNEXURE-2

Bharath Institute of Higher Education and Research

Sri Lakshmi Narayana Institute of Medical Sciences

Participant list of Value-added course: **ACNE VULGARIS - DR06**
(Nov 2017– Feb- 2018)

2nd Year MBBS Student			
Sl. No	**Name of the Student**	**Reg No**	**Signature**
1	SRIRAM .S	U16MB381	
2	SUBALAKSHMI .D	U16MB382	
3	SUNITHA .A	U16MB383	
4	SURENDAR RAJ .S	U16MB384	
5	SUSMITHA .V	U16MB385	
6	SWATI GUPTA	U16MB386	
7	SWATI KUMARI	U16MB387	
8	THAMARAIK KANNAN	U16MB388	
9	THEEPTHI .T	U16MB389	
10	UDDIP DATTA RAY	U16MB390	
11	SANDHYA	U16MB371	
12	SARA R	U16MB372	
13	SARASWATHI N	U16MB372	
14	SHIKHA SONI	U16MB376	
15	SNEHA	U16MB379	

Dr. A. BUVANARATCHAGAN, MD
Dr. Buvanaratchagan
Asst. Professor, Dermatology
Sri Lakshmi Narayana Institute of Medical Sciences
Osudu, Puducherry-605 502

RESOURCE PERSON

PROFESSOR & HEAD
DEPT. OF DERMATOLOGY
SRI LAKSHMI NARAYANA INSTITUTE OF MEDICAL SCIENCES
OSUDU, PUDUCHERRY
Dr. K. Harsha Vardhan

COORDINATOR

ANNEXURE-3

SRI LAKSHMI NARAYANA INSTITUTE OF MEDICAL SCIENCES

ACNE VULGARIS

Annexure- III

MULTIPLE CHOICE QUESTIONS

COURSE CODE:DR06

ANSWER ALL QUESTIONS

1. What is the most common causative agent of Acne Vulgaris?
   A. Herpes simplex
   B. Propionibacterium acnes
   C. Staphylococcus aureus
   D. Trichophyton rubrum

2. The pathological process that leads to Acne Vulgaris is:
   A. Alteration of follicular keratinization
   B. Follicular colonization
   C. Increased and altered sebum production
   D. All of the above

3. The most common manifestation of hyperandrogenism
   A. Acne
   B. Hirsuitism
   C. Amenorrhea
   D. Infertility

4. Which part of skin does acne affect?
   A. Epidermis
   B. Dermis
   C. Hair follicles
   D. Hair shaft

5. Which of these hormones trigger acne in adolescents?
    A. Androgen
    B. Estrogen
    C. Endorphin
    D. Norepinephrine

6. Acne can be treated with which of these?
    A. Skin cleansers
    B. Oral antibiotics
    C. Oral Vitamin A medicines
    D. All of the above

7. Comedones are seen in
    A. Acne vulgaris
    B. Lichen planus
    C. Adenoma sebaceum
    D. Pityriasis

8. A patient is presenting with nodulocystic acne on the face. The drug of choice is:
    A. Retinoids
    B. Antibiotics
    C. Steroids
    D. UV Light

9. Antibiotics useful in acne include all, except:
    A. Topical clindamycin
    B. Topical framycetin
    C. Topical erythromycin
    D. Minocycline

10. Acne vulgaris is due to involvement of?
    A. Sebaceous gland
    B. Pilosebaceous gland
    C. Eccrine gland
    D. Apocrine gland

ANNEXURE-3

SRI LAKSHMI NARAYANA INSTITUTE OF MEDICAL SCIENCES

Swathi gupta

ACNE VULGARIS

Annexure- III

MULTIPLE CHOICE QUESTIONS

COURSE CODE:DR06

ANSWER ALL QUESTIONS

1. What is the most common causative agent of Acne Vulgaris?
   A. Herpes simplex
   B. Propionibacterium acnes
   C. Staphylococcus aureus
   D. Trichophyton rubrum

10/10

2. The pathological process that leads to Acne Vulgaris is:
   A. Alteration of follicular keratinization
   B. Follicular colonization
   C. Increased and altered sebum production
   D. All of the above

Vardhan KV 24/1/18

3. The most common manifestation of hyperandrogenism
   A. Acne
   B. Hirsutism
   C. Amenorrhea
   D. Infertility

4. Which part of skin does acne affect?
   A. Epidermis
   B. Dermis
   C. Hair follicles
   D. Hair shaft

5. Which of these hormones trigger acne in adolescents?
   A. Androgen
   B. Estrogen
   C. Endorphin
   D. Norepinephrine

6. Acne can be treated with which of these?
   A. Skin cleansers
   B. Oral antibiotics
   C. Oral Vitamin A medicines
   D. All of the above

7. Comedones are seen in:
   A. Acne vulgaris
   B. Lichen planus
   C. Adenoma sebaceum
   D. Pityriasis

8. A patient is presenting with nodulocystic acne on the face. The drug of choice is:
   A. Retinoids
   B. Antibiotics
   C. Steroids
   D. UV Light

9. Antibiotics useful in acne include all, except:
   A. Topical clindamycin
   B. Topical framycetin
   C. Topical erythromycin
   D. Minocycline

10. Acne vulgaris is due to involvement of?
   A. Sebaceous gland
   B. Pilosebaceous gland
   C. Eccrine gland
   D. Apocrine gland

ANNEXURE-3

SRI LAKSHMI NARAYANA INSTITUTE OF MEDICAL SCIENCES

Sriram - 2

ACNE VULGARIS

Annexure- III

MULTIPLE CHOICE QUESTIONS

COURSE CODE:DR06

ANSWER ALL QUESTIONS

1. What is the most common causative agent of Acne Vulgaris?
   A. Herpes simplex
   B. Propionibacterium acnes
   C. Staphylococcus aureus
   D. Trichophyton rubrum

10/10

Vandhana KA
24/1/18

2. The pathological process that leads to Acne Vulgaris is:
   A. Alteration of follicular keratinization
   B. Follicular colonization
   C. Increased and altered sebum production
   D. All of the above

3. The most common manifestation of hyperandrogenism
   A. Acne
   B. Hirsuitism
   C. Amenorrhea
   D. Infertility

4. Which part of skin does acne affect?
   A. Epidermis
   B. Dermis
   C. Hair follicles
   D. Hair shaft

5. Which of these hormones trigger acne in adolescents?
   A. Androgen
   B. Estrogen
   C. Endorphin
   D. Norepinephrine

6. Acne can be treated with which of these?
   A. Skin cleansers
   B. Oral antibiotics
   C. Oral Vitamin A medicines
   D. All of the above

7. Comedones are seen in
   A. Acne vulgaris
   B. Lichen planus
   C. Adenoma sebaceum
   D. Pityriasis

8. A patient is presenting with nodulocystic acne on the face. The drug of choice is:
   A. Retinoids
   B. Antibiotics
   C. Steroids
   D. UV Light

9. Antibiotics useful in acne include all, except:
   A. Topical clindamycin
   B. Topical framycetin
   C. Topical erythromycin
   D. Minocycline

10. Acne vulgaris is due to involvement of?
   A. Sebaceous gland
   B. Pilosebaceous gland
   C. Eccrine gland
   D. Apocrine gland

ANNEXURE-IV

Student Feedback Form

Course Name: **ACNE VULGARIS**

Subject Code: **DR06**
Name of Student: _____ Roll No.: _____

We are constantly looking to improve our classes and deliver the best training to you. Your evaluations, comments and suggestions will help us to improve our performance

Sl. NO	Particulars	1	2	3	4	5
1	Objective of the course is clear					
2	Course contents met with your expectations					
3	Lecturer sequence was well planned					
4	Lectures were clear and easy to understand					
5	Teaching aids were effective					
6	Instructors encourage interaction and were helpful					
7	The level of the course					
8	Overall rating of the course	1	2	3	4	5

**** Rating: 5 – Outstanding; 4 - Excellent; 3 – Good; 2– Satisfactory; 1 - Not-Satisfactory***

Suggestions if any:

Date:24-01-2018

Signature

ANNEXURE-IV

Student Feedback Form

Course Name: **ACNE VULGARIS**

Subject Code: **DR06**
Name of Student: Sriram S Roll No: U16MB381

We are constantly looking to improve our classes and deliver the best training to you. Your evaluations, comments and suggestions will help us to improve our performance

Sl. NO	Particulars	1	2	3	4	5
1	Objective of the course is clear				✓	
2	Course contents met with your expectations					✓
3	Lecturer sequence was well planned				✓	
4	Lectures were clear and easy to understand			✓		
5	Teaching aids were effective				✓	
6	Instructors encourage interaction and were helpful		✓			
7	The level of the course					✓
8	Overall rating of the course	1	2	3	4	5

** Rating: 5 – Outstanding; 4 - Excellent; 3 – Good; 2– Satisfactory; 1 - Not-Satisfactory*

Suggestions if any:

Date:24-01-2018

Signature

ANNEXURE-IV

Student Feedback Form

Course Name: **ACNE VULGARIS**

Subject Code: **DR06**
Name of Student: [redacted] Roll No.: 016MD296

We are constantly looking to improve our classes and deliver the best training to you. Your evaluations, comments and suggestions will help us to improve our performance

Sl. NO	Particulars	1	2	3	4	5
1	Objective of the course is clear				✓	
2	Course contents met with your expectations					✓
3	Lecturer sequence was well planned				✓	
4	Lectures were clear and easy to understand					✓
5	Teaching aids were effective			✓		
6	Instructors encourage interaction and were helpful					✓
7	The level of the course				✓	
8	Overall rating of the course	1	2	3	4	5

** Rating: 5 – Outstanding; 4 - Excellent; 3 – Good; 2– Satisfactory; 1 - Not Satisfactory*

Suggestions if any:

Signature

Date 24-01-2018

Annexure-5

Sri Lakshmi Narayana Institute of Medical Sciences

Affiliated to Bharath Institute of Higher Education & Research

(Deemed to be University under section 3 of the UGC Act 1956)

CERTIFICATE OF MERIT

This is to certify that Dr. [illegible] has actively participated in the Value Added Course on Acne Vulgaris held during Nov 2017– Feb 2018 organized by Sri Lakshmi Narayana Institute of Medical Sciences, Pondicherry- 605 502, India.

Dr. A. BUVANARATCHAGAN, MD.
PROFESSOR & HEAD
DEPT. OF DERMATOLOGY
Sri Lakshmi Narayana Institute of Medical Sciences
Oulgaret, Puducherry-605 502

Dr. Buvanaratchagan
RESOURCE PERSON

PROFESSOR & HEAD
DEPT. OF DERMATOLOGY
Sri Lakshmi Narayana Institute of Medical Sciences
Oulgaret, Puducherry-605 502

Dr. K. Harsha Vardhan
COORDINATOR

Sri Lakshmi Narayana Institute of Medical Sciences

Affiliated to Bharath Institute of Higher Education & Research
(Deemed to be University under section 3 of the UGC Act 1956)

CERTIFICATE OF MERIT

This is to certify that Swathi Guptha has actively participated in the Value Added Course on Acne Vulgaris held during Nov 2017– Feb 2018 organized by Sri Lakshmi Narayana Institute of Medical Sciences, Pondicherry- 605 502, India.

Dr. A. BUVANARATCHAGAN, MD.

Dr. Buvanaratchagan
RESOURCE PERSON

PROFESSOR & HEAD
DEPT. OF DERMATOLOGY

Dr. K. Harsha Vardhan
COORDINATOR

Course completion letter

Date 27-01-2018

From
Dr. K. Harsha Vardhan
Department of Dermatology
Sri Lakshmi Narayana Institute of Medical Sciences
Bharath Institute of Higher Education and Research,
Chennai.

Through Proper Channel

To
The Dean,
Sri Lakshmi Narayana Institute of Medical Sciences
Bharath Institute of Higher Education and Research,
Chennai.

Sub: Completion of value-added course: acne vulgaris

Dear Sir,

With reference to the subject mentioned above, the department has conducted thevalue-added course titled: **acne vulgaris** on 20-11-17. We solicit your kind action to send certificates for the participants, that is attached with this letter. Also, I am attaching the photographs captured during the conduct of the course.

Kind Regards

Dr. K. Harsha Vardhan

<HOD Sign and Seal>

Encl: Certificates

Photographs

Course completion letter

From
Dr. K. Harsha Vardhan
Department of Dermatology
Sri Lakshmi Narayana Institute of Medical Sciences
Bharath Institute of Higher Education and Research,
Chennai.

Date 27-01-2018

Through Proper Channel

To
The Dean,
Sri Lakshmi Narayana Institute of Medical Sciences
Bharath Institute of Higher Education and Research,
Chennai.

Sub: Completion of value-added course: acne vulgaris

Dear Sir,

With reference to the subject mentioned above, the department has conducted thevalue-added course titled: **acne vulgaris** on 20-11-17. We solicit your kind action to send certificates for the participants, that is attached with this letter. Also, I am attaching the photographs captured during the conduct of the course.

Kind Regards

Vardhan KH

Dr. K. Harsha Vardhan,

<HOD Sign and Seal>

Encl: Certificates

Photographs