E-ISSN: XXXX-XXXX; DOI: 10.36962/PSCIA

VOLUME 01, ISSUE 01, 2021

PROCEEDINGS

Proceedings of The Southern Caucasus İnternational Academy of Modern Sciences

MULTIDISCIPLINARY JOURNAL
REFEREED SCIENTIFIC JOURNAL

Applied Social Research & Behavioral Sciences

E-ISSN: XXXX-XXXX; DOI: 10.36962/PSCIA

VOLUME 01, ISSUE 01, 2021

PROCEEDINGS

Proceedings of The Southern Caucasus İnternational Academy of Modern Sciences

MULTIDISCIPLINARY JOURNAL
REFEREED SCIENTIFIC JOURNAL

LONDON 2021

© THE EUROPE SCIENTIFIC JOURNALS
PROCEEDINGS
THE SOUTHERN CAUCASUS INTERNATIONAL ACADEMY

E-ISSN: XXXX-XXXX, DOI: 10.36962 / PSCIA
PSCIA
MULTIDISCIPLINARY JOURNAL
REFEREED SCIENTIFIC JOURNAL

©Publisher: SCIAMS. LTD (United Kingdom, London), C/N 13298740.
Director & Shareholder: Namig Isazade
Registered Address: 71-75 Shelton Street, Covent Garden, London, WC2H 9JQ, UK.
©Editorial office: 71-75 Shelton Street, Covent Garden, London, WC2H 9JQ, UK.
Telephones: +994 55 241 70 12; +994 51 864 88 94
Website: http://scia.website/
E-mail: sc.mediagroup2017@gmail.com

E – ISSN: XXXX – XXXX
VOLUME 01 ISSUE 01 2021
PROCEEDINGS
THE SOUTHERN CAUCASUS INTERNATIONAL ACADEMY

TABLE OF CONTENTS

PROCEEDINGS
THE SOUTHERN CAUCASUS INTERNATIONAL ACADEMY
E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

DYNAMICS OF PULMONARY FUNCTIONAL INDICES IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Ketevan Lobzhanidze[1], Maia Sulaqvelidze[2], Revaz Tabukashvili [3]

[1]N. Kipshidze Central University Clinic, Tbilisi, Georgia, Primary Care Physician,

Email: keti221@yahoo.com.

[2]N.Kipshidze Central University Clinic, Outpatient Department, Head of the Department. European University,

Professor, Email: maiasulaq@gmail.com

[3]Tbilisi State Medical University, Department of Internal Medicine Propaedeutics, Head of the Department , Professor.

ABSTRACT

The study aimed to provide a detailed analysis of correlations between FEV-1 and other indices of pulmonary function, including forced vital capacity (FVC%), Tiffeneau-Pinelli index (FEV1/FVC%), measurements of peak expiratory flow (FEF/PEF), forced expiratory flow over the middle half of FVC (FEF25%, FEF50%, FEF75%), as well as correlations between FEV1 and grades of MMRC (Modified Medical Research Council Questionnaire) by using of the self-evaluation questionnaire.

The study was conducted at the "N. Kipshidze Central University Clinic". 78 patients with chronic obstructive pulmonary disease (COPD) were involved in the study. The functional status of respiratory system and clinical condition of the patient were assessed by spirometry and MMRC.

According to study objectives patients were divided into three groups: the group #1 – untreated patients, without any inhaled therapy (n=26); the group #2 – patients taking inhaled salbutamol monotherapy (n=28), the group #3 - patients taking inhaled combination therapy with LABA/IC - long-acting beta-agonists and corticosteroids (n=24).

The study results revealed statistically significant correlation between FEV1 and other parameters of respiratory function, such as FVC, FEV1/FVC and FEF 50%, as well as statistically significant correlation between FEV-1 and MMRC in COPD patients, which increases the value of the self-evaluation questionnaire.

According to study results we can conclude that the favorable prognosis of COPD is greatly depends on the time of onset and adequacy of therapy. The onset of adequate therapy soon after confirmation the diagnosis by spirometry greatly influence the cause and the prognosis of the disease. Thus, Spirometry is the most important diagnostic tool in making proper diagnosis of COPD, identifying high risk groups of patients with worst prognosis, starting adequate therapy and prevent progression and poor outcome of the disease. At the same time, the wide implementation of self-assessment questionnaire in clinical practice might be helpful in identifying COPD patients in which poor prognosis and worst outcome is expected.

Keywords: Chronic obstructive pulmonary disease (COPD), spirometry, forced expiratory volume per second – FEV1, lung function decline, mMRC.

Introduction: Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and /or alveolar abnormalities usually caused by significant exposure to noxious

particles or gases [6] and associated with progressive decline of pulmonary function and characterized with various degree of dyspnea and exacerbations. [1]
COPD as a progressive illness leading to high mortality rate due to chronic hypoxemia and complications which are closely associated with this chronic condition. COPD is the third leading cause of mortality [5] [10]. Its importance is related to its high prevalence in both developing and developed countries, therefore treatment and prevention of the disease poses a great challenge to the healthcare system [4][11]. According to the World Health Organization, COPD is a major cause of morbidity, mortality and represents a problem for modern world [16][9]. Higher burden of *COPD* is expected in future owing to environmental pollution and increased life expectancy of the population [6]. The forced expiratory volume in the first second – FEV1 is established as a main determinant of COPD severity [6][12]. FEV1 is recognized as a reliable prognostic index and is used for assessment of COPD severity, reduced FEV1 is related with frequent exacerbations and increased risk of mortality [8] [18][17].
Despite the importance of the problem, researchers are trying to identify factors, which significantly correlate with the dynamics of decrease in FEV1. Due to complexity of the problem, disparity between different studies raises further questions. [6][7].
The main goal of COPD management is to control symptoms, prevent exacerbations and delay progression of the disease. Taking into consideration high prevalence of the disease, the goal of any scientific research is to develop the COPD management strategy which will provide better control of risk factors, reduce frequency of exacerbations and delay progression of the disease.

Aim of the Study: The study aimed to provide a detailed analysis of dynamics of FEV, which is the main tool for the assessment of pulmonary function and is used as an indicator of disease severity and progression. We also intended to assess correlations between FEV-1 and other indices of pulmonary function, including forced vital capacity (FVC%), Tiffeneau-Pinelli index (FEV1/FVC%), measurement of peak expiratory flow (FEF/PEF), forced expiratory flow over the middle half of FVC (FEF25%, FEF50%, FEF75%), as well as correlations between FEV1 and grades of MMRC (Modified Medical Research Council Questionnaire) by using of the self-evaluation questionnaire.

Materials and methods: The study was conducted at "Academition N. Kipshidze Central University Clinic" using data obtained from COPD patients including initial and follow-up visits. Clinical assessment of patients included the following: demographics (gender, age) and constitutional data (BMI), information about COPD provoking risk-factors (active or former smoker), the associated diseases and self-assessment questionnaire (MMRC, CAT) results. The self-assessment questionnaire for dyspnea (MMRC - Modified Medical Research Council Questionnaire) is designed by the Council of Medical Research. It is used for evaluation of patients' clinical status [2] [6][3] and risk of mortality[6][10] [14] [13]. MMRC in combination with spirometry results is considered as a useful tool for the assessment of prognosis and risk of future complications. MMRC is a 5-point scale questionnaire, which is used for estimation of severity of breathlessness related with physical activity. Grades are distributed from 0 (breathlessness with strenuous physical activity) to 5 (dyspnea at minimal physical activity) [19].
Pulmonary functional status was assessed by spirometry. COPD severity was measured by GOLD criteria: GOLD 1 – mild: FEV1/FVC < 0,70, FEV1 ≥ 80% of predicted; GOLD 2 – moderate:

FEV1/FVC < 0,70, 50% ≤ FEV1 < 80% of predicted; GOLD 3 - severe: FEV1/FVC < 0,70 30% ≤ FEV1 < 50% of predicted; GOLD 4 – very severe: FEV1/FVC < 0,70, FEV1 < 30% of predicted. Spirometry was performed in every 3 months and a detailed analysis of results was made.
The study included 78 patients. Demographic and clinical characteristics of the patients are given : Gender- Male -50 (64,10%), Female- 28 (35,90%), Age 61,56 ± 10,72, Age of starting COPD complaints-54,92 ± 10,52, Duration of COPD-6,64 ± 4,05, Former Smoker-50,00 (64,10%), Smoker-28,00 (35,90%), P/Y-35,21 ± 25,72, Duration of smoking-28,45 ± 10,77, BMI-28,45 ± 10,77, Normal Body Mass-20(25,64%), Excessive weight-18(23,08%), Obesity-40(51,28%), Treatment in History- Was not treated-26 (33,33%), Salbutamol-28(35,90%), Combined therapy-24 (30,77%), Exacerbation in history- No-62 (79,49%) , Yes-16(20,51%), Mmrc-gradation- Grade2- 42(53,85%), Grade3- 36(46,15%), Questionnaire on Lung function-12,36 ± 2,78, Arterial Hypertension-70(89,74%), CAD. angina of effort -26(33,33%), Heart failure-10(12,82%), Atrial fibrillation-2 (2,56%), Sd 2-16(20,51%), dl-38(48,72%), Tqd-2(2.56%).

Statistics: Statistical analysis were performed using SPSS 22.0 software. Student's T-test was applied for comparing quantitative data between groups. Pearson's correlation coefficient was used for the assessment of correlations between variables. The P value was set <0.05 for the evaluation of statistical significance.

Results: Table 2 shows a correlation of pulmonary functional indices with FEV1 values at the beginning of the study.

Table 2: Correlation of Pulmonary Functional Indices at the Beginning of the Study

Index (mark in model)	FEV1	FVC	FEV1/ FVC	FEF (PEF)	FEF 25-75%	FEF 25%	FEF 50%	FEF 75%
FEV1 (Y)		0.6179	0.4766	0.2908	0.2741	0.4144	0.5052	0.4455
FVC (X1)	0.6179		-0.2736	0.0874	0.0348	0.1703	0.0445	0.0677
FEV1/FVC (X2)	0.4766	-0.2736		0.4382	0.2354	0.6374	0.5976	0.4405
FEF (PEF) (X3)	0.2908	0.0874	0.4382		0.0626	0.6115	0.3521	-0.1617
FEF 25-75% (X4)	0.2741	0.0348	0.2354	0.0626		0.2505	0.3194	0.3841
FEF 25% (X5)	0.4144	0.1703	0.6374	0.6115	0.2505		0.7759	0.4775
FEF 50% (X6)	0.5052	0.0445	0.5976	0.3521	0.3194	0.7759		0.7217
FEF 75% (X7)	0.4455	0.0677	0.4405	-0.1617	0.3841	0.4775	0.7217	

(cells with statistically significant correlations are colored).

Multiple linear regressive analysis revealed statistically significant positive correlation between FEV1 and other parameters of respiratory function, including FVC, FEV1/FVC and FEF 50%. These results clearly indicate that progression of the disease and worsening of pulmonary function is significantly associated with reduction of FEV1, as well as with considerable worsening of

FEV1/FVC, FVC and FEF 50% parameters. This possible explanation of results is that progression of COPD is characterized by a total decline of vital capacity of the lungs with simultaneous severe peripheral airway dysfunction.
Results showing a correlation between functional indices at 30 months of follow-up are given in Table 3.

Table 3: Correlation of Functional Indices at 30 months of follow-up

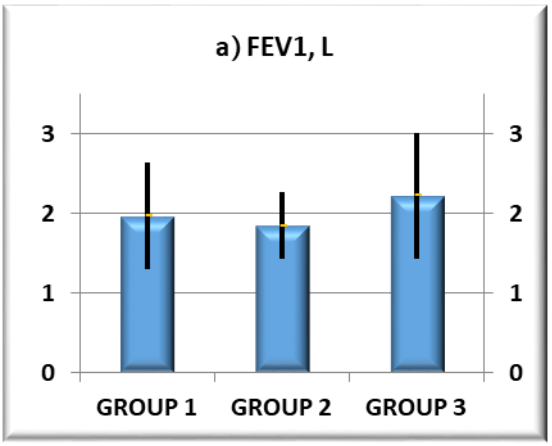
Index (mark in model)	FEV1	FVC	FEV1/ FVC	FEF (PEF)	FEF 25-75%	FEF 25%	FEF 50%	FEF 75%
FEV1 (Y)		**0.6192**	**0.4531**	**0.3211**	0.2107	**0.3111**	**0.2739**	**0.2984**
FVC (X1)	**0.6192**		**-0.2783**	-0.0466	0.0106	0.1964	0.0658	0.1040
FEV1/FVC (X2)	**0.4531**	**-0.2783**		**0.4782**	0.1236	0.05906	0.1222	0.1614
FEF (PEF) (X3)	**0.3211**	-0.0466	**0.4782**		0.0589	0.0477	0.0622	-0.1238
FEF 25-75% (X4)	0.2107	0.0106	0.1236	0.0589		**0.7569**	**0.8369**	**0.7731**
FEF 25% (X5)	**0.3111**	0.1964	0.05906	0.0477	**0.7569**		**0.8169**	**0.6580**
FEF 50% (X6)	**0.2739**	0.0658	0.1222	0.0622	**0.8369**	**0.8169**		**0.7936**
FEF 75% (X7)	**0.2984**	0.1040	0.1614	-0.1238	**0.7731**	**0.6580**	**0.7936**	

(cells with statistically significant correlations are colored).

After a 30-month follow-up period, a multiple linear regressive analysis still revealed a statistically significant positive correlations between FEV1 and FVC, FEV1/FVC and FEF 50% ($p<0.0001$), which was seen at the beginning of the study. The abovementioned denotes that FVC, FEV1/FVC and FEF 50% are indices of pulmonary functional status which are in direct proportional correlation with FEV1 index. Obstructive type of ventilation disturbance is characterized with decrease in FEV1/FVC ratio on the background of normal FVC[18], on the background of disease progress airiness of pulmonary tissue decreases and correspondingly vital capacity of lungs (FVC) decreases as well, however, despite importance of the issue, looking for correlation of other spirometry indices with dynamics of FEV1 decrease is still the field of observation in the medicine.
In order to find a relationship between dynamics of FEV1, grades of the MMRC revealed by the questionnaire and treatment outcomes (or information was not available), the study contingent was divided into three groups: the group #1 – untreated patients without any inhaled therapy (n=26); the group #2 – patients taking inhaled salbutamol monotherapy (n=28), the group #3 - patients taking inhaled combination therapy with LABA/IC (n=24).

E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

Diagram 1: Distribution average values of FEV1 (expressed in Liters) in all three groups



As study results showed, an average values of FEV1 expressed in liters is definitely increased in the third group of patients who started COPD management with inhaled combination therapy with LABA/IC. This clearly suggests that therapy with combination of drugs with various mechanisms of action is superior over monotherapy in terms of improved FEV 1 values.
In all three groups we investigated a correlation between FEV1 dynamics and grade of dyspnea revealed by the self-assessment questionnaire (MMRC). According to study results, an improvement of both FEV 1 and dyspnea grade were observed in the third group. Findings indicate that there is strong correlation between FEV-1 and the dyspnea grade in COPD patients. Thus, based on study results self-assessment questionnaire is very important tool in objective evaluation of respiratory functional status and might be widely implemented in clinical practice.
The distribution of dyspnea self-evaluation questionnaire scores in all the three groups is given in Table 4.

Table 4: Distribution of Dyspnea Self-Evaluation Questionnaire scores in all three Groups

Parameters	Group 1	Group 2	Group 3
Score by the questionnaire of pulmonary function	**11,00** ± 3,02	**12,86** ± 2,49	**13,25** ± 2,33
	p_{1-2} = 0.0177	**p_{1-3} = 0.0055**	p_{2-3} = 0.5646 (NS)

(cells with statistically significant correlations are colored).

Conclusions: A statistically significant correlation was observed between FEV1 values and other parameters of pulmonary functional test, including FVC, FEV1/FVC and FEF 50%. Results clearly show that progression of the diseases and worsening of pulmonary function are strongly correlated with total decline and deterioration of almost all pulmonary functional indices.
Progression of COPD and functional impairment of peripheral airways of lungs are total and represents by deterioration of almost all indices received by spirometry investigation.

Timely starting treatment of COPD with inhaled combination of long-acting β2 agonists and steroids LABA/IC is significantly associated with improvement of FEV1 in dynamics.
Correlation between FEV-1 value and dyspnea grade is statistically significant in COPD patients which increases usefulness of self-evaluation questionnaire for assessment of disease severity and risk of complications as well as for prognostic purposes.
Study results suggest some recommendations for better control of COPD, prevention of complications and improvement of the outcomes.
Timely starting and adequate treatment of COPD is an important factor for favorable prognosis.
Spirometry is an important tool for making proper diagnosis of COPD, identifying high risk groups and planning adequate treatment strategy as soon as possible in order to delay the progression of the disease.
Wide implementation of the self-evaluation questionnaire is helpful tool for identifying and objectively assess high risk patients with poor prognosis.

REFERENCES

1. Almagro P, Soriano JB, Cabrera FJ, et. al. Working Group on COPD, Spanish Society of Internal Medicine. Short- and medium-term prognosis in patients hospitalized for COPD exacerbation: the CODEX index. Chest. 2014 May;145(5):972-80.
2. Anelise B Munari, Aline A Gulart, Karoliny dos Santos, Raysa S Venâncio, Manuela Karloh and Anamaria F Mayer Respiratory Care January 2018,63(1):77-85. DOI: https://doi.org/10.4187/respcare.05636
3. Bestal JC, Paul EA, Garrod R, Garnham R, Jones PW, Wedzicha JA. Usefullness of the Medical Research Council (MRC) dispnoea scale as a measure of disability in patients with chronic obstructive pulmnonary disease. Thorax 1999; 54(7):581-6.
4. Frank E, Speizer MD, Ware JH. Exploring Different Phenotypes of COPD. N Engl J Med 2015,373:185-186.
5. Gavidia M. COPD Mortality Rate Drops in Some Countries, While Total Mortality Rises, Study Finds. AJMC, Assessed on: November 27, 2019 at https: //www.ajmc.com/view/copd-mortality-rate-drops-in-some-countries-while-total-mortality-rises-study-finds
6. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Updated 2017, http://goldcopd.org/gold-2017-global-strategy-diagnosis-management-prevention-copd/
7. Guo Y, Zhang T, Wang Z, et al. Body mass index and mortality in chronic obstructive pulmonary disease: A dose-response meta-analysis. Medicine (Baltimore) 2016;95:e4225. 10.1097/MD.0000000000004225
8. Hurst JR, Vestbo J, Anzueto A et al. Susceptibility to exacerbation in chronic obstructive pulmonary disease. N Engl J Med, 2010,363:1128-1138.
9. Iribarren M. R, Pérez T. A, Gómez Punter R.A, Noval A. R., Soriano J. B, Bermúdez J. A, Vázquez Espinosa E . Smoking habit in COPD patients European Respiratory Journal 2019 54: PA4488; DOI: 10.1183/13993003.congress-2019.PA4488 .
10. Lortet-Tieulent J, Soerjomataram I, López-Campos JL, et al. International trends in chronic obstructive pulmonary disease mortality, 1995–2017. Eur Respir J, 2019,54(6):1901791. doi: 10.1183/13993003.01791-2019.

E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

11. Lowe KE, Regan EA, Anzueto A et. al. COPD Gene 2019: redefining the diagnosis of chronic obstructive pulmonary disease. *Chronic Obstr Pulm Dis*. 2019, 6(5): 384-399.
12. Matarese A, Sardu C, Shu J, Santulli G. Why is chronic obstructive pulmonary disease linked to atrial fibrillation? A systematic overview of the underlying mechanisms. Int J Cardiol, 2019,276:149-151.
13. Nishimura K, Izumi T, Tsukino M, Oga T. Dyspnea is a better predictor of 5-year survival than airway obstruction in patients with COPD. Chest 2002;121(5): 1434-40.
14. Sundh J, Janson C, Lisspers K, Stallberg B, Montgomery S. The Dyspnoea, Obstruction, Smoking, Exacerbation (DOSE) index is predictive of mortality in COPD. Prim Care Respir J 2012;21(3): 295-301.
15. Sunmin Kim, Jisun Oh ,Yu-Il Kim, Differences in classification of COPD group using COPD assessment test (CAT) or modified Medical Research Council (mMRC) dyspnea scores: a cross-sectional analyses, BMC Pulmonary Medicine, Published: 03 June 2013
16. Vestbo J, Hurd SS, Agustí AG et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med, 2013,187:347-365
17. Авдеев С. Н. Стратегии профилактики обострений хронической обструктивной болезни легких // Доктор.Ру. 2017.10(139)
18. Будневский, А. В. Биомаркеры как предикторы исходов хронической обструктивной болезни легких (обзор литературы) / А. В. Будневский, Е. С. Овсянников, А. В. Чернов, 2014:5(64).125-128. https://moluch.ru/archive/64/10332/ (дата обращения: 22.09.2020).
19. https:/www.moh.gov.ge/uploads/guidelines/2017/06/07/220973bd4d84475ad37c50818b23a85c.pdf

E – ISSN: XXXX – XXXX
VOLUME 01 ISSUE 01 2021
PROCEEDINGS
THE SOUTHERN CAUCASUS INTERNATIONAL ACADEMY

EFFECTİVE WAYS FOR BRAND CREATİON AND BRAND BUİLDİNG

Khalig Gurbanov

"Economics and management of energy and petrochemical industries" Department, Senior teacher.
Azerbaijan State Oil and Industry University. Email: ibrahimovasadagat06@gmail.com

ABSTRACT

Great brands are not accidents. They are a result of thoughtful and imaginative planning. A brand must offer a compelling and credible reason for choosing it over the other options. In determining whether an attribute or benefit for a brand can serve as point-of-difference, there are three key considerations. The brand association must be seen as desirable, deliverable, and differentiating. Customer-based brand equity occurs when the consumer has a high level of awareness and familiarity with the brand and holds some strong, favorable, and unique brand associations in memory. The CBBE concept approaches brand equity from the perspective of the consumer—whether the consumer is an individual or an organization or an existing or prospective customer. The basic premise of the CBBE concept is that the power of a brand lies in what customers have learned, felt, seen, and heard about the brand as a result of their experiences over time. Thus marketers must also convince consumers that there are meaningful differences among brands. Brand awareness consists of brand recognition and brand recall performance: Brand recognition is consumers' ability to confirm prior exposure to the brand when given the brand as a cue. Brand recall is consumers' ability to retrieve the brand from memory when given the product category, the needs fulfilled by the category, or a purchase or usage situation as a cue.
Keywords: brand, consumer, marketing, brand marketing, brand equity, consumer, brand building, marketers, brand knowledge

Great brands are not accidents. They are a result of thoughtful and imaginative planning. Anyone building or managing a brand must carefully develop and implement creative brand strategies. One of the crucial aspects of it occurs to be Positioning, which requires defining our desired or ideal brand knowledge structures, and also establishing points-of-parity and points-of-difference to establish the right brand identity and brand image. Unique, meaningful points-of-difference (PODs) provide a competitive advantage and the "reason why" consumers should buy the brand. On the other hand, some brand associations can be roughly as favorable as those of competing brands, so they function as points-of-parity (POPs) in consumers' minds—and negate potential points-of-difference for competitors. In other words, these associations are designed to provide "no reason why not" for consumers to choose the brand.

A brand must offer a compelling and credible reason for choosing it over the other options. In determining whether an attribute or benefit for a brand can serve as point-of-difference, there are three key considerations. The brand association must be seen as desirable, deliverable, and differentiating. These three considerations for developing an optimal positioning align with the three perspectives on which any brand must be evaluated, namely the consumer, the company, and the competition. Desirability is determined from the consumer's point of view, deliverability is based on a company's inherent capabilities, and differentiation is determined relative to the competitors.

E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

To function as a POD, consumers ideally would see the attribute or benefit as highly impor-tant, feel confident that the firm has the capabilities to deliver it, and be convinced that no other brand could offer it to the same extent. If these three criteria are satisfied, the brand association should have sufficient strength, favorability, and uniqueness to be an effective POD. Each of these three criteria has a number of considerations.

Desirability Criteria. Target consumers must find the POD personally relevant and important. Brands that tap into growing trends with consumers often find compelling PODs. For example, Apple & Eve's pure, natural fruit juices have ridden the wave of the natural foods movement to find success in an increasingly health-minded beverage market.

Just being different is not enough—the differences must matter to consumers. For example, at one time a number of brands in different product categories (colas, dishwashing soaps, beer, de-odorants, gasoline) introduced clear versions of their products to better differentiate themselves. The "clear" association has not seemed to be of enduring value or to be sustainable as a point-of-difference. In most cases, these brands experienced declining market share or disappeared altogether.

Deliverability Criteria. The deliverability of an attribute or benefit brand association depends on both a company's actual ability to make the product or service (feasibility) as well as their effectiveness in convincing consumers of their ability to do so (communicability), as follows:

• Feasibility: Can the firm actually supply the benefit underlying the POD? The product and marketing must be designed in a way to support the desired association. It is obviously easier to con-vince consumers of some fact about the brand that they were unaware of or may have overlooked than to make changes in the product and convince consumers of the value of these changes. As noted above, perhaps the simplest and most effective approach is to point to a unique attribute of the product as a proof point or reason-to-believe. Thus, Mountain Dew may argue that it is more energizing than other soft drinks and support this claim by noting that it has a higher level of caffeine. On the other hand, when the point-of-difference is abstract or image based, support for the claim may reside in more general associations to the company that have been developed over time. Thus, Chanel No. 5 perfume may claim to be the quintessential elegant, French perfume and support this claim by noting the long association between Chanel and haute couture.

Communicability: The key issue in communicability is consumers' perceptions of the brand and the resulting brand associations. It is very difficult to create an association that is not consistent with existing consumer knowledge, or that consumers, for whatever reason, have trouble believing in. What factual, verifiable evidence or "proof points" can marketers communicate as support, so that consumers will actually believe in the brand and its desired associations? These "reasons-to-believe" are critical for consumer acceptance of a potential POD. Any claims must pass legal scrutiny too. The makers of category leader POM Wonderful 100% Pomegranate Juice have battled with the Federal Trade Commission over what the FTC deems as "false and unsubstantiated claims" about treating or preventing heart disease, prostate cancer, and erectile dysfunction.

Differentiation Criteria. Finally, target consumers must find the POD distinctive and supe-rior. When marketers are entering a category in which there are established brands, the challenge is to find a viable, long-term basis for differentiation. Is the positioning preemptive, defensible, and difficult to attack? Can the brand association be reinforced and strengthened over time? If these are the case, the positioning is likely to last for years.

Two questions often arise in brand marketing: What makes a brand strong? and How do you build a strong brand? The challenge for marketers in building a strong brand is ensuring that customers have the right type of experiences with products and services and their accompanying marketing programs

so that the desired thoughts, feelings, images, beliefs, perceptions, opinions, and experiences become linked to the brand.

Although a number of useful perspectives concerning brand equity have been put forth, the customer-based brand equity (CBBE) concept provides a unique point of view on what brand equity is and how it should best be built, measured, and managed.

The CBBE concept approaches brand equity from the perspective of the consumer - whether the consumer is an individual or an organization or an existing or prospective customer. Understanding the needs and wants of consumers and organizations and devising products and programs to satisfy them are at the heart of successful marketing.

The basic premise of the CBBE concept is that the power of a brand lies in what customers have learned, felt, seen, and heard about the brand as a result of their experiences over time. In other words, the power of a brand lies in what resides in the minds and hearts of customers.

A brand has positive customer-based brand equity when consumers react more favorably to a product and the way it is marketed when the brand is identified than when it is not (say, when the product is attributed to a fictitious name or is unnamed). Thus, customers might be more accepting of a new brand extension for a brand with positive customer-based brand equity, less sensitive to price increases and withdrawal of advertising support, or more willing to seek the brand in a new distribution channel. On the other hand, a brand has negative customer-based brand equity if consumers react less favorably to marketing activity for the brand compared with an unnamed or fictitiously named version of the product.

Let's look at the three key ingredients to this definition: (1) "differential effect," (2) "brand knowledge," and (3) "consumer response to marketing." First, brand equity arises from differences in consumer response. If no differences occur, then the brand-name product can essentially be classified as a commodity or a generic version of the product. Competition, most likely, would then just be based on price. Second, these differences in response are a result of consumers' knowledge about the brand, that is, what they have learned, felt, seen, and heard about the brand as a result of their experiences over time. Thus, although strongly influenced by the marketing activity of the firm, brand equity ultimately depends on what resides in the minds and hearts of consumers. Third, customers' differential responses, which make up brand equity, are reflected in perceptions, preferences, and behavior related to all aspects of brand marketing, for example, including choice of a brand, recall of copy points from an ad, response to a sales promotion, and evaluations of a proposed brand extension.

When consumers report different opinions about branded and unbranded versions of identical products - which almost invariably happens - it must be the case that knowledge about the brand, created by whatever means (past experiences, marketing activity for the brand, or word of mouth), has somehow changed customers' product perceptions. This result has occurred with virtually every type of product - conclusive evidence that consumers' perceptions of product performance are highly dependent on their impressions of the brand that goes along with it. In other words, clothes may seem to fit better, a car may seem to drive more smoothly, and the wait in a bank line may seem shorter, depending on the particular brand involved.

Thus, according to the customer-based brand equity concept, consumer knowledge drives the differences that manifest themselves in terms of brand equity. This realization has important managerial implications. For one thing, brand equity provides marketers with a vital strategic bridge from their past to their future.

E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

Brands as a Reflection of the Past. Marketers should consider all the dollars spent on manufacturing and marketing products each year not so much as "expenses" but as "investments" in what consumers saw, heard, learned, felt, and experienced about the brand. If not properly designed and implemented, these expenditures may not be good investments, in that they may not have created the right knowledge structures in consumers' minds, but we should consider them investments nonetheless. Thus, the quality of the investment in brand building is the most critical factor, not the quantity beyond some minimal threshold amount. In fact, it is possible to "overspend" on brand building if money is not being spent wisely. Conversely, some brands are considerably outspent but amass a great deal of brand equity through marketing activities that create valuable, enduring memory traces in the minds of consumers.

Brands as a Direction for the Future. The brand knowledge that marketers create over time dictates appropriate and inappropriate future directions for the brand. Consumers will decide, based on their brand knowledge, where they think the brand should go and grant permission (or not) to any marketing action or program. Thus, at the end of the day, the true value and future prospects of a brand rest with consumers and their knowledge about the brand.

No matter how we define brand equity, though, its value to marketers as a concept ultimately depends on how they use it. Brand equity can offer focus and guidance, providing a means to interpret past marketing performance and design future marketing programs. Everything the firm does can help enhance or detract from brand equity. Those marketers who build strong brands have embraced the concept and use it to its fullest as a means of clarifying, communicating, and implementing their marketing actions.

One great example providing invaluable information on brand building is The Discovery Channel, which was launched with the motto "Explore Your World" and well-defined brand values of adventure, exploration, science, and curiosity. After a detour to reality programming featuring crime and forensics shows and biker and car content, the channel returned to its mission of producing high-quality work that the company could be proud of and that was beneficial for people. Today, Discovery's 13 U.S. channels cumulatively reach 745 million subscribing households, and its 120 overseas channels in 180 countries reach 969 million homes. One hundred fifty thousand hours of content supplied by Discovery Education is used by more than 1 million teachers in half of all schools in the United States. Discovery's Web sites attract 24 million unique visitors every month. The company also launched Discovery Channel Magazine in Asia.

Using the associative network memory model, let's think of brand knowledge as consisting of a brand node in memory with a variety of associations linked to it. We can consider brand knowledge as having two components: brand awareness and brand image. Brand awareness is related to the strength of the brand node or trace in memory, which we can measure as the consumer's ability to identify the brand under different conditions. It is a necessary, but not always a sufficient, step in building brand equity. Other considerations, such as the image of the brand, often come into play.

Brand image has long been recognized as an important concept in marketing. Although marketers have not always agreed about how to measure it, one generally accepted view is that, consistent with our associative network memory model, brand image is consumers' perceptions about a brand, as reflected by the brand associations held in consumer memory. In other words, brand associations are the other informational nodes linked to the brand node in memory and contain the meaning of the brand for consumers. Associations come in all forms and may reflect characteristics of the product or aspects independent of the product.

What causes brand equity to exist? How do marketers create it? Customer-based brand equity occurs when the consumer has a high level of awareness and familiarity with the brand and holds some strong, favorable, and unique brand associations in memory. In some cases, brand awareness alone is enough to create favorable consumer response; for example, in low-involvement decisions when consumers are willing to base their choices on mere familiarity. In most other cases, however, the strength, favorability, and uniqueness of brand associations play a critical role in determining the differential response that makes up brand equity. If customers perceive the brand as only representative of the product or service category, then they'll respond as if the offering were unbranded.

Thus marketers must also convince consumers that there are meaningful differences among brands. Consumers must not think all brands in the category are the same. Establishing a positive brand image in consumer memory - strong, favorable, and unique brand associations - goes hand-in-hand with creating brand awareness to build customer-based brand equity. Let's look at both these sources of brand equity.

Brand awareness consists of brand recognition and brand recall performance:

Brand recognition is consumers' ability to confirm prior exposure to the brand when given the brand as a cue. In other words, when they go to the store, will they be able to recognize the brand as one to which they have already been exposed?

Brand recall is consumers' ability to retrieve the brand from memory when given the product category, the needs fulfilled by the category, or a purchase or usage situation as a cue. In other words, consumers' recall of Kellogg's Corn Flakes will depend on their ability to retrieve the brand when they think of the cereal category or of what they should eat for breakfast or a snack, whether at the store when making a purchase or at home when deciding what to eat.

If research reveals that many consumer decisions are made at the point of purchase, where the brand name, logo, packaging, and so on will be physically present and visible, then brand recognition will be important. If consumer decisions are mostly made in settings away from the point of purchase, on the other hand, then brand recall will be more important. For this reason, creating brand recall is critical for service and online brands: Consumers must actively seek the brand and therefore be able to retrieve it from memory when appropriate.

Note, however, that even though brand recall may be less important at the point of purchase, consumers' brand evaluations and choices will still often depend on what else they recall about the brand given that they are able to recognize it there. As is the case with most information in memory, we are generally more adept at recognizing a brand than at recalling it.

Advantages of Brand Awareness. What are the benefits of creating a high level of brand awareness? There are three - learning advantages, consideration advantages, and choice advantages.

Learning Advantages: Brand awareness influences the formation and strength of the associa-tions that make up the brand image. To create a brand image, marketers must first establish a brand node in memory, the nature of which affects how easily the consumer learns and stores additional brand associations. The first step in building brand equity is to register the brand in the minds of consumers. If the right brand elements are chosen, the task becomes easier.

Consideration Advantages: Consumers must consider the brand whenever they are making a purchase for which it could be acceptable or fulfilling a need it could satisfy. Raising brand awareness increases the likelihood that the brand will be a member of the consideration set, the handful of brands that receive serious consideration for purchase. Much research has shown that consumers are rarely loyal to only one brand but instead have a set of brands they would consider

E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

buying and another - possibly smaller - set of brands they actually buy on a regular basis. Because consumers typically consider only a few brands for purchase, making sure that the brand is in the consideration set also makes other brands less likely to be considered or recalled.

Choice Advantages: The third advantage of creating a high level of brand awareness is that it can affect choices among brands in the consideration set, even if there are essentially no other associations to those brands. For example, consumers have been shown to adopt a decision rule in some cases to buy only more familiar, well-established brands. Thus, in low-involvement decision settings, a minimum level of brand awareness may be sufficient for product choice, even in the absence of a well-formed attitude.

One influential model of attitude change and persuasion, the elaboration-likelihood model, is consistent with the notion that consumers may make choices based on brand awareness considerations when they have low involvement. Low involvement results when consumers lack either purchase motivation (they don't care about the product or service) or purchase ability (they don't know anything else about the brands in a category).

Consumer purchase motivation: Although products and brands may be critically important to marketers, choosing a brand in many categories is not a life-or-death decision for most consumers. For example, despite millions of dollars spent in TV advertising over the years to persuade consumers of product differences, 40 percent of consumers in one survey believed all brands of gasoline were about the same or did not know which brand was best. A lack of perceived differences among brands in a category is likely to leave consumers unmotivated about the choice process.

Consumer purchase ability: Consumers in some product categories just do not have the nec-essary knowledge or experience to judge product quality even if they so desired. The obvious examples are products with a high degree of technical sophistication, like telecommunica-tions equipment with state-of-the-art features. But consumers may be unable to judge quality even in low-tech categories. Consider the college student who has not really had to cook or clean before, shopping the supermarket aisles in earnest for the first time, or a new manager forced to make an expensive capital purchase for the first time. The reality is that product quality is often highly ambiguous and difficult to judge without a great deal of prior experience and expertise. In such cases, consumers will use whatever shortcut or heuristic they can come up with to make their decisions in the best manner possible. Sometimes they simply choose the brand with which they are most familiar and aware.

Establishing Brand Awareness. How do you create brand awareness? In the abstract, creating brand awareness means increasing the familiarity of the brand through repeated exposure, although this is generally more effective for brand recognition than for brand recall. That is, the more a consumer "experiences" the brand by seeing it, hearing it, or thinking about it, the more likely he or she is to strongly register the brand in memory.

Thus, anything that causes consumers to experience one of a brand's element - its name, symbol, logo, character, packaging, or slogan, including advertising and promotion, sponsor-ship and event marketing, publicity and public relations, and outdoor advertising - can increase familiarity and awareness of that brand element. And the more elements marketers can reinforce, usually the better. For instance, in addition to its name, Intel uses the "Intel Inside" logo and its distinctive symbol as well as its famous four-note jingle in TV ads to enhance awareness.

Repetition increases recognizability, but improving brand recall also requires linkages in memory to appropriate product categories or other purchase or consumption cues. A slogan or jingle creatively pairs the brand and the appropriate cues (and, ideally, the brand positioning as well, helping to build

a positive brand image). Other brand elements like logos, symbols, characters, and packaging can also aid recall.

The way marketers pair the brand and its product category, such as with an advertising slogan, helps determine the strength of product category links. For brands with strong category associations, like Ford cars, the distinction between brand recognition and recall may not matter much - consumers thinking of the category are likely to think of the brand. In competitive markets or when the brand is new to the category, it is more important to emphasize category links in the marketing program. Strong links between the brand and the category or other relevant cues may become especially important over time if the product meaning of the brand changes through brand extensions, mergers, or acquisitions.

For instance GANNETT can be a great example to consider for most companies. In March 2011, Gannett launched its first nationwide branding and advertising campaign, themed "It's All Within Reach." The company traces its origins to a small newspaper in Elmira, NY, in 1906 and over the decades has grown into a leading international media and marketing solutions company. Gannett's media properties include USA TODAY; 81 U.S. community newspapers (such as the Arizona Republic, Indianapolis Star, and Detroit Free Press); 23 broadcasting stations; over 100 digital properties; Point Roll, an industry leader in rich media advertising solutions; Career Builder, the nation's top employment site; and Captivate, a digital programming and advertising network with nearly 10,000 elevator and lobby screens in about 1,000 buildings. Then-Chairman and CEO Craig Dubow explained the campaign as, "Today, Gannett offers consumers and businesses everything they need to connect and engage with what matters most to them - anywhere, anytime and on every platform. It's important for our brand to reflect and promote our company as it is today and the tremendous value we bring."

Many marketers have attempted to create brand awareness through so-called shock adver-tising, using bizarre themes. For example, at the height of the dot-com boom, online retailer Outpost.com used ads featuring gerbils shot from cannons, wolverines attacking marching bands, and preschoolers having the brand name tattooed on their foreheads. The problem with such approaches is that they invariably fail to create strong category links because the product is just not prominent enough in the ad. They also can generate a fair amount of ill will. Often coming across as desperate measures, they rarely provide a foundation for long-term brand equity. In the case of Outpost.com, most potential customers did not have a clue what the company was about.

Creating brand awareness by increasing the familiarity of the brand through repeated exposure (for brand recognition) and forging strong associations with the appropriate product category or other relevant purchase or consumption cues (for brand recall) is an important first step in building brand equity. Once a sufficient level of brand awareness is created, marketers can put more emphasis on crafting a brand image.

Strength of Brand Associations. The more deeply a person thinks about product information and relates it to existing brand knowledge, the stronger the resulting brand associations will be. Two factors that strengthen association to any piece of information are its personal relevance and the consistency with which it is presented over time. The particular associations we recall and their salience will depend not only on the strength of association, but also on the retrieval cues present and the context in which we consider the brand.

In general, direct experiences create the strongest brand attribute and benefit associations and are particularly influential in consumers' decisions when they accurately interpret them. Word-of-mouth is likely to be particularly important for restaurants, entertainment, banking, and personal services.

E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

Starbucks, Google, Red Bull, and Amazon are all classic examples of companies that created amazingly rich brand images without the benefit of intensive advertising programs. Mike's Hard Lemonade sold its first 10 million cases without any advertising because it was a "discovery" brand fueled by word-of-mouth.

On the other hand, company-influenced sources of information, such as advertising, are often likely to create the weakest associations and thus may be the most easily changed. To overcome this hurdle, marketing communication programs use creative communications that cause consumers to elaborate on brand-related information and relate it appropriately to existing knowledge. They expose consumers to communications repeatedly over time, and ensure that many retrieval cues are present as reminders.

Favorability of Brand Associations. Marketers create favorable brand associations by convincing consumers that the brand possesses relevant attributes and benefits that satisfy their needs and wants, such that they form positive overall brand judgments. Consumers will not hold all brand associations to be equally important, nor will they view them all favorably or value them all equally across different purchase or consumption situations. Brand associations may be situation-or context-dependent and vary according to what consumers want to achieve in that purchase or consumption decision. An association may thus be valued in one situation but not another.

For example, the associations that come to mind when consumers think of FedEx may be "fast," "reliable," and "convenient," with "purple and orange packages." The color of the packaging may matter little to most consumers when actually choosing an overnight delivery service, although it may perhaps play an important brand awareness function. Fast, reliable, and convenient service may be more important, but even then only under certain situations. A consumer who needs delivery only "as soon as possible" may consider less expensive options, like USPS Priority Mail, which may take one to two days.

Because the brand is linked to the product category, some category associations may also become linked to the brand, either specific beliefs or overall attitudes. Product category attitudes can be a particularly important determinant of consumer response. For example, if a consumer thinks that all brokerage houses are basically greedy and that brokers are in it for themselves, then he or she probably will have similarly unfavorable beliefs about and negative attitudes toward any particular brokerage house, simply by virtue of its membership in the category.

Thus, in almost all cases, some product category associations will be shared with all brands in the category. Note that the strength of the brand associations to the product category is an important determinant of brand awareness.

Brand positioning is at the heart of marketing strategy. It is the "act of designing the company's offer and image so that it occupies a distinct and valued place in the target customer's minds." As the name implies, positioning means finding the proper "location" in the minds of a group of consumers or market segment, so that they think about a product or service in the "right" or desired way to maximize potential benefit to the firm. Good brand positioning helps guide marketing strategy by clarifying what a brand is all about, how it is unique and how it is similar to competitive brands, and why consumers should purchase and use it.

Deciding on a positioning requires determining a frame of reference (by identifying the target market and the nature of competition) and the optimal points-of-parity and points-of-difference brand associations. In other words, marketers need to know who the target consumer is, who the main competitors are, how the brand is similar to these competitors, and how the brand is different from them.

REFERENCES

1. Strategic Brand Management, 4th Edition, ISBN: 978-0-13-266425-7 by Kevin Lane Keller, published by Pearson Education, Inc., 2013.
2. Barbara Loken, Rohini Ahluwalia, and Michael J. Houston, eds., Brands and Brand Management: Contemporary Research Perspec-tives (New York: Taylor & Francis, 2010).
3. www.tescoforschoolsandclubs.co.uk.
4. Parsu Parasuraman, and Arvind Malhotra, "Understanding e-Service Quality", pre-sentation made at MSI Board of Trustees Meeting, "Marketing Knowledge in the Age of e-Commerce", November 2000.

PROCEEDINGS
THE SOUTHERN CAUCASUS INTERNATIONAL ACADEMY
E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

STUDIES OF INTERACTION OF THE SURFACTANT-CONTAINING CHEMICAL PRODUCT WITH VIGNA RADIATA

Cai X.[1,2], Ostroumov S.A. [1,2]

[1]Faculty of Biology, Lomonosov Moscow State University, Russia
[2]Shenzhen MSU-BIT University, Shenzhen, PR China;
Email: ar55@yandex.ru

ABSTRACT

In the paper, new data on research of effects of a chemical product which contains synthetic surfactants on plant seedlings are presented. The chemical product studied was a shampoo made in China. This was a herbal shampoo (HS) that contained lauryl polyether ammonium sulfate, ammonium lauryl sulfate, and components of two medicinal plants. Its effects on seedlings of *Vigna radiata* were studied. It was shown that at some concentrations, water solutions of the HS produced toxic effects. At a concentration of 0.5%, the HS produced a toxic effect that caused inhibition of the root length more than 50%. The new data are in accord with the previous results obtained by the research group of S.A.Ostroumov at M.V.Lomonosov Moscow State University.
Keywords: environmental hazards, ecotoxicology, plant science, phytotest, phytotoxicity, aquatic toxicology, surfactants, bioassay, plant seedlings,

Introduction: In previous studies, the bioassay of several surfactants and surfactant-containing chemical products were studied [1-18]. The concentrations of these chemicals in water which produced toxic effects on a number of biological species were determined [1-11, 13, 16, 17, 18]. Other laboratories also use similar approaches to test toxicity and environmental hazards from chemicals. [19, 20].
Recently these studies were continued using detergents and biological species Lens culinaris and Vigna radiata [18].
The goal of this study is to continue the research of potential biological effects (including toxicity) of surfactant-containing chemical products using the biological species Vigna radiata.

Methods: The chemical tested in the study was a Chinese herbal shampoo (the name of the shampoo: Ginger Polygonum Multiflorum Nutrient Shampoo). It was produced by BAWANG International (Group) Holding Co., Ltd (Guangzhou, China). The nontransparent liquid shampoo appears brown color. The formulation of the commercial shampoo are lauryl polyether ammonium sulfate, ammonium lauryl sulfate, cocamidopropyl betaine, cocamide MEA, glycol distearate, PDMS (polydimethylsiloxane), fragrance, sodium chloride, piroctone olamine, polyquaternium-47, polyquaternium-10, DMDM hydantoin, panthenol, EDTA-Na2, methylparaben, zingiber officinal (a type of extract from ginger roots), polygonum multiflorum (a Chinese medicine), and water.
The method was described in detail in the books [16, 17] and our other publications [18]. The seeds were put in Petri dishes. The tested water solution of the chemicals studied were added to the Petri dishes. The quantitative parameters of seed germination and the seedling growth were measured and the average values were calculated. Statistical data analysis was performed using Microsoft Excel 2019 Program.

Number of seeds was 30 per Petri dish.
The volume of shampoo solution added to each Petri dish was 20 mL.
The isometric volume (20 mL) of ultrapure water was used as the control.
Temperature of the incubation of the Petri dishes was 25.0±1.0 °C.
Other details of the method of the experiments were described in [16-18].

Results and discussion: The main results are presented in Table 1.
It is seen from Table 1 that increased concentrations of the chemical texted produced increased toxicity on the biological species used, Vigna radiata.
The increased concentrations induced a decrease in the root length.
The largest concentration tested (5%) produced the most pronounced toxic effect.
The interpretation of the data obtained is presented in Table 2.
The obtained results are in accord with the previous results of research projects conducted in the group of S.A. Ostroumov at Moscow State University [1-18]. Previous data obtained in this group demonstrated phytotoxicity of surfactants and several surfactant-containing chemical mixtures to higher plants [1-11, 13-18, 21], both terrestrial [1-11, 13, 16, 17, 18] and aquatic ones [9, 21].
The new results presented in this publication add new additional examples of toxicity of the chemical mixtures that contain surfactants.

Table 1 The mung beans (Vigna radiata) tests for the 96-h exposure to various concentrations of the water solution of the shampoo (20 mL) at 25.0±1.0 °C. The tested chemical was the Chinese herbal shampoo (the name of the shampoo: Ginger Polygonum Multiflorum Nutrient Shampoo).

Concentrations of the tested chemical (%)	0.0 %	0.5%	5.0%
Root length, average (mm)	58.47	22.36	0.35
Standard error (mm)	1.70	1.38	0.13

Table 2 Interpretation of the results obtained in this study on biological effects of the tested chemical (Ginger Polygonum Multiflorum Nutrient Shampoo) which was tested at various concentrations using Vigna radiata.

Concentration (%) of the chemical product tested	Interpretation of the results of the phytotest in this study	Comments
0	No toxicity	No inhibition of growth of roots
0.5	A pronounced toxicity	Inhibition of root growth, more than 50%
5.0	Lethal effect as a result of high toxicity	No root growth observed

It is worth noting that the chemical product (chemical mixture) studied in this publication is a broadly used body-care product.
The chemical products of this type are manufactured and sold in large quantities. The discharge of these chemicals into aquatic environment is massive. The aquatic environment pollution with these chemicals is substantial. Therefore, the potential environmental impact of the water pollution with these chemicals is of substantial importance. The ecotoxicological considerations connected with

water pollution with surfactants and surfactant-containing chemical products were analyzed in the previous publications, namely, the books [16, 17]. The new data support the main conclusions made in these books.

Conclusions: 1. It was found the the phytotest with Vigna radiata is an effective method to study biological effects of a shampoo.
2. It was discovered that at certain concentrations and time exposures the chemical tested, namely, the Chinese herbal shampoo (the name of the shampoo: Ginger Polygonum Multiflorum Nutrient Shampoo), produced toxic effects on the plant seedlings.

REFERENCES

1. Goryunova S.V., Ostroumov S.A. Effects of an anionic detergent on green algae and some angiosperms. // Biological Sciences. 1986, No.7: p.84-86.
2. Nagel H,Ostroumov S.A., Maximov V.N. Inhibition of elongation of seedlings of buckwheat under the effect of sodium dodecylsulphate. // Biological Sciences. 1987, No.12: 81-84; https://www.academia.edu/44213751/;
3. Maximov V.N., Nagel H., Ostroumov S.A. Biotesting waters containing a surfactant (sulfonol) and DNOC. // Hydrobiological Journal, 1988. 24 (4): 54-55. https://www.academia.edu/1436246/ ;
4. Maximov V.N., Nagel H., Kovaleva T.N., Ostroumov S.A. Biotesting of water polluted by sulfonol. // Water Resources. 1988. 1: 165-168.
5. Ostroumov S.A. Certain Aspects of Evaluating Biological Activity of Xenobiotics // Vestnik MGU, Series 16, Biologiya, 1990. p. 27-34.
6. Ostroumov S.A., Xing B. Effects of three types of metal oxide nanoparticles (TiO2, CuO, Al2O3) on the seedlings of the higher plant Lens culinaris. // Ecologica. 2012. Vol.19 (65), 10-14.
7. Ostroumov S.A., L.S. Samoilenko, M.M. Telitchenko. Studies on some aspects of ecotoxicology and biochemical ecology of surfactants // Biodeterioration and Biodegradation.1995. Vol. 9, 641-641.
8. Ostroumov S.A., Golovko A.E. Biotesting of surfactant (sulphonol) toxicity using rice seedings as a test-object // Gidrobiologičeskij žurnal (Kiev) [Gidrobiologicheskiy Zhurnal, Hydrobiological Journal]. 1992. Vol.28 (3), 72-75.
9. Ostroumov S.A., Kotelevtsev S.V. Assessing environmental hazards of chemicals: the efficient method with higher plants // Black Sea Scientific Journal of Academic Research. 2015. Vol.26 (8), p.8;
10. Ostroumov, S.A., and Kotelevtsev, S.V., 2015. Using agricultural plants in order to access toxicity of chemical pollutants to control pollution of the environment: informational biotechnology. // International Symposium of ISB- INMA TEH. Agricultural and Mechanical Engineering, Bucharest, Romania, 29-31 October 2015 (pp. 405-408). INMA Bucharest.
11. Ostroumov S.A., Solomonova E.A. Phytotoxicity of a surfactant-containing product towards macrophytes // Russian Journal of General Chemistry. 2013. 83 (13), 2614-2617; https://www.academia.edu/27074231/ ;

12. Lazareva E.V., Ostroumov S.A. Accelerating the reduction of the concentration of surface-active substances in water microcosms in the presence of plants: Innovations for phytotechnology // Doklady Akademii Nauk. 2009. 425 (6), 843-845; https://www.academia.edu/43779198/;
13. Poklonov V.A., Kotelevtsev S.V., Ostroumov S.A. On the effect of detergents on Vigna radiata and Lens culinaris under biotest conditions // Toxicological Bulletin. 2012. No. 5. p.49-53. [Poklonov V. A., Kotelevtsev S. V., Ostroumov S. A. O vozdeystvii detergentov na Vigna radiata i Lens culinaris v usloviyakh biotesta // Toksikologicheskiy vestnik. 2012. № 5. s.49-53].
14. Electronic resource. 2010. Using plants in ecological and environmental studies: List of publications, S.A. Ostroumov;. https://library.by/portalus/modules/biology/readme.php?subaction=showfull&id=1281291046& archive=&start_from=&ucat=& ; last viewed 04.05.2020;
15. Electronic resource. 160 articles, environment, water, ecology, toxicology, remediation, bioassay, aquatic, higher plants, macrophytes…; in English, in Russian. 50-page list. http://5bio5.blogspot.com/2015/07/160-articles-environment-water-ecology.html; last viewed 04.05.2020;
16. Ostroumov S. A., Biological Effects of Action of Surfactants on Organisms, MAKS-Press, Moscow (2001), p. 334. (in Rus.). [translit of the title of the book: Biologicheskiie effekty pri vozdeistvii poverkhnostno-aktivnykh veshchestv na organizmy]; https://www.worldcat.org/title/biologicheskiie-effekty-pri- vozdeistvii-poverkhnostno-aktivnykh-veshchestv-na-organizmy/oclc/263630756;
17. Ostroumov S.A., 2006. Biological effects of surfactants. CRC Press. https://www.academia.edu/826799/; https://www.academia.edu/782323/;
18. Cai X., Ostroumov S.A. Discovery of detergent toxicity using non-animal bioassay. Biogeochemical Innovations, Vol.2, p.216-219 (2020). https://www.academia.edu/44455943/;
19. Eze, M.O., George, S.C. and Hose, G.C., 2021. Dose-response analysis of diesel fuel phytotoxicity on selected plant species. Chemosphere, 263, p.128382.
20. Das, P., Bora, P., Paul, N. and Bhattacharyya, N., 2021. Vegetation composition and assessment of phytotoxicity in a paper mill dumpsite. Plant Science Today, 8(1), pp.140-147.
21. Solomonova E. A., Ostroumov S. A.. Tolerance of an Aquatic Macrophyte Potamogeton crispus L. to Sodium Dodecyl Sulphate. - Moscow University Biological Sciences Bulletin, 2007, Vol. 62, No. 4, p. 176–179. DOI: 10.3103/S0096392507040074; http://www.scribd.com/doc/45556848 ;

PROCEEDINGS
THE SOUTHERN CAUCASUS INTERNATIONAL ACADEMY
E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

STUDYING THE IMITATION MODEL OF THE SYSTEM SECURITY INFORMATION IN SERVICE NETWORKS

Balami Ismayılov

National Aviation Academy, Doctor of technical sciences, Associate professor, Azerbaijan.
Email: balemi@rambler.ru

ABSTRACT

Information security systems (ISS), including the N-th number of security features, are considered. The system is represented as a multichannel queuing system (QS) with a Poisson flow of requests at the input. The goal of building of this structure is pursued. At the same time, the process of servicing unauthorized access (UA) request is also random. Security features in the ISS convert the source stream into streams of detected and skipped (undetected) unauthorized access requests. Models of ISS have been developed and simulation experiments have been carried out, the results obtained have been analyzed.
Keywords: Information security systems, queuing systems, security features, unauthorized access.

REZÜME

N sayda müdafiə vasitəsindən ibarət informasiya təhlükəsizliyi sisteminə (İTS) baxılmışdır. Sistemə girişində puasson axını olan çoxkanallı kütləvi xidmət sistemi (KXS) kimi baxılmışdır. Onun strukturunun qurulması məqsədi nəzərdə tutulur. İcazəsiz müdaxiləli (İM) xidmət prosesində - sorğular da təsadüfidir. İTS-də müdafiə vasitəsi ilkin axını aşkarlanmış və buraxılmış (aşkarlanmamış) İM sorğularına çevirir. İTS modeli işlənmiş, imitasiya eksperimenti aparılmış,alınmış nəticələr təhlil edilmişdir.
Açar sözlər: İnformasiya təhlükəsizliyi sistemi, kütləvi xidmət sistemi, müdafiə vasitəsi, icazəsiz müdaxilə.

Introduction: The problem associated with the creation of an ISS in service networks is one of the most urgent tasks. In the literature there are known works that study the nature of negative impacts on service networks [1-5]. Impacts on service networks are carried out mainly from the global Internet, which are not only a means of finding information, but, unfortunately, the medium of spread of viruses. ISS in service networks are created between various kinds of service networks on the one hand and a global network on the other. This is a kind of gateway (gateway), whose functions include the inspection and filtering of information passing through it. Such a structure of interconnections allows drastically reducing the threats of UA in service networks by using the "masquerading" method, i.e. when all outgoing traffic from the service network is sent on behalf of the ISS, making the network almost "invisible" [1]. In addition, in the problem of information security of networks, there are problems of building the structure of security systems, including modern hardware and software to control the transmitted information. ISS mainly contains a set of programs that require a certain amount of memory [1-3].
In the literature, various approaches have been proposed for the study of the characteristics of ISS in service networks for finding the optimal structure of an ISS [1–4]. To solve the problem of studying

the characteristics of the ISS in [1], the method of a generalized reduced gradient was used and the mathematical expectation of the probability of loss from the untimely distribution of messages after filtering the network was chosen as an indicator of efficiency. In [5, 6], mathematical models of a hardware-software complex for protecting information from unauthorized access are considered.
Note that in contrast to [1,5,6], here, the main models are considered to be models of ISS from UA in service networks, representing the N- th number of protection tools (PT) with a limited queue and taking into account missing (undetected) UA requests. They interact with streams of random events - attempts to tamper with UA, which are caused not only by the actions of intruders, but also by errors in software and hardware systems.
ISS perform the following functions:
- carry out protection against intruders;
- perform attempts to detect UA;
- carry out actions for their classification;
- give appropriate solutions for blocking UA.
In [2] it is noted that a similar process, i.e. UA attempts in the network can be described by extraordinary random flows.
In [6], in order to simplify the model, the ordinary recurrent flow of UA attempts was considered. Note that unauthorized service requests arise not only because of the actions of the attacker, but also because of the following reasons:
- software errors;
- incorrect settings of access rights;
- non-compliance of the operating conditions of the İSS with the requirements of the technical conditions.
In the model, the process of serving UA requests can be considered random for the following reasons:
- randomness of the moment of appearance of requests;
- the randomness of the state of the processing at this moment and the randomness of its possible states at subsequent points in time
Based on the above provisions, the structure of the original model of ISS from UA can be provided in the following form (Figure 1).

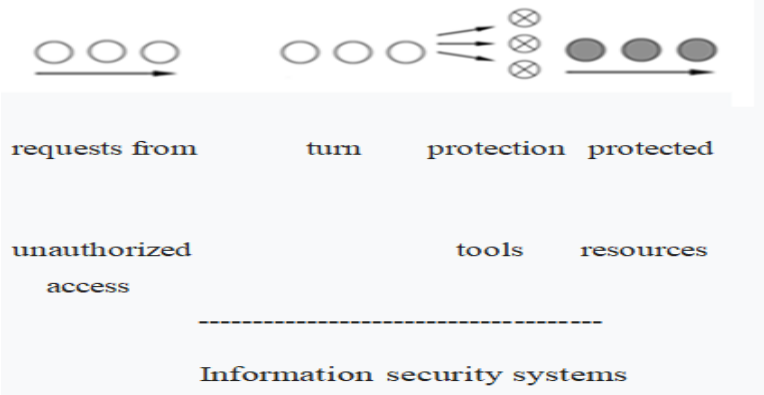


Figure 1 The structure of the model of ISS from UA

E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

In the system, the attacker is not exposed to input, but tries to implement various threats in the service network. Incoming requests from UA appear with intensity λ at the input of the ISS, including the N-th number of PT. Protection tools convert the original UA flow to the streams of detected and missed (i.e. sparse) UA queries with intensity $\bar{\lambda}$. Each PT in an ISS is characterized by the probability of missing UA and the probability of providing protection.
If we consider the protective equipment functioning in the ISS as service devices, and the incoming requests for UA as requirements, then the ISS as a whole can be considered as a multi-channel queuing system, which is shown in Fig.2.

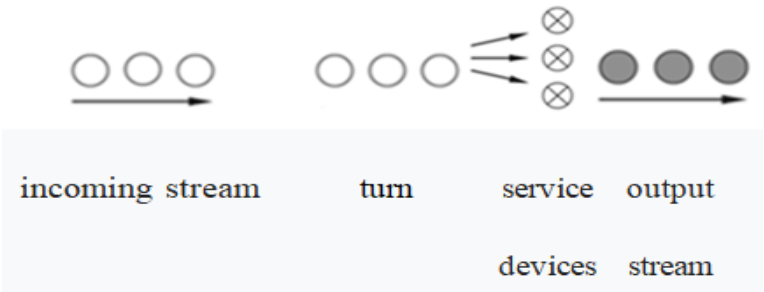
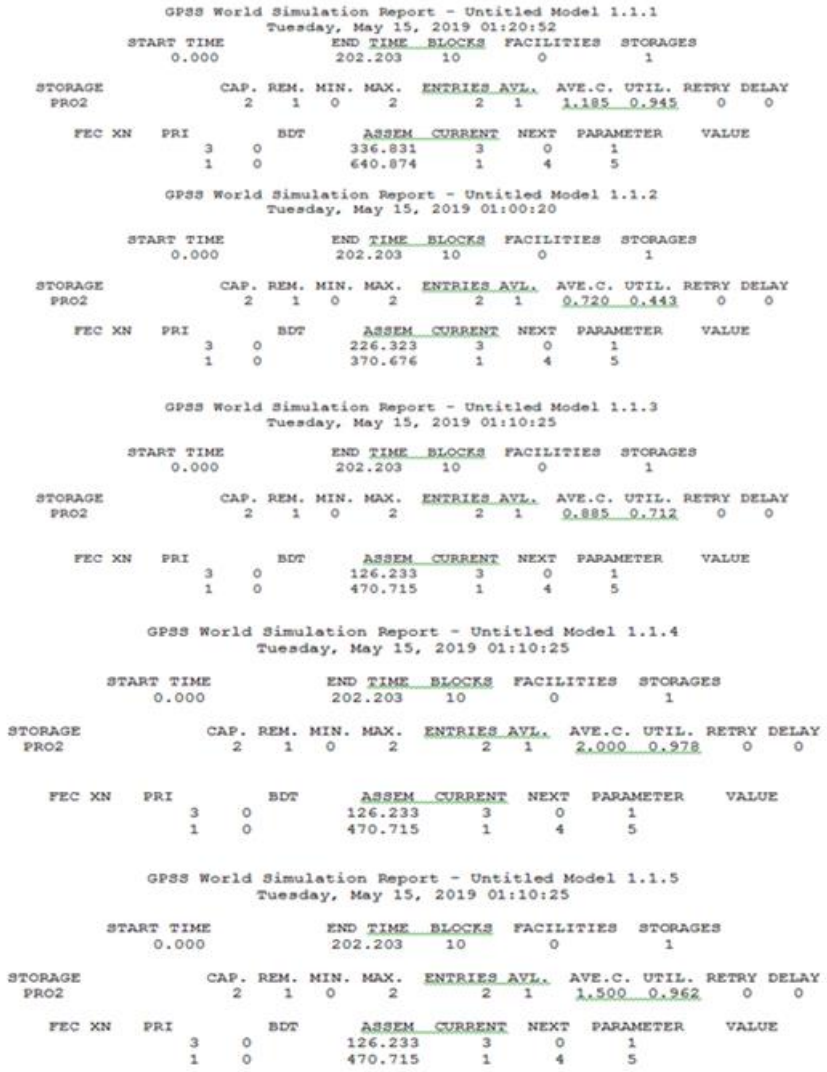


Figure 2 Multichannel queuing system

A simulation model of the system in the GPSS language (General purpose simulation system), which is an algorithm describing the behavior of the QS, i.e. changes in the state of the system over time for a given stream of requests arriving at the input of the system. Input flows determine the external parameters of the system. The parameters of the output streams describe the property of the system functioning and are its output parameters. The output parameters of the system are considered the number of occupied devices in the system, the utilization rate of service devices, etc.

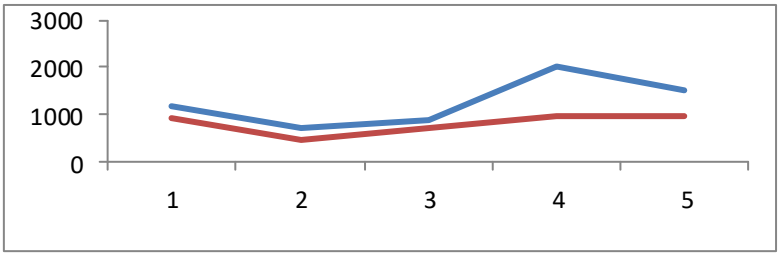
The algorithm of the imitational model of ISS: A multichannel QS is considered, including the N-th number of an PT with a limited queue as service devices and as transacts - incoming requests for UA. The state of the QS is characterized by the states of servicing devices, transactions and queues in service devices. The state of service devices is characterized by a logical variable, the values of which are defined as "busy" or "free." The variable describing the state of the transaction may have the values of "service" or "wait". The queue state is determined by the number of transacts in it.
It is assumed that the number of intruder's revenues over a certain period of time depends only on the length of the observation period. The average intensity of intruders is determined by the Poisson law [6].
In order to build a simulation model of an ISS from UA controllers, algorithms have been developed for constructing a simulation model of an ISS in service networks, which include the following items:
1) generation of transactions to simulate the receipt of requests for UA;
2) if there is a free PT in the ISS - incoming transaction are passed into the system, otherwise the transition to item 6 is carried out;
3) queuing to simulate the request buffer PT;

4) the implementation of the delay in order to simulate the processing of the PT of incoming requests for UA;
5) is carried out the destruction of transactions to eliminate requests for UA both missed and screened PT;
6) the value of the probability of skipping UA (for example, 0.1) and the probability of providing protection (for example, 0.9), depending on the set values of these probabilities in the algorithm, either the transaction is destroyed or proceeds to step 2.
Based on this algorithm, a simulation model of an ISS was developed in the GPSS language, and the results presented in Figure 3 for five runs were obtained.
At the same time, for the performed runs of the imitation model, the characteristics of the İSS in the service networks are investigated and the following trends in its main characteristics are defined as:
- the number of occupied devices in the system;
- utilization rate of service devices in the system.



```
                GPSS World Simulation Report - Untitled Model 1.1.1
                        Tuesday, May 15, 2019 01:20:52

      START TIME            END TIME  BLOCKS  FACILITIES  STORAGES
          0.000              202.203     10          0          1

STORAGE             CAP. REM. MIN. MAX.  ENTRIES AVL.  AVE.C. UTIL. RETRY DELAY
 PRO2                 2    1    0    2         2    1    1.185  0.945     0     0

   FEC XN   PRI          BDT        ASSEM   CURRENT  NEXT  PARAMETER    VALUE
                3    0          336.831       3       0       1
                1    0          640.874       1       4       5

                GPSS World Simulation Report - Untitled Model 1.1.2
                        Tuesday, May 15, 2019 01:00:20

      START TIME            END TIME  BLOCKS  FACILITIES  STORAGES
          0.000              202.203     10          0          1

STORAGE             CAP. REM. MIN. MAX.  ENTRIES AVL.  AVE.C. UTIL. RETRY DELAY
 PRO2                 2    1    0    2         2    1    0.720  0.443     0     0

   FEC XN   PRI          BDT        ASSEM   CURRENT  NEXT  PARAMETER    VALUE
                3    0          226.323       3       0       1
                1    0          370.676       1       4       5


                GPSS World Simulation Report - Untitled Model 1.1.3
                        Tuesday, May 15, 2019 01:10:25

      START TIME            END TIME  BLOCKS  FACILITIES  STORAGES
          0.000              202.203     10          0          1

STORAGE             CAP. REM. MIN. MAX.  ENTRIES AVL.  AVE.C. UTIL. RETRY DELAY
 PRO2                 2    1    0    2         2    1    0.885  0.712     0     0

   FEC XN   PRI          BDT        ASSEM   CURRENT  NEXT  PARAMETER    VALUE
                3    0          126.233       3       0       1
                1    0          470.715       1       4       5

                GPSS World Simulation Report - Untitled Model 1.1.4
                        Tuesday, May 15, 2019 01:10:25

      START TIME            END TIME  BLOCKS  FACILITIES  STORAGES
          0.000              202.203     10          0          1

STORAGE             CAP. REM. MIN. MAX.  ENTRIES AVL.  AVE.C. UTIL. RETRY DELAY
 PRO2                 2    1    0    2         2    1    2.000  0.978     0     0

   FEC XN   PRI          BDT        ASSEM   CURRENT  NEXT  PARAMETER    VALUE
                3    0          126.233       3       0       1
                1    0          470.715       1       4       5

                GPSS World Simulation Report - Untitled Model 1.1.5
                        Tuesday, May 15, 2019 01:10:25

      START TIME            END TIME  BLOCKS  FACILITIES  STORAGES
          0.000              202.203     10          0          1

STORAGE             CAP. REM. MIN. MAX.  ENTRIES AVL.  AVE.C. UTIL. RETRY DELAY
 PRO2                 2    1    0    2         2    1    1.500  0.962     0     0

   FEC XN   PRI          BDT        ASSEM   CURRENT  NEXT  PARAMETER    VALUE
                3    0          126.233       3       0       1
                1    0          470.715       1       4       5
```

Figure 3 The results of the simulation model of ISS



number of runs

Figure 4 Tendencies of change in the number of occupied devices (blue line) in the system and utilization rate of service devices (red line) (scale1: 1000)

The revealed results show that with detected and missed requests in the system, the trend in the number of occupied devices in the system and the utilization rate of the service devices are respectively 1,185; 0.720; 0.885; 2.000; 1500 and 0.945; 0.443; 0.712; 0.978; 0.962 (Figure 4).
The obtained results confirm the assumptions made that the appearance of the missed and detected transacts depends on the length of the observation period. The results can be used in networks for various purposes.

Conclusion: An approach to the study of the characteristics of SBI in service networks is proposed. Algorithms and models for the study of the characteristics of the SME have been developed, simulation experiments have been carried out, and corresponding results have been obtained. The latter can be used to build new or modify existing PBIs in networks of various purposes.

REFERENCES

1. Б.Г. Исмайлов Исследование характеристик систем защиты информации распределенной сети//Автоматика и Вычислительная Техника. Рига, 2006, №3, с.51-59.
2. В.А. Герасименко, А.А. Малюк Основы защиты информации. М.: Наука, 1997, 224 с.
3. E.Gelenbe, P.Glynn, K.Sigmann Queues with negative arrivals//J.Appl.Prob.1991.V 28.pp. 245- 250.
4. Р.Манзо, Н.Касконе, Р.В. Разумчик Экспоненциальная система массового обслуживания с отрицательными заявками и бункером для вытесненных заявок. Автоматика и Телемеханика,2008, вып.9, 103-113с.
5. В. В. Карпов Вероятностная модель оценки защищенности средств вычислительной техники с аппаратно-программным комплексом защиты информации от несанкционированного доступа. «Программные продукты и системы » № 1, 2003 с.31-36.
6. В.А. Герасименко, А. В. Карпов Имитационная модель системы защиты информации.«Программные продукты и системы » № 2, 2005 с.26-30.

E – ISSN: XXXX – XXXX
VOLUME 01 ISSUE 01 2021
PROCEEDINGS
THE SOUTHERN CAUCASUS INTERNATIONAL ACADEMY

DEVELOPMENT OF TOURISM IN THE REGION IN THE CONTEXT OF THE STRATEGY OF INTERCULTURAL DIALOGUE

Alona Obozna[1], Anna Pinchuk[2], Ivan Fedotov[3]

[1]Mykolaiv Branch of Kyiv National University of Culture and Arts, PhD of Economics, Ukraine,
Email: helensj532@gmail.com
[2]Mykolaiv Branch of Kyiv National University of Culture and Arts, PhD of Economics, Ukraine,
Email: 666135303d@gmail.com
[3]Mykolaiv Branch of Kyiv National University of Culture and Arts, Lecturer Ukraine,
Email: fedotovivan91@gmail.com

ABSTRACT

Introduction: It is culture that encourages various forms of creative self-expression and at the same time the study and renewal of traditions, promotes the development of creative economy, innovation policy and active public participation in building a modern and democratic state.
In Mykolayiv region there is an extensive network of cultural institutions that have a strong potential for consolidation of society, its focus on European values, Ukraine's integration into the European community, improving the quality of life of region, ensuring equal access to information, knowledge and cultural heritage.

Results: The state cultural policy is implemented without clearly defined priorities that would meet the challenges of the new century. There is a growing awareness that the development of the creative sector, including in the field of culture, can directly or indirectly affect the economy, improving its performance and creating jobs, stimulating innovation and promoting sustainable social development.

Conclusion: Modern international relations of Ukraine are characterized by rather intensive integration processes, among which the interregional and cross-border cooperation in which the Nikolaev area is involved also plays an important role.]

Introduction: The goal of the tourism industry, which we are opening today, is to present our best experience in this area, as well as to develop the main tasks for the development of the tourism industry in our regions.
We live in the south of Ukraine, in the city of Mykolaiv and we work in the field of tourism at the MB «University of KNUKiM». We want to briefly tell you about this amazingly interesting and tourist place. We will visit some corners of Mykolaiv that want and can develop tourism. At the same time, we are developing various tourist destinations that will become priorities in our work.
These are the places that tourists are already visiting and with which we already have plans for cooperation.
The Mykolaiv area has powerful recreational and tourist potential and nature reserve fund, which are capable to surprise and entertain having a rest. Due to the unique relief and climate, many different types of tourism are developing here today.

E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

In addition to relaxing on the sandy beaches of the Black Sea coast, you can go yachting, rafting, kiting, windsurfing, cycling and hiking, go on excursions to unique canyons, nature reserves, get acquainted with the incredibly beautiful corners of nature, breathe without and broaden their horizons and develop erudition.

In order to promote Mykolaiv region as an area attractive for tourism and recreation in the most attractive places of the region, festivals and other mass events are held annually, which are attended by many vacationers among adults and children.

The most popular types of tourism in the city of Mykolaiv are recreational, historical and cultural, improving. The basis of a powerful tourist-recreational and health-improving and medical complex are the recreational territories of the settlements of Kobleve, Rybakivka, Chornomorka and Ochakiv.

Availability in the area of the sea coast with a length of about 140 km, mineral water sources with approved reserves of up to 1 thousand cubic meters. deposits of therapeutic mud, especially Tiligul and Beikush estuaries with geological reserves of more than 2 million cubic meters. creates conditions for the announcement of these recreational and tourist areas climatic and balneological resorts of local and national importance.

Mykolaiv is a festival city.

To get acquainted with the ethnographic features and cultural heritage of the city and the region, annual festival events have been launched:

- Open Children's Rock Festival "Eternal Youth" - the only one in Ukraine, takes place in the Cultural and Game Complex "Children's Town" Fairy Tale ";
- Youth "STARtfest" - a festival of youth talents: vocals, theater;
- Festival of street cultures "Skills" - modern dance cultures;
- All-Ukrainian Festival of National Cultures "Friendship" - the establishment of the principles of interethnic peace and harmony in society, promotion of cultural heritage, folk traditions, language, decorative and applied arts of the ethnic groups of Ukraine;
- FEST-Mriya festival - a holiday of Ukrainian traditions and popularization of folk;
- "Mykolaiv RIVER-FEST" - a large-scale water festival in the city of gentle water, a real symbiosis of efforts of citizens;

Every year in Mykolaiv under the auspices of the Mykolaiv regional state administration the International investment forum "Mykolaiv investment" is carried out. The purpose of the Forum is a broad presentation of investment opportunities in the region, innovative and investment projects, attracting investment for small and medium business development, establishing business contacts with Ukrainian and foreign partners.

One of the main directions of development of the tourist industry of the region is the provision of quality services.

Today the subjects of tourist activity offer the following excursion routes for vacationers and tourists:

"Gray Kinburn - the pearl of the Black Sea Coast",
"Granite-steppe Pobuzhye",
"City of the ancient Greeks - Olvia",
"Wine tour to Radsad",
"Ochakiv - the pearl of the Black Sea Coast ",
"Excursion tour of the city of Mykolaiv ".

Acquaintance with the city of St. Nicholas" with a visit to the best in Ukraine and one of the oldest in Europe ZOO and others.

The list of topics and authors of the excursion product is constantly updated and forms a database of the Department of Foreign Relations, Foreign Economic Activity, European Integration, Tourism and Resorts of Mykolaiv.
The goal of the tourism industry that we are opening today is to present our best experience in this area, as well as to develop the main tasks for the development of the tourism industry in our region. We will visit all corners of Mykolaiv that want and can develop tourism.
At the same time, we are developing various tourist destinations that will become priorities in our work. These are the places that tourists are already visiting and with which we already have plans for cooperation. Mykolayiv City Council has signed 14 cooperation agreements with cities and regions of Belarus, Bulgaria, Greece, Georgia, Italy, China, Romania and Turkey. The city of Voznesensk has 6 sister cities in Georgia, Lithuania, South Africa, Poland and Hungary. The Pervomaisk City Council signed an Agreement on Friendship and Cooperation with the City of Dobrich (Bulgaria).

Conclusion: The most promising areas of tourism development are ecological, rural, historical and cultural, industrial, industrial, youth, active types of tourism (rafting, kiting, jumping, hiking, orienteering, etc.).

REFERENCES

1. A.O. Obozna, MV Мерлянов, O.B. Havrilova Development of cultural and historical tourism in Mykolayiv Black Sea Economic Studies. 2018. - Issue 29. - P. 42-45.
A. Obozna, O. Gavrilova, I. Fedotov Analysis of the state of development of the domestic tourism industry in accordance with international recommendations of statistical indicators. Efektyvna ekonomika. № 6, June, 2019. - Access mode: http://www.economy.nayka.com.ua/pdf/6_2019/65.pdf.
2. MYKOLAIV REGIONAL STATE ADMINISTRATION Development strategy of the Nikolaev area for the period up to 2027.Project

PROCEEDINGS
THE SOUTHERN CAUCASUS INTERNATIONAL ACADEMY
E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

CO-INFECTIONS OF COVID-19 PATIENT WITH HAIRY-CELL LEUKEMIA AND BACTEREMIA CAUSED BY SALMONELLA : A CASE REPORT

Tamar Didbaridze[1], Levan Ratiani[2], Kakhaber Chelidze[3], Inga Gvasalia[4], Nino Gogokhia[5] Malvina Javakhadze[5], Lia Tevzadze[6], Lile Malania[6]

[1]TSMU. Department of Microbiology, Associate Professor, MD, PhD. Georgia.
[2]TSMU. The First University Clinic, Anesthesiology/Resuscitation Department. Georgia.
[3]TSMU. Head of Internal Medicine #1 Department, Full Professor, MD, PhD. Georgia.
[4]Physitian of infection diseases, MD, PhD. Georgia.
[5]Head of Clinical Laboratory. TSMU the First University Clinic, TSMU Professor. Georgia.
[5]TSMU. Department of infectious diseases, Associate Professor, MD, PhD. Georgia.
[6]NCDC. Reference laboratory. Georgia.
Email: didbaridzetamar@gmail.com

ABSTRACT

The life-threatening Salmonella infection may develop if a pathogen spreads to the bloodstream. Salmonella septicemia can be caused by any of the Salmonella bacteria, which are found in contaminated food and water. The infection is systemic and affects virtually every organ system. The most common symptom is an intermittent fever.
In this case report, we will discuss a presentation of hairy-cell leukemia with Salmonella spp. bacteremia and COVID-19 disease. The patient with hairy-cell leukemia and persistent high fever (without prior symptomatic intestinal infection) was eventually tested for COVID-19 and found to be positive. An immunocompromised state predisposes to invasive infection with intracellular organisms, such as Salmonella spp. even with the early-stage of leukemia.
To our knowledge, this is the first reported case of Invasive non-typhoidal Salmonella (iNTS)-in a COVID-19 patient.
Keywords: Salmonella, sepsis, COVID-19, leukemia.

Introduction: Salmonella is gram-negative non-spore-forming facultative intracellular anaerobes that cause a wide spectrum of disease, especially in the warm season.[1] The clinical presentation depends on the serotype of Salmonella and host factors and can range from gastroenteritis, enteric fever, bacteremia, focal infections, to a convalescent lifetime carrier state.[2] The non-typhoidal species of Salmonella tend to produce a more localized response including a self-limited form of gastroenteritis because they are believed to lack the human-specific virulence factors.[1] Therefore, extra-intestinal non-typhoidal Salmonella (NTS) is uncommon and usually occurs in patients with predisposing factors such as immune deficiency or occult urologic problems. About 95% of cases of Salmonella infection are food-borne; however, the incidence of direct contact exposure with animal carriers is uprising.[3]
Salmonella spp are estimated to cause over 93 million new infections annually[4], and are responsible for a variety of clinical manifestations in humans. The primary Salmonella-induced diseases in humans are gastroenteritis (caused by non-typhoidal Salmonella; NTS) and typhoid fever (caused by S. Typhi and the various S. Paratyphi pathovars). Infections with S. Typhi are responsible for

approximately 21 million new cases of typhoid each year, globally (5). Annual mortality from typhoid is estimated to be >190,000 and has increased by 39% between 1990 and 2010.[6] Although rarely encountered in western countries, typhoid is not a conquered disease; a recent analysis of global mortality data revealed that, in highly endemic regions such as Southeast Asia and sub-Saharan Africa, the relative years of life lost to typhoid ranked similarly to those lost to breast cancer, prostate cancer, and leukemia in North America.[7] Non-typhoidal Salmonella (NTS) is an important pathogen that causes gastroenteritis, bacteremia, and focal infections. Salmonella Typhi and Paratyphi A are host-restricted pathogens whose reservoir is humans. Unlike other Salmonella serovars that primarily cause local intestinal inflammation and diarrhea, Salmonella Typhi and Paratyphi A, B, and C characteristically invade from the gastrointestinal tract into the bloodstream, survive and reproduce within macrophages, and in 1–4% of cases result in a chronic carriage (8). Salmonella Typhi and Salmonella Paratyphi A, collectively known as typhoidal Salmonella, are causal agents for a serious, invasive (bacteremia), sometimes fatal disease of humans called typhoid fever or paratyphoid fever (also called enteric fevers). The bacteremia of typhoid fever persists for several weeks if antibiotic therapy is not given. The symptoms and signs of typhoid fever are not due to circulating endotoxin. Most patients have no serum endotoxin except patients who present with severe clinical disease and septic shock syndrome, in whom circulating endotoxin can be demonstrated.[9]

Clinical Case presentation: A 39-year-old male with a 2-month history of hairy-cell leukemia was hospitalized at the Department of Internal Medicine (The First University Clinic of TSMU, Tbilisi, Georgia) with a persistent high fever. The patient worked as a diver and his habitual diet mainly consisted of half-raw seafood.

Along with a mild elevation of WBCs blood culture collected at admission returned positive innumerable Salmonella species within 48 hours. Further, it was identified as Salmonella enterica serovar Typhi (ST) O: 9,12, when sent to the NCDC reference laboratory for serotyping.

One set of blood cultures drawn on admission resulted positive in one out of two bottles two days after they were drawn, identified as Salmonella enterica serovar Typhi (ST) O:9,12 group and also serotyped by NCDC reference laboratory. The antimicrobial susceptibility test was performed by using the Kirby-Bauer disk diffusion method following the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines.

Based on a local susceptibility test results IV Ceftriaxone 2 g/d was administered and repeated blood culture was obtained after ten-days of antimicrobial treatment. Despite clearance of bacteremia fever was persisted. Because of this SARS-CoV-2 infection was tested by RT-PCR. The test result was positive.

The patient was discharged in a stable health condition on the day 24th of admission.

Conclusion: In conclusion, we have described a case of simultaneous invasive non-typhoidal salmonella (iNTS) infection and COVID-19 in leukemia patient, who was successfully treated with antimicrobials.

Discussion: Our patient was diagnosed with a Hairy-cell leukemia and hence had the extraintestinal manifestation of Salmonella. Salmonella bacteremia is a well-known manifestation of immunosuppression in patients with hematology malignancy, and these patients have 20- to 100-fold

E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

increased prevalence of acquiring Salmonella infection and bloodstream invasion versus the general population.

REFERENCES

1. Majowicz SE, et al. The global burden of nontyphoidal Salmonella gastroenteritis. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America. 2010;50:882–889.
2. Crump JA, et al. The global burden of typhoid fever. Bulletin of the World Health Organization. 2004;82:346–353.
3. Lozano R, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380:2095–2128. Coburn B, Grassl GA, Finlay BB. Salmonella, the host and disease: A brief review. Immunol Cell Biol. 2007;85:112–8.
4. Yang CH, Tseng HH, Chen KJ, Liu JD. Salmonella infections: A retrospective 10-year analysis of 134 cases in a regional hospital in Taiwan. Scand J Infect Dis. 1996;28:171–5.
5. Linam WM, Gerber MA. Changing epidemiology and prevention of Salmonella infections. Pediatr Infect Dis J. 2007;26:747–8.
6. Wistrom J, Jertborn M, Ekwall E, Norlin K, Söderquist B, Strömberg A, et al. Empiric treatment of acute diarrheal disease with norfloxacin. A randomized, placebo-controlled study. Swedish Study Group. Ann Intern Med. 1992;117:202–8
7. Sirinavin S, Garner P. Antibiotics for treating Salmonella gut infections. Cochrane Database Syst Rev. 2000 CD001167.
8. Centers for Disease Control and Prevention. National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS): Human Isolates Final Report. 2004
9. Lee SC, Yang PH, Shieh WB, Lasserre R. Bacteremia due to non-typhi Salmonella: Analysis of 64 cases and review. Clin Infect Dis. 1994;19:693–6

E – ISSN: XXXX – XXXX
VOLUME 01 ISSUE 01 2021
PROCEEDINGS
THE SOUTHERN CAUCASUS INTERNATIONAL ACADEMY

CLINICAL AND LABORATORY ANALYSIS OF SPINAL MENINGITIS: A CASE REPORT

Levan Ratiani[1], Tamar Didbaridze[1], Ketevan Machavariani[1], Magda Rurua[1], Nana Saralidze[1], Nino Gogokhia, Zurab Zaalishvili[2]

[1]Tbilisi State Medical University, The First University Clinic, Georgia.
[2]American MD program of Tbilisi State Medical University, Georgia.
Email: didbaridzetamar@gmail.com

ABSTRACT

Spinal meningitis is a very rare complication of spinal anesthesia. Over the course of 1952 to 2005, only 179 cases have been described in the medical literature. Risk factors for spinal meningitis include spinal anesthesia, a diagnostic lumbar puncture, myelography, epidural anesthesia, head trauma, epidural corticosteroid injection, and the dissemination of nosocomial bacteremia. The causative agents of spinal meningitis are usually representative of normal oropharyngeal, upper respiratory, and skin flora: Streptococcus salivarius, S. mitis, S.gravis, S.sanguinis, Enterococcus fecalis, S. uberis, S. microaerophilia, Corynebacterium xerosis, Abiotrophia defective, Acinetobacter spp, S. aureus, S. epidermidis. However, it should be noted that CSF culture is usually negative.
We report a case of the 26-year-old previously healthy male who underwent extracorporeal lithotripsy for urolithiasis preceded by spinal anesthesia on Jul 3, 2020 and wad admitted
in the First University Clinic of TSMU ICU department in 2020 of 21july. CSF culture yielded coagulase-negative Staphylococcus epidermidis. Antibiotic therapy was started with intravenous ceftriaxone and vancomycin. Then the patient was switched to meropenem and vancomycin.
Keywords: meningitis, Staphylococcus epidermidis, treatment, spinal anesthesia.

Introduction: Spinal meningitis is a very rare complication of spinal anesthesia. Over the course of 1952 to 2005, only 179 cases have been described in the medical literature. 50% of these cases were attributed to spinal anesthesia while 9% were associated with a diagnostic lumbar puncture. Spinal meningitis is usually caused by the inoculation of subarachnoid space by exogenous bacteria. This concept is supported by the fact that out of those 179 cases mentioned earlier, 114 of them (63%) were associated with the normal oropharyngeal flora of medical staff while 1% of cases were caused by endogenous microbes. Risk factors for spinal meningitis include spinal anesthesia, a diagnostic lumbar puncture, myelography, epidural anesthesia, head trauma, epidural corticosteroid injection, and the dissemination of nosocomial bacteremia.
The exact incidence of spinal meningitis after spinal and epidural anesthesia is not known; however, according to several retrospective studies, it ranges from 0 to 0.04%. The underlying cause of spinal meningitis might be inappropriate aseptic techniques or hematogenous dissemination of asymptomatic bacteremia in patients undergoing lumbar puncture. Two patients from the care of the same neurosurgeon, four patients from the clinical practice of the same anesthesiologist, and two patients from the same operating room after spinal anesthesia were diagnosed with spinal meningitis. This observation indicates the essential role of clinical in the pathogenesis of spinal meningitis. The causative agents of spinal meningitis are usually representative of normal oropharyngeal, upper respiratory, and skin flora:Streptococcus salivarius, S. mitis, S.gravis, S.sanguinis, Enterococcus

E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

fecalis, S. uberis, S. microaerophilia, Corynebacterium xerosis, Abiotrophia defective, Acinetobacter spp, S. aureus, S. epidermidis. However, it should be noted that CSF culture is usually negative. This phenomenon might be explained by the fact that microorganisms mentioned above have low virulence and they do not grow well on standardized bacterial media. However, they can replicate fast in CSF and cause spinal meningitis.[4-7] Quagliarello and Scheld posed a possible theory of the mechanisms that are employed by bacteria to penetrate the blood-brain barrier and replicate in CSF: IgA proteaseↃ, bacterial pili, biofilm, complement inhibitors, and binding epitopes.[3] 2-3 hours are usually needed for spinal meningitis to manifest clinically after bacterial inoculation in CSF.
In the beginning, there are pro-inflammatory cytokines such as TNF-a in CSF. It is scientifically proven that these cytokines and interleukins cause inflammation and disrupt the blood-brain barrier. Another possible mechanism is that toxic metabolites produced by leukocyte-induced bacterial digestion cause vasogenic edema. This disrupts CSF autoregulation which can cause cerebral hyper or hypoperfusion. Veringa *et.al*[10] studied the source of spinal meningitis caused by S. salivarius. This infection was associated with the myelography procedure. They amplified the genetic material of bacteria isolated from CSF and confirmed a specific fatty acid pattern of S. salivarius. Then they compared their findings to the bacteria isolated from the nasopharyngeal swab of the surgeon and his assistant. Similarly, Trautman *et. al*[(11)] published the case of S. aureus-induced spinal meningitis and epidural abscess after epidural anesthesia during twin delivery. They studied nasopharyngeal bacteria of an anesthesiologist, nine nurses, and two obstetricians all of whom participated in delivery. They separated large DNA molecules via gel electrophoresis. There was a concordance between CSF culture results and that of anesthesiologist's nasopharyngeal flora.

Case report: A 26-year-old previously healthy male underwent extracorporeal lithotripsy for urolithiasis preceded by spinal anesthesia on Jul 3, 2020. 24 hours after surgery he developed severe occipital and bilateral temporal headache initially diagnosed as a headache of unknown origin. There were no changes in CSF analysis at this time. An epidural blood patch was not performed. The patient was treated in an inpatient setting for UTI from Jul 11 to Jul 20, 2020.
On Jul 21, he was transferred to TSMU First University Clinic. He had a high fever, severe headache, vomiting, photophobia, nuchal rigidity, and positive Kernig sign.
The site of previous spinal anesthesia was neither erythematous nor painful. The patient was noted to have left-sided hemiparesis with left lower extremity plegia. Brain MRI revealed ischemic foci in the left cerebellar hemisphere. Subarachnoid cisterns were moderately enlarged. The patient was placed in ICU. CSF obtained via lumbar puncture was not clear.CSF analysis revealed a leukocyte count of 2000/mm^3, a glucose level of 2,22mmol/L (Normal range 2.22-4.44mmol/l), a protein level of 0.45 g/L (Normal range 0.15-0.45 g/L). CSF culture yielded coagulase-negative Staphylococcus epidermidis. Antibiotic therapy was started with intravenous ceftriaxone and vancomycin. Then the patient was switched to meropenem and vancomycin.

Discussion: A post-dural puncture headache is an uncommon (incidence 1-3%) but expected complication after spinal anesthesia (1). Spinal meningitis is an extremely rare finding after spinal anesthesia. (2) In this case, a causal relationship between the patient's meningitis and spinal anesthesia is unclear, because the chemistry of CSF showed leukocytosis, but glucose and protein levels were in the normal range. Also, it is important to take into consideration ischemic stroke.

REFERENCES

1. Halpern S, Preston R: Postdural puncture headache and spinal needle design. Metanalyses. Anesthesiology 1994; 81:1376-83.
2. Chestnut DH: Spinal anesthesia in the febrile patient. Anesthesiology 1992; 76:667-9.
3. Quagliarello VJ, Scheld WM: Bacterial meningitis: Pathogenesis, pathophysiology, and progress. N Engl J Med 1992; 327:864–72Quagliarello, VJ Scheld, WM
4. Lyytikainen O, Rautio M, Carlson P, Anttila V, Vuento R, Sarkkinen H, Kostiala A, Vaisanen ML, Kanervo A, Ruutu P: Nosocomial bloodstream infections due to viridans streptococci in hematological and non-hematological patients: Species distribution and antimicrobial resistance. J Antimicrob Chemother 2004; 53:631–4Lyytikainen, O Rautio, M Carlson, P Anttila, V Vuento, R Sarkkinen, H Kostiala, A Vaisanen, ML Kanervo, A Ruutu, P
5. Wisplinghoff H, Reinert R, Cornely O, Seifert H: Molecular relationships and antimicrobial susceptibilities of viridans group streptococci isolated from the blood of neutropenic cancer patients. J Clin Microb 1999; 37:1876–80Wisplinghoff, H Reinert, R Cornely, O Seifert, H
6. Pfaller MA, Jones RN, Doern GV, Sader HS, Kugler KC, Beach ML: Survey of bloodstream infections attributable to gram-positive cocci: Frequency of occurrence and antimicrobial susceptibility to isolates collected in 1997 in the United States, Canada, and Latin America from the SENTRY Antimicrobial Surveillance Program. SENTRY Participants Group. Diagn Microbiol Infect Dis 1999; 33:283–97Pfaller, MA Jones, RN Doern, GV Sader, HS Kugler, KC Beach, ML
7. Facklam R: What happened to the streptococci: an overview of taxonomic and nomenclature changes. Clin Microbiol Rev 2002; 15:613–30Facklam, R
8. Weed LH, Wegeforth P, Ayer J, Felton L: Influence of certain experimental procedures upon the production of meningitis by intravenous inoculation. Monogr Rockefeller Inst Med Res 1920; 12:57–112Weed, LH Wegeforth, P Ayer, J Felton, L
9. Carp H, Bailey S: The association between meningitis and dural puncture in bacteremic rats. Anesthesiology 1992; 75:667–9Carp, H Bailey, S
10. Veringa E, van Belkum A, Schellekens H: Iatrogenic meningitis by Streptococcus salivarius following lumbar puncture (letter). J Hosp Infect 1995; 29:316–8Veringa, E van Belkum, A Schellekens, H

PROCEEDINGS
THE SOUTHERN CAUCASUS INTERNATIONAL ACADEMY
E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

EPIDERMOLYSIS BULLOSA AND STEM CELL THERAPY

Maia Matoshvili, Davit Tophuria, Natia Kvizhinadze

Dermato-Venerology Department, Human Normal Anatomy Department, Pharmacy Department, Tbilisi State Medical University.

ABSTRACT

The main goal of regeneration or sustained genetic correction of damaged tissue, advanced tissue-engineering techniques are especially applicable for many dermatological diseases including wound healing, genodermatoses (like the severe blistering disorder epidermolysis bullosa) and chronic (auto-)inflammatory diseases. This review summarizes general aspects as well as current and future perspectives of stem cell therapy in dermatology.
Keywords: Epidermolysis bullosa, Bone-marrow transplantation, MSC-cell therapies.

Introduction: Stem cells (SCs), common to all multicellular organisms, are specified as undifferentiated self-replicating cells possessing the ability to generate, sustain and replace terminally differentiated cells. They show two key features: self-renewal (cell divisions with maintenance of the undifferentiated state), and capability of in vivo and in vitro reconstitution of a given tissue via differentiation into specialized cell types1. SCs are commonly subdivided into two main entities, embryonic stem cells (ESCs) (pluripotent) and adult SCs (multipotent or unipotent).

Methodology: 1.MSC-cell therapies SC therapies are increasingly established in the experimental treatment of genetic diseases, recently also in patients with recessive dystrophic EB (RDEB), a rare genetic blistering disease. RDEB patients lack genes for synthesis of Collagen VII. These symptoms mainly account for more severe disease complications, such as mitten deformities of hands and feet and aggressive epithelial cancers. Therapeutic approaches, either with intravenous infusion or direct local administration of MSCs to chronic wounds have started however, to provide novel insight into key BM cells and mechanisms germane to repair and regeneration of the epithelium. Initially, intradermal injections of human BM-MSCs showed a dose-dependent, significant higher production and in loco deposition of type VII collagen associated with restoration of immature anchoring fibrils and superior dermal-epidermal integrity compared to controls with intradermal phosphate-buffered saline-injections in DEB mouse models. In line with this preclinical data, Conget et al.126 described the replenishment of type VII collagen at the dermal–epidermal junction upon intradermal BM-MSC injection provided from healthy donors into chronic wounds of two RDEB individuals3. The administration led to a reduced blister formation (up to 6 months) and an increased reepithelialisation of chronic ulcers. Tissue remodeling activity of the transplanted MSCs, owing to both, their integration into the skin and their secretion of growth factors and cytokines participating in the regulation of tissue regeneration, might activate self-healing mechanisms in RDEB skin. Subsequent studies questioned a predominant impact of SC on phenotypic amelioration 1. Petrof et al.10 showed that a single intradermal injection of allogeneic fibroblasts accelerated the initial rate of wound healing in patients with RDEB within the first 28 days although this effect diminished thereafter. In another study, both the injection of allogeneic cultured fibroblasts in suspension solution as well as of the suspension solution alone led to a similar increase in type VII collagen expression and

improved wound healing in chronic non-healing ulcers of RDEB patients, independently of type VII collagen regeneration The mechanical stimulus in the course of intradermal injection itself was thus supposed as a potential cause of improved wound healing, reflecting an elevated expression of heparin binding-EGF-like growth factor in response to subclinical inflammations that occur after injections into the human skin. Providing a clinically feasible approach of systemic treatment, also the infusion of allogeneic BM-derived SCs led to a phenotypic improvement in RDEB patients, showing reduced blistering and tissue fragility 2. Transplanted SCs from healthy donors are believed to engraft into the skin, differentiate to fibroblasts and keratinocytes, synthesize the missing type VII collagen anchoring fibers and thereby improve the fragile skin and shearing off of the epidermis63. In this respect, it has been shown that low levels of restored expressions of collagen VII (below 30%) are sufficient to significantly improve the RDEB phenotype and even a correction of about 3% COL7A1 mRNA seemed to be adequate for phenotypic reversion in a mouse model. Ten RDEB children who received systemic (intravenous) allogeneic (wild-type) BM-MSCs showed improved wound healing, reduced skin redness, a subjective improvement in quality of life and high tolerability. As skin biopsies at 2 months post-treatment revealed no increase in type VII collagen nor new anchoring fibrils, phenotypic improvement possibly reflected a predominant immune suppressive and immune modulating effect of MSCs 11. In another study with RDEB patients fewer blistering and significantly shortened healing time after treatment with BM-MSCs was demonstrated, either with or without concomitant cyclosporine 12. In this cohort, electron microscopic examination additionally confirmed an increase in anchoring fibrils after treatment. In summary, intradermal or intravenous injections of MSCs have shown some clinical benefits for RDEB patients. However, feasible application techniques as well as optimal cell dosage and frequency schedules for administration of allogeneic MSCs still have to be established and evaluated in future clinical trials. Further, biological and pratical limitations, like the ephemerality of the transplanted cells and potential immune rejection towards neo-antigens hitherto hinder the clinical applicability.

2) Bone-marrow transplantation. Following the demonstration of successful BM SC transplantation in murine RDEB, a clinical trial of whole BMT was performed in children with RDEB13. The first step included a high-dose chemotherapy to immunoablate patients to ensure more dependable lymphohematopoietic engraftment. Unfiltered cell populations of the donor BM were used based on previous observations that both hematopoietic and mesenchymal BM-derivedSCs have the potential to increase the production of C7134. All six patients, who underwent BMT had some clinical improvement and five of the six showed increased C7 at the DEJ at the time biopsies where taken between day 100 and 200. Three of the six individuals showed an immense clinical improvement, with a reduction from 50% blistering area of the body surface to less than 10%. The remaining three patients exhibited a moderate improvement with less than 25% of the body surface area affected 4. However, toxicities occurred, as one patient died before the BMT due to heart failure possibly related to cyclophosphamide toxicity and pre-existing renal failure. Another individual died 6 months after transplantation because of an infection related to graft failure. Therefore, BMT protocols are currently refined by considering the use of reduced intensity conditioning and targeting of distinct subpopulations of BM cells.

3) Gene therapy A low worldwide incidence of rare (or “orphan”) genetic skin diseases limits the accrual of data for research and suspends advancements in developing therapeutic concepts for these skin conditions. But since all of the most devastating forms of such inherited skin diseases like EB are mostly resulting from monogenic defects, in theory, their remediation at the genetic level should

E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

be more feasible 5. Sustained gene correction of continuously renewing tissue like skin, however, relies on the efficient molecular targeting of SCs.

A proof-of-principle study with somatic gene therapy in EB has been published 14. Via a retroviral vector, a LAMB3 transgene has been inserted into autologous keratinocytes that were then grafted back as a confluent sheet onto the thigh of an adult patient with generalized intermediate junctional EB. In the following years, the graft has continued to express laminin-332 at the dermoepidermal junction, leading to a clinical improvement and long-term epidermal stability. This remarkable benefit was achieved although the number of holoclone SCs was reduced in the patient, probably a repercussion of long-term skin blistering resulting in niche destruction and SC depletion or exhaustion. In the future, optimized protocols, with the goal to effectively isolate a sufficient amount of autologous EpSC, before being corrected by gene transfer, might facilitate the procedure9. These cells, after building grafts and being transplanted, have the potential to induce long-term (if not permanent) regeneration of wounded skin. So far, promising observations of the use of genetically corrected skin grafts include (1) a total engraftment, yielding a morphologically and functionally normal, non-blistering skin that is able to resist mechanical stress, (2) continuing laminin beta-3-protein and laminin 332 expression that consequently strengthens the epidermal-dermal junction over a period of at least 8 years, (3) the ability to persistently and effectively restore the epidermis with only a few transgenic EpSC, which accounted only for a small subpopulation of transduced cells (most transduced keratinoctes have been shorter-living transit-amplifying progenitors) 10. With regard to hitherto limited and/or transient efficacy as well as safety/tolerability issues, optimal therapy for EB is doubtful to involve justllogeneic cells. More promise may hold a combination of gene, protein, drug, and cell therapies 6.

4) iPSCs iPSCs therapies are therapeutically promising for genetic skin disease, because they can be rather easily exploited to be genetically manipulated. In addition, this approach makes modeling of skin diseases via targeted mutagenesis of the relevant genes possible forgoing the usage of ESCs15. The successful establishment of iPSC-based therapies for hereditary skin diseases mainly relies on four steps: First, via a patient's skin biopsy cells have to be isolated. Second, these cells have to be transformed into iPSCs via genetic reprogramming. Third, genetic aberrations in obtained iPSCs have to be (safely) corrected, preferably through homologous recombination (HR) 7.

In cell culture models, successfully generated iPSc from either gene corrected (autologous) RDEB fibroblasts or healthy (allogenic) individuals are able to differentiate into hematopoietic SCs and MSCs that can home to mucocutaneous blistering areas where they differentiate into keratinocytes and fibroblasts69, 8. Additionally, autologous grafting of in vitro generated 3-dimensional (3D) skin equivalents by iPSCs shows generation of stratified epidermis in vitro and in vivo (animal models). The first attempt to use revertant cell therapy in an individual with generalized intermediate junctional EB yielded no functional benefits after (successful) grafting of isolated revertant keratinocytes, which were expanded to epidermal sheets. Of note, cultured keratinocytes showed 30% reversion, whereas the number of reverted keratinocytes dropped to 3% in the graft, probably becauseof lacking holoclones15. An alternative approach using punch graft transplantation of revertant skin, however, has been used successfully to heal chronic erosions with enhanced expression of laminin-332 in a patient with a similar form of junctional EB and mutated LAMB3 gene. The improved skin integrity was maintained for at least 18 months.The future impact of this approach thus relies on methods to more efficiently expand revertant keratinocytes in culture and to

generate grafts containing adequate numbers of revertant SC to yield functional repair and regeneration of the skin.

REFERENCES

1. Kumar D, Talluri TR, Anand T, Kues WA. Transposon-based reprogramming to induced pluripotency. Histol Histopathol. 2011;30:
2. Bilousova G, Roop DR. Induced pluripotent stem cells in dermatology: potentials, advances, and limitations. Cold Spring Harb Perspect Med. 2011
3. Beaver CM, Ahmed A, Masters JR. Clonogenicity: holoclones and meroclones contain stem cells. PLoS One. 2012
4. Gola M, Czajkowski R, Bajek A, Dura A, Drewa T. Melanocyte stem cells: biology and current aspects. Med Sci Monit. 2012
5. Nemeth K, Mezey E. Bone marrow stromal cells as immunomodulators. A primer for dermatologists. J Dermatol Sci. 2015
6. Tanabe S. Signaling involved in stem cell reprogramming and differentiation. World J Stem Cells. 2015
7. 7Van Camp JK, Beckers S, Zegers D, Van Hul W. Wnt signaling and the control of human stem cell fate. Stem Cell Rev. 2014
8. Blanpain C, Fuchs E. Epidermal stem cells of the skin. Annu Rev Cell Dev Biol. 2016
9. Barrandon Y, Green H. Three clonal types of keratinocyte with different capacities for multiplication. Proc Natl Acad Sci U S A. 2015
10. Claudinot S, Nicolas M, Oshima H, Rochat A, Barrandon Y. Long-term renewal of hair follicles from clonogenic multipotent stem cells. Proc Natl Acad Sci U S A. 2015
11. Blanpain C, Fuchs E. Epidermal homeostasis: a balancing act of stem cells in the skin. Nat Rev Mol Cell Biol. 2009;10:207–217. [PMC free article] [PubMed] [Google Scholar]
12. Senoo M. Epidermal stem cells in homeostasis and wound repair of the skin. Adv Wound Care (New Rochelle) 2013
13. Rompolas P, Mesa KR, Kawaguchi K, Park S, Gonzalez D, Brown S, et al. Spatiotemporal coordination of stem cell commitment during epidermal homeostasis. Science. 2016
14. Hsu YC, Li L, Fuchs E. Emerging interactions between skin stem cells and their niches. Nat Med. 2018;
15. Kaur P, Li A. Adhesive properties of human basal epidermal cells: an analysis of keratinocyte stem cells, transit amplifying cells, and postmitotic differentiating cells. J Invest Dermatol. 2019

PROCEEDINGS
THE SOUTHERN CAUCASUS INTERNATIONAL ACADEMY
E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

MELANOCYTIC DISEASES

Maia Matoshvili, Davit Tophuria, Natia Kvizhinadze

Dermato-Venerology Department, Human Normal Anatomy Department, Pharmacy Department, Tbilisi State Medical University. Email: mmatoshvili@hotmail.com

ABSTRACT

It was traditionally assumed that cancer cells of melanoma arise from melanocytes. Recently, however, a hypothesis was posed that melanoma could also descend in extrafollicular SCs altered by harming factors such as ultraviolet (UV) A and UVB 5. Experimental studies are currently ongoing to investigate the mechanisms capable of causing damage to the DNA of SCs, as to ascertain this hypothesis.
Keywords: Melanocytic diseases, Melanocyte development, Melanoma.

Introduction: McSCs are essential to maintain melanocyte populations in human skin and its appendages. Studies on McSCs have elucidated molecular mechanisms underlying ordinary melanocytic development as well as melanocyte-related pathological conditions like vitiligo and melanoma, although still many questions regarding the characterization of McSCs remain unsolved 3. Human iPSCs may be useful for the characterization of human McSCs, since this application allows the acquirement of a sufficient amount of patient-specific melanocytes along the differentiation of iPSCs. These cells could then be applies for disease modeling and evaluation of potentially therapeutic approaches156. The use of HSCs transplantation, adjuvant to chemotherapy and immunotherapy for patients with metastatic melanoma, has been already evaluated in clinical trials. These strategies should allow the use of increased chemotherapy doses for more efficient eradication of tumor cells. However, definitive results are still missing A distinct type of pluripotent, non-tumorigenic (in vivo) MSCs refer to the term multilineage-differentiating stress-enduring cells (Muse cells). These cells can be conveniently obtained from mesenchymal tissues (such as dermis and bone marrow) and human mesenchymal cultured cells (such as dermal fibroblasts). After culturing in a specific differentiation medium containing ten factors (Wnt3a, stem cell factor, endothelin-3, basic fibroblast growth factor, linoleic acid, cholera toxin, L-ascorbic acid, 12-O-tetradecanoyl-phorbol 13-acetate, insulin–transferrin–selenium, and dexamethasone), Muse cells derived from dermal fibroblasts have been shown to readily transform into functional melanocytes 2. These differentiated Muse cells expressed melanocytic markers, grew in 3D cultured skin and produced melanin after transplantation to the back skin of immunodeficient mice 1. However, in contrast to other pSCs such as ES cells and iPS cells, Muse cells show low telomerase activity and are not able to grow tumors in vivo. This technique might be the basis for new treatment approaches to melanocytic diseases like vitiligo.

Methodology: 1) Cancer stem cells Several years ago, it was discovered that a small sub-population of acute myeloid leukemia cells could reestablish tumors in severe combined immunodeficiency mice, while the vast majority of the tumor cells could not 5. This study underlies the cancer SC hypothesis, which implicates that cancer SCs have characteristics comparable to the SC population of their tissue of origin (i.e., self-renewal, differentiation potential) 6. They are assumable very rare

within the tumor and are thought to produce progenitor cells that can generate all types of cells comprising the tumor. CSCs pose a challenge for cancer therapies, because eradicating the bulk tumor usually does not include all CSCs, leaving enough of them at liberty to re-establish the complete heterogeneity of cancer tissue. In addition, these SCs might be more resistant to chemotherapy, and even targeted molecular therapies via their relatively high expression of the multi-drug resistance genes (e.g., MDR-1, BRCP1), a common feature of many SCs. Furthermore, owing to their ability to rapidly induce DNA repair mechanisms, CSCs are often highly resistant to radiation therapy. Finally, they appear to be particularly adept in stimulating angiogenesis, nurturing tumor development CSCs can switch between quiescence (tumor dormancy) and active cell division with subsequent varying chemosensitivity, a behavior that mainly depends on changes in the microenvironmental niche and involves complex signaling pathways regulating tumorigenic growth and dormant arrest 10. CSCs further possess the capability to create new niches during the metastatic process160,161. These “metastatic niches” are defined by specific locations (e.g., metastatic cells occupying native SC and perivascular niches), signaling pathways (e.g., PI3K-AKT pathway as a critical survival input for metastatic cancer cells), incorporated stromal (e.g., endothelial) cell types and ECM proteins (e.g., tenascin C which strongly promotes SC functions). The components of this micromilieu support the survival, self-renewal and expansion of disseminated metastatic CSCs. Beside melanocytic SCs or melanoma cancer SCs probably involved in the pathogenesis of melanoma, CSCs have also been demonstrated in non-melanoma skin cancer such as squamous cell carcinoma (SCC) in mice. The proliferation and expansion of these CSCs are markedly influenced by their ability to respond to TGF-β receptor II and integrin/focal adhesion kinase-mediated signaling at the tumor–stroma interface. This pathway is crucially important in human cancer 6. It acts initially tumor suppressive (inhibition of proliferation) but promotes metastasis in later stages in response to a tumor associated altered cellular context and variable environmental signaling profiles. Studies have revealed that several distinct CSC populations coexist in SCC and that tumor initiation and metastatic potential of these populations can be uncoupled 7. Therefor understanding CSC biology it is critical to develop novel CSC-targeted therapies, especially for patients with cancer and a poor prognosisNew therapeutics may be designed to specifically target these cells to block cancer progression. At the moment many chemotherapeutics attack rapidly dividing cells, so that it is easy for slowly dividing cancer SCs to evade these therapies40. Whether skin tumors like melanoma follow a cancer SC model for tumor development or a hierarchical model of tumor growth and progression (or combinatory/ other models) remains to be determined. These features of tumor dynamics, however, have implications on drug development in order to increase the efficacy of CSCs targeting 9. Cancer SCs from solid tumors usually express organ-specific markers. However, many caveats impede the discovery and identification of cancer SC markers for diagnostic and therapeutic purposes, to include the potential that the expression of these cell surface markers is not stable, that daughter cells may express different markers, that markers may not be unique to the cancer SCs but expressed in other cell types as well and that these surface protein markers may not have any role in cancer SC biology 8. Beside the isolation of CSCs by flow cytometry according to CSC-specific cell surface markers, CSCs can be identified by so-called “side population chains (SP)” within a tumor. The latters refer to a subpopulation of tumor cells that is highly conserved in human cancer cell lines and linked to SC characteristics (clonogenic). It further features drug transport property with multidrug resistance and might serve as a “evolutionary backup” to keep alive at least a sub-fraction of cells when exposure to cytotoxic compounds occurs. SP show differential efflux activity to the main cell population usually measured by efflux of the fluorescent DNA binding dye

E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

Hoechst 3334. Moreover, CSCs may be determined through sphere assays, since tumorigenic cells showing SC characteristics have the ability to grow as floating spheres in serum-free medium The significant role of aberrant Wnt signaling in cancer and CSC has engendered substantial efforts into the development of therapeutic approaches to target this pathway 9. Several small molecules, involved in tumor signaling, have been identified that selectively block the p300/β-catenin interaction, thereby increasing the CBP/β-catenin interaction, which maintains long-term pluripotency in a variety of SC populations. Thus the therapeutic potential of CBP/β-catenin antagonists (e.g., ICG-001) has been studied in various preclinical tumor models, where it has demonstrated the ability to safely eliminate drug-resistant tumor-initiating cells.

REFERENCES

1. Yang RH, Qi SH, Shu B, Ruan SB, Lin ZP, Lin Y, et al. Epidermal stem cells (ESCs) accelerate diabetic wound healing via the Notch signalling pathway. Biosci Rep. 2016.
2. Jiménez F, Garde C, Poblet E, Jimeno B, Ortiz J, Martínez ML, et al. A pilot clinical study of hair grafting in chronic leg ulcers. Wound Repair Regen. 2012.
3. Jackson WM, Nesti LJ, Tuan RS. Concise review: clinical translation of wound healing therapies based on mesenchymal stem cells. Stem Cells Transl Med. 2012.
4. Liu JQ, Zhao KB, Feng ZH, Qi FZ. Hair follicle units promote re-epithelialization in chronic cutaneous wounds: a clinical case series study. Exp Ther Med. 2015.
5. Tartarini D, Mele E. Adult stem cell therapies for wound healing: biomaterials and computational models. Front Bioeng Biotechnol. 2016.
6. Isakson M, de Blacam C, Whelan D, McArdle A, Clover AJ. Mesenchymal stem cells and cutaneous wound healing: current evidence and future potential. Stem Cells Int. 2015.
7. Zahorec P, Koller J, Danisovic L, Bohac M. Mesenchymal stem cells for chronic wounds therapy. Cell Tissue Bank. 2015.
8. Wu Y, Chen L, Scott PG, Tredget EE. Mesenchymal stem cells enhance wound healing through differentiation and angiogenesis. Stem Cells. 2017.
9. Badiavas EV, Falanga V. Treatment of chronic wounds with bone marrow-derived cells. Arch Dermatol. 2018.
10. Falanga V, Iwamoto S, Chartier M, Yufit T, Butmarc J, Kouttab N, et al. Autologous bone marrow-derived cultured mesenchymal stem cells 2019.

E – ISSN: XXXX – XXXX
VOLUME 01 ISSUE 01 2021
PROCEEDINGS
THE SOUTHERN CAUCASUS INTERNATIONAL ACADEMY

STEM CELL NICHES AND SKIN DISORDERS

Maia Matoshvili, Davit Tophuria

Dermato-Venerology Department, Human Normal Anatomy Department. Tbilisi State Medical University.
Email: mmatoshvili@hotmail.com

ABSTRACT

Skin SCs reside in specialized morphological and functional units with a specific microenvironment. These so-called niches may contain various SCs as well as supportive cells providing framework or signaling to the SCs. Within human skin, at least five different niches have been delineated (basal layer of the epidermis, HF bulge, base of sebaceous gland, dermal papillae and dermis), that harbor different types of skin SCs:
Keywords: Stem Cells, Dermal niches, Skin.

Introduction: a) Interfollicular epidermal SCs are scattered singly across the dermal-epidermal junction. In the mucosa and on the palms and soles, SCs are located at the base of the rete ridges. They constitute about 1%~7% of epidermal basal cells. Several human SC markers have been described, including high surface expression of α6 and β1 integrins that may be relevant for sustaining the attachment of epidermal SC to their basement membrane through hemidesmosomes 1. Progenies from epidermal SCs that withdraw from the cell cycle, show a suppression of integrin α6 expression, before they start differentiating and moving towards the skin surface, where they slough off along terminal differentiation after approximately 4 weeks33. Furthermore, p63 (a homologue of tumor suppressor p53), a low expression of transferring receptor (CD71) and desmoglein 3 as well as LRIG1, the scaffold protein FERM lineated (basal layer of the epidermis, HF bulge, base of sebaceous gland, dermal papillae and dermis), that harbor different types of skin SCs 2:

a) Interfollicular epidermal SCs are scattered singly across the dermal-epidermal junction. In the mucosa and on the palms and soles, SCs are located at the base of the rete ridges. They constitute about 1%~7% of epidermal basal cells. Several human SC markers have been described, including high surface expression of α6 and β1 integrins that may be relevant for sustaining the attachment of epidermal SC to their basement membrane through hemidesmosomes. Progenies from epidermal SCs that withdraw from the cell cycle, show a suppression of integrin α6 expression, before they start differentiating and moving towards the skin surface, where they slough off along terminal differentiation after approximately 4 weeks33. Furthermore, p63 (a homologue of tumor suppressor p53), a low expression of transferring receptor (CD71) and desmoglein 3 as well as LRIG1, the scaffold protein FERM domain-containing protein 4A (FRMD4A), and CD46 have been established as interfollicular SC markers.

b) Beside tissue regeneration interfollicular SCs have been shown to be invested with the ability of generating hairs32. In HFs, several distinct SC-types have been identified. One multipotent SC population resides in the bulge located at the base of the HF (during telogene phase of hair development) or beneath the HF-associated sebaceous gland (in anagen phase). This follicular component is established during embryonic hair morphogenesis and resists periodic degeneration during the hair growth cycle. Stimulation of these SC to exit their niche as well as their proliferation

E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

and differentiation to form mature HFs is closely linked to the hair growth cycle 3. HF bulge SC show expression of the molecular markers such as cluster of differentiation 200 (CD200), keratin 15 (K15), Lgr5+ and pleckstrin homology-like domain family A, member 1 (PHLDA1) as well as transcription factors Sox9+, Lhx2+ and NFATc126,36,37 Beside these epidermal SCs, another multipotent precursor cell population resides in HFs and dermal papillae that originate from the embryonic neural crest. These epidermal neural crest SCs (EPI-NCSCs) hold clonal multipotency that can give rise to melanocytic, neuronal and myogenic cell lineages in vitro and show differentiation potential toward mesenchymal lineages, as they are able to give rise to adipocyte, chondrocyte, and osteocyte progeny. Because of their advantageous physiological plasticity, multipotency, simple accessibility and non-controversial ethical issues, these EPI-NCSCs are considered promising donor cells for the repair of nervous system injuries 4.

Methodology: a) Sebaceous glands, attached to the HFs, are supposed to descend from different follicle SC populations, including Krt15+ bulge cells, LGR6+ and junctional zone SCs. Other studies describe the existence of periglandular Blump1-expressing sebaceous progenitors and a SC population within the gland itself 5. Progenitors give rise to terminally differentiated sebocytes that degenerate along holocrine secretion, releasing lipid-rich sebum into the hair canal that maintain an adequate lubrication of the skin surface 5.

b) Melanocyte SCs derive from the neural crest and permanently reside in the HF bulge, basal epidermis and probably also in the dermis 6. They give rise to pigment-producing melanocytes in the epidermis and the hair matrix. The fate of the melanocytes within the follicle is connected to the HF phases, where melanocytes proliferate and differentiate during anagen, and diminish through apoptosis in catagen 7. Dysfunction of this SC population results in pigmentation defects that phenotypically manifest as hair graying. The latter underlies an increased apoptosis of melanocyte SCs due to higher oxidative stress subsequent to the deficiency of anti-apoptotic Bcl2 protein that occurs with aging 8.

c) The steady remodeling of the dermis and fibroblasts as their primary cellular component is managed via mesenchymal SCs. They are located in the connective tissue within the dermis, surround HFs (especially in the follicular sheath and papillae) or are found among pericytes around blood vessels. Beside fibroblasts, dermal mesenchymal SCs generate myofibroblasts, endothelial cells, nerves, blood vessels, osteoblasts, chondrocytes and adipocytes 9. Morevoer, they are crucial for the coordination of the complex process of wound healing by attracting other host cells, growth factors and extracellular matrix (ECM) secretory proteins. Dermal SCs lack uniform distinctive markers but adhere to plastic in contrary to other SCs 10.

REFERENCES

1. Kim K, Doi A, Wen B, Ng K, Zhao R, Cahan P, et al. Epigenetic memory in induced pluripotent stem cells. Nature. 2011
2. Polo JM, Liu S, Figueroa ME, Kulalert W, Eminli S, Tan KY, et al. Cell type of origin influences the molecular and functional properties of mouse induced pluripotent stem cells. Nat Biotechnol. 2012
3. Nashun B, Hill PW, Hajkova P. Reprogramming of cell fate: epigenetic memory and the erasure of memories past. EMBO J. 2015

4. Muchkaeva IA, Dashinimaev EB, Terskikh VV, Sukhanov YV, Vasiliev AV. Molecular mechanisms of induced pluripotency. Acta Naturae. 2013
5. Miura K, Okada Y, Aoi T, Okada A, Takahashi K, Okita K, et al. Variation in the safety of induced pluripotent stem cell lines. Nat Biotechnol. 2016
6. Mayshar Y, Ben-David U, Lavon N, Biancotti JC, Yakir B, Clark AT, et al. Identification and classification of chromosomal aberrations in human induced pluripotent stem cells. Cell Stem Cell. 2016
7. Gore A, Li Z, Fung HL, Young JE, Agarwal S, Antosiewicz-Bourget J, et al. Somatic coding mutations in human induced pluripotent stem cells. Nature. 2015
8. Cheng L, Hansen NF, Zhao L, Du Y, Zou C, Donovan FX, et al. Low incidence of DNA sequence variation in human induced pluripotent stem cells generated by nonintegrating plasmid expression. Cell Stem Cell. 2017;
9. Szabo E, Rampalli S, Risueño RM, Schnerch A, Mitchell R, Fiebig-Comyn A, et al. Direct conversion of human fibroblasts to multilineage blood progenitors. Nature. 2018
10. Araki R, Uda M, Hoki Y, Sunayama M, Nakamura M, Ando S, et al. Negligible immunogenicity of terminally differentiated cells derived from induced pluripotent or embryonic stem cells. Nature. 2019

PROCEEDINGS
THE SOUTHERN CAUCASUS INTERNATIONAL ACADEMY
E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

Characteristics of the management of hyperglycemia in critically ill patients with inpatient Covid-19 and diabetes mellitus to whom glucocorticoids were administered

Levan Ratiani[1], Karen Grigoriani[1], Ketevan Machavariani[1], Vakhtang Shoshiashvili[1], Eka Khuchua[1], Luiza Gabunia[2], Tamar Didbaridze[1], Giorgi Sordia[1], Zurab Zaalishvili [3]

[1]Tbilisi State Medical University First University Clinic. Georgia
[2]TSMU, Pharmacology Department, associate professor. Georgia
[3]American MD program of Tbilisi State Medical University. Georgia
Email: didbaridzetamar@gmail.com

Abstract

The article discusses the possible pathogenesis of the development of hyperglycemia during COVID-19 and hyperglycemia caused by glucocorticoids. Optimal periods for the determination of glycemia during COVID-19 when prescribing glucocorticoids are also indicated. Mention is made of insulin therapy regimens (postprandial and mixed) when prescribing prednisolone in the morning and the peculiarities of insulin therapy when reducing the dose of glucocorticoids while taking dexamethasone.
Keywords:COVID-19, glucocorticoids, glucocorticoid-induced diabetes, insulin therapy, hyperglycemia COVID-19.

Introduction: 2020 can be distinguished as the year of fighting the new type of SARS-CoV - 2 (Severe acute Respiratory Syndrome-Coronavirus 2) pandemic. The disease caused by SARS-CoV - 2 is known as COVID-19 (Corona Virus Disease 2019) (1). In the fight against this pandemic, cultural and entertainment events were restricted, education in schools and other higher education institutions became remote, public transport was suspended, and people traveling between cities and countries were severely restricted. Georgia is no exception, even in the 90s of the hard 20th century our country did not stop studying in wood-burning classrooms, stopping public transport, especially Tbilisi Metro Ltd., moving people between cities and countries. These strict restrictions only add to the importance of the problem. According to the data of February 2, 2021, the number of COVID-19 patients in Georgia is 259209, and 3208 dead (https://stopcov.ge/). In over the world, by February 2, 2021, according to Johns Hopkins University (https: //coronavirus.jhu.edu/map.html) 103,523, 528 infected, and 2,236,348 dead, and most importantly, the end of the pandemic has not yet been seen, despite the registration of vaccines.

Diabetes mellitus is one of the major risk factors: COVID-19 patients with high comorbid backgrounds (elderly, male, cardiovascular disease, heart failure, hypertension, chronic obstructive pulmonary disease, chronic kidney disease, and of course diabetes mellitus) have a higher risk of morbidity and mortality than patients without these comorbidities (1, 2, 3). In a retrospective study conducted by Greek science, 36 (20.9%) of COVID-19-confirmed patients and 22 (71%) of patients who died of COVID-19 pneumonia had diabetes mellitus (DM) comorbid pathology (4). In a study by the Chinese, 172 (16.2%) of patients with severe general condition had concomitant disease DM. (5). Also, 270 (17%) of the patients lying in intensive care units in Italy had DM. In the United States (US) DM was the most common (32% / 148) concomitant pathology in patients lying in the intensive care unit with COVID-19 infection.

Possible mechanisms of hyperglycemia: Glycemic decompensation is one of the complications of COVID-19 infection in patients with DM, which may be manifested by an intensification of glycemic corrective therapy, e.g. increasing insulin doses (6). This can be explained by several mechanisms: on the one hand, hyperglycemia directly increases SARS-CoV - 2 replication in human monocytes, on the other hand, glycolysis by mitochondrial reactive oxidative radicals and hypoxia-induced factor 1α products also increases the viral replication process (7). COVID-19 is characterized by an increase in markers of severe inflammatory processes (interleukin 6, lactate dehydrogenase, inflammatory cytokines), which may increase insulin resistance (8). There are several mechanisms by which it is possible to explain the increased resistance caused by viral inflammation. Both COVID-19 pneumonia, SARS-CoV - 2, and MERS (Middle Eastern respiratory syndrome (MERS -CoV) cause not only cellular infiltration into lung tissue, but similar processes can develop in smooth muscle and liver, tissues, and organs playing a major role in the absorption of insulin-induced glucose (9, 10, 11).

The SARS-CoV - 2 virus uses its own receptor, the angiotensin-converting enzyme type 2 (ACE2), to penetrate the human cell. In large quantities, its expression is in the mucous membranes of the mouth, throat, and nasopharynx (e.g. "invasion door"), in enterocytes of the rectum, myocardial cells, proximal ducts of the kidneys and pancreas (12, 13, 14, 15). The presence of receptors in various organs can explain the atypical manifestations of COVID-19 disease, such as loss of taste, diarrhea, and transient hyperglycemia (16). After binding to the receptor, the transmembrane serine protease "cuts" the ACE2 receptor by invading the spike virus into the cell and subsequently applying it (15). Experimental studies have shown that ACE2-receptor expression is increased in mice under conditions of hyperglycemia (17). It has also been shown to increase not only ACE 2-receptor expression in hyperglycemic conditions, but also its glycosylation in lung tissue (binding of a protein to glucose), which promotes binding of the SARS-CoV - 2 virus to the ACE-receptor (18).

It is known that SARS-CoV - 2 virus is detected by immune-competent cells after its invasion into the human body, induction of "cytokine storm" induced by pro-inflammatory cytokines (TNF, IL-1β, IL-6, IL-8, IL-17 Etc.) and is characterized by the separation of chemokines (MCP1, IP10, MIP1α) (16, 19). Recent studies have shown that cytokine storms in patients with COVID-19 and diabetes are more severe and aggressive than in patients without COVID-19 without diabetes (3, 5, 20). Such an aggressive current can be explained by the fact that for all processes, as well as for the immune response, energy supplies are needed e.g. "Fuel", and the degree of its intensity directly depends on the amount of glucose absorbed by immune cells. There is also a direct correlation between IL-6, IL-8, and glycemic index (20). As far back as 2002, when the atypical pneumonia pandemic developed, scientists observed that the lethality was high in patients with DM who had a relatively high sugar level (21). A similar pattern has occurred during the new coronavirus pandemic: mortality in China was 3 times higher in patients with AD and glycemia at 184 mg / dL (10.2 Mmol / L) than in patients with glycemia at 116 mg/dl (6.4 Mmol / L) (28.8 and 6% respectively). Mortality was also high in 40/96 patients with COVID-19 and uncontrolled glycemia in the US, and 13/88 in patients with controlled glycemia (14.8%, p <.001) (20). These studies once again suggest that DM dysglycemia is a risk factor for COVID-19 severe current and lethal outcome.

When considering DM as a risk factor, you should also indicate obesity, which is a comorbid pathology in patients with DM. It should be emphasized that obesity is an independent risk factor for COVID-19 infection. According to the US Epidemiological Survey (COVID-NET), between March 1 and March 30, 2020, 48% of patients hospitalized in the US for COVID-19 were obese (22). In

E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

France, COVID-19 patients with body mass index (BMI)> 35 kg /m2 independently with the presence of other risk factors (arterial hypertension, DM, age) 1.6 times more frequently underwent artificial lung ventilation (ARV), than those, with BMI<35 kg /m2 (23).
According to the currently available data, the immunotoxic response plays an important role in COVID-19 pathophysiology. Studies are therefore underway to better manage COVID-19 before somehow inhibiting this immune response. Glucocorticoids (GCs) are known to be effective in fighting this disease with their antimicrobial properties (24, 25, 26, 27). 5-8 days after receiving GC, decreased levels of IL-8, MCP1, IP10 in the blood. GC also inhibits IL-6, IFN-N (Th1-response), IL-4 (Th2-response) production (28). The World Health Organization recommends low-dose GC (4-6 mg dexamethasone or 50 mg hydrocortisone every 8 hours) for 7 to 10 days only in patients with severe COVID-19 and adult respiratory distress syndrome (COPD) (25). Accordingly, GCs are the first treatment at this stage to have a proven positive effect on COVID-19 treatment. There are papers in the literature (29, 30, 31, 32, 33) that evaluate the benefits of GC in patients with new coronavirus, although each of them has a share in the RECOVERY study, where for the first time in a multicenter randomized controlled trial in a large number of patients (2104 patients in a study group and 4321 patients in the control group) taking 6 mg dexamethasone intravenously or orally over 10 days reduced mortality by 35% in critically ill patients (invasive artificial ventilation patients) and also reduced mortality by 20% in COVID-19 patients on oxygen therapy (24). In addition, it should be noted that the dexamethasone group significantly reduced the number of hospitalization days and the likelihood of discharge before hospitalization (34). Along with the positive aspects of GC appointment, there are disadvantages: high mortality due to prolongation of viremia in patients with influenza-induced pneumonia, high risk of developing a secondary infection (35). There is a high risk of developing autoimmune and cardiac processes during the GK appointment. GCs may also cause resistance to muscle relaxants, which are widely used during mechanical ventilation (31, 35). We should not forget about GC-induced side effects such as dysglycemia / newly detected DM, lipolysis, and protein catabolism (32, 36). So hyperglycemia/dysglycemia SARS-CoV - 2 Infection with the virus can be caused by increased insulin resistance due to cytokine "storm", suppression of insulin production, and GK action, which requires special attention from endocrinologists/diabetologists (37). Financial costs in Europe during the COVID-19 pandemic are higher in patients with DM than in those without DM (38).
The literature already recommends the management of hyperglycemia in patients with DM and COVID-19 by prescribing priority medications or insulin therapy based on the patient's general condition and comorbidities (16, 39, 40, 41). In our article, we discuss the features of the management of hyperglycemia in severely ill patients with DM and COVID-19 in the setting of GC. There are already reports of insulin therapy features in patients undergoing artificial lung ventilation (42, 43, 44)

Detection of diabetes mellitus and hyperglycemia: In each patient infected with the SARS-CoV - 2 virus, glycemia should be determined several times over a period of 2 days (e.g., fasting, before meals, and at bedtime) from the start of GC. In the case of glycemia <180 mg / dL (10 mmol / L) at all points taken, it is possible to continue the determination of glycemia once a day (eg at 17-18: 00) until discontinuation of GC (37). It is also noteworthy that fasting glycemia is often not elevated in the setting of GC intake, and a high glycemic rate is observed postprandially after 2 hours (45). Thus, fasting glycemia is not a parameter characteristic of GK-induced dysglycemia.

If glycemia> 200 mg / dL is detected, a diagnosis is made. Newly detected patients should be diagnosed with glycated hemoglobin in their blood for a mean 3-month glycemic index (46).

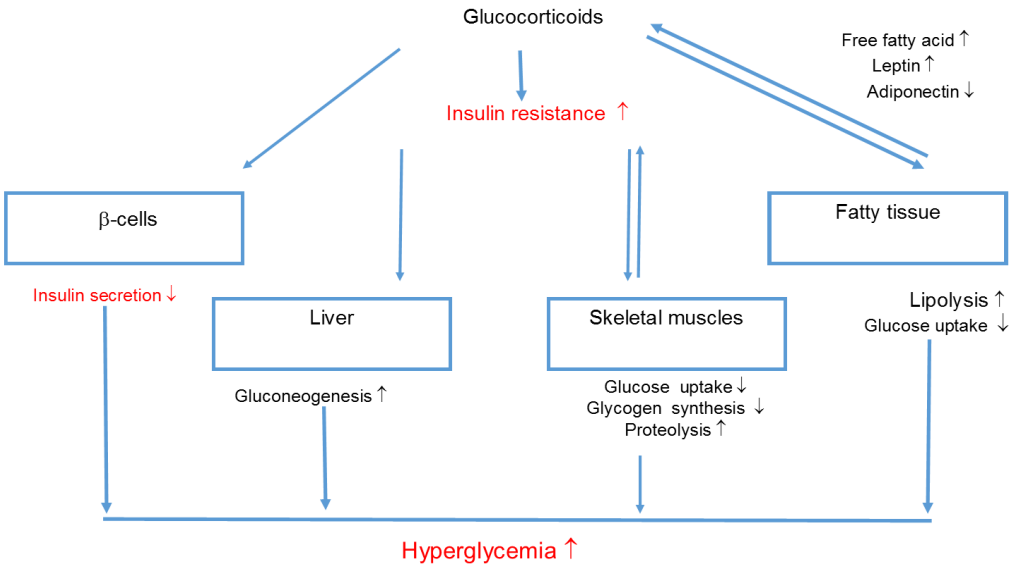
The course of hyperglycemia during the appointment of glucocorticoids: The effect of GC on glycemia depends mainly on the dose of GC, their effectiveness, duration of action and does not depend on the path of its penetration into the body. Distinguish between short-acting (hydrocortisone), medium-acting (prednisone, prednisolone), and long-acting GC (dexamethasone, betamethasone, and triamcinolone) (45). The potency of GC is always based on a comparison of the effect with hydrocortisone, the potency of which is conventionally equal to "1". Accordingly, the potency of prednisolone is "4" and that of dexamethasone is "30-40" (Table 1) (45).

Table 1 Characteristic properties of glucocorticoids

Glucocorticoids	Duration of action (h)	Dose equivalent	Half-life of elimination (h)
Cortisone/ Hydrocortisone	Short (8-12)	1	1-1.5
Prednisone/ Prednisolone	Medium (12-16)	5	3
Methylprednisolone	Medium (12-16)	4	1-2
Dexamethasone	Long (36-72)	30-40	3-5

GC, through its receptors, induces increased insulin resistance in target organs, β-cell dysfunction, and increased blood glucagon secretion (47, 48). In skeletal muscle, GC also inhibits the absorption of insulin-dependent glucose (approximately 30-50%) and glycogen synthesis (approximately 70%) due to blockade of insulin signal cascades by targeting glucose-4-transporter (GLUT4) translocation to target muscle cells (49, 50). After receiving GC, increased gluconeogenesis in the liver is accompanied by an increased expression of phosphoenolpyruvate carboxykinase (PEPCK) and glucose-6-phosphatase (51)., Increased lipolysis and proteolysis induced by GC, in turn, contribute to increased insulin resistance (Figure 1) (47).

Figure 1 Effects of glucocorticoids on metabolism (45, 52)



August 22, 2014, At the conference "Diabetes in Rheumatism" held in Pfeiffer (Switzerland), Swiss Professor Peter Dima During the report, expressed the following opinion: “In some patients with type 1 DM, a relevant amount of C-peptide or a certain amount of residual insulin reserves can be found even after 10 years. After 5 years, 15% of diabetics retain their residual insulin secretion, but after taking prednisolone, we see a picture of dysglycemia as if such patients no longer have their own insulin secretion ”(53).

Regardless of the prednisolone administration route (p/o or i.v.) 4-6 hours later, the maximum effect of prednisolone on glucose metabolism begins, lasting 14-16 hours. There is also an increase in insulin resistance 4 hours after taking dexamethasone, although unlike prednisolone, it has a longer duration of action (lasting more than> 24 hours) (Table 1) (54, 55, 56).

As already mentioned, when prescribing GC, the prerequisite for detecting hyperglycemia / DM is to determine the glycemia several times a day. Once again, in glucocorticoid-induced diabetes, hyperglycemia is manifested mostly after 2 hours postprandial (57). Determination of fasting glycemia alone or glycated hemoglobin in the blood is not of informative value for steroid-induced hyperglycemia /DM, as very often they are within the norm (53, 57, 58). According to experts, when taking GC in the morning, it is optimal to determine blood glucose in the middle of the day 2 hours after eating. Insulin resistance induced by GC is maximal at this time because food-induced hyperglycemia (52, 54, 59) is added to β-cell counts.

Treatment: Hyperglycemia /DM is not a contraindication to the appointment of GC, especially when at this stage they (especially dexamethasone) have a proven effect in the fight against COVID-19 (24, 34, 60). Attention should be paid to the prescribed GC dose, the effect of their action, and the presence of DM. Since GCs significantly increase insulin resistance, the patient should choose to limit easily absorbed carbohydrates, remove pre-existing intervals between main foods, and minimize the number of carbohydrates in the intake (57, 58). The inpatient glycemic index for GC is 108 mg/dL - 180 mg /dL (6.0 mmol/L - 10 mmol / L) (37). If these glucose levels can be achieved overnight through dietary measures, then glucose control should be continued. Glycemia>195–270

mg/dL (13–15 mmol/L) It is advisable to prescribe insulin therapy because GC is ineffective in severe and critically severe COVID-19 patients where oral Prescribing antipyretics is shown to be counterproductive or ineffective depending on the general condition of the patients (24, 32, 34).

There are 2 types of insulin therapy (postprandial and mixed inulin), once a day in the morning with the appointment of GC (45).

The insulin therapy regimen depends on the duration of action of the GC action (frequency of moderate or prolonged action) and the duration of hyperglycemia. E.g. When prednisolone is taken 1 time in the morning, hyperglycemia develops after 4 hours, which lasts 12-16 hours, and at night after the end of prednisolone action due to the corresponding reduced insulin resistance also decreases blood glucose levels (61). In the case of postprandial administration, normal human insulin is injected 3-4 times a day before meals. Normal human insulin has a longer duration of action than human ultra-short-acting insulin and is therefore preferred for the management of hyperglycemia (45, 56). The starting dose of insulin is conventionally 03-0.5 units/kg/day divided into 3 injections (eg 40% -40% -20%) (37, 41, 62).

An alternative principle of glycemic management is the combination of isophane and normal human insulin before a meal in the morning with a single-dose GC of moderate duration. Here, too, the starting dose of insulin is conventionally 01-0.3 one / kg/day. As with human insulin, experts and researchers prioritize isophane insulin over long-acting human insulin analogs (Glargine, Determir) (57, 58, 63, 64).

Glycemic management tactics are different when prescribing a medium-duration GC several times a day or for a long-acting GC. At this time, GC-induced hyperglycemia lasts for more than 24 hours as during endogenous hypercortisolism. Accordingly, this heading should be considered when prescribing insulin (37, 56, 57, 60). It is important to note that the demand for both basal secretion and bolus secretion is growing significantly. In this case, one of the options for glycemic management is to divide the starting total dose (03-0.5 units/kg/day) into 4 injections and subcutaneously every 6 hours (56). However, in medical practice, the basal-bolus regimen of insulin therapy is mainly used to prescribe GC several times a day or for long-acting GC (64).

Patients (both type 1 and type 2) who have been taking intensive or traditional insulin therapy before receiving GC, should continue to take their usual insulin regimen, increasing their total daily insulin dose by 30-100% and controlling their glycemia (37, 58). . There is no upper dose limit for insulin. (65).

It is recommended that for patients receiving insulin by the pump, the dose of insulin (starting at 03-0.5 units/kg/day) be divided into three prolonged boluses at the time of GC appointment. For example, 20% of the basal dose calculated within 3 hours after GC should be administered, then for 6 hours - 60% and for a further 4 hours - 30%. Corrective insulin can be made if needed (45). For example, B.M. Lobnig in his paper (2012) increased the basal velocity of an insulin pump by morning injection of 100-250 mg solumedrol as follows: 12-14 h. + 0.5 units/h, 14-16 h + 1.5 units/h, 16-20h + 3.0 units/h, 20-22 h. +1.5 units/h (56).

Glycemic control: Glucose monitoring should be performed several times a day continuously. Glycemic control is especially important 2 hours after dinner (45, 52, 53). The insulin regimen and dose should be titrated according to the glycemic index. Despite a number of algorithms for calculating and managing the starting insulin dose, experts and practice show that each patient should be prescribed an insulin regimen, doses, and subsequent titration of insulin individually, GC type, duration of action, duration of administration/injectability, frequency of disease. Considering

other peculiarities (58), it must also be emphasized that when reducing/stopping GC doses, insulin should be reduced/stopped taking into account the duration of GC action. Otherwise, there is a high risk of developing severe hypoglycemia after cessation of GC intake (37, 45, 58, 66).

Complications: As mentioned earlier, hyperglycemia during COVID-19 is associated with higher mortality, longer hospital stays, and increased costs (37, 38). There is no equivocal answer as to whether hyperglycemia always returns to normoglycemia after cessation of GC. GC appointment, duration, duration of hyperglycemia (2-8 weeks), remaining insulin supply volume (58, 60) should be considered at this time. E.g. According to B.M. Lobnig (2012), when taking GC, if high hyperglycemia persists for 2-8 weeks, there is a high probability that the insulin secretion supply is stagnant for 6 months or more. It may be necessary at this time to transfer patients from oral antihypertensive drugs to insulin therapy to compensate for glycemia (60). There is also a risk of developing the following complications caused by hyperglycemia when prescribing GC: hyperosmolar condition (in the case of glycemia> 350 mg/dL), exicosis and its associated manifestations (hypovolemia and drop in blood pressure, thrombosis, blurred vision,), impaired immunity (urinary tract infections, nosocomial pneumonia) (60). It should also be noted that the RECOVERY study had the same percentage of patients with DM (approximately 25%) in both the dexamethasone group and the control group (32).
Therefore, the management of hyperglycemia during COVID-19 with proven GC efficacy is also a significant challenge, on which the outcome of the disease in patients also depends.

References:

1. Hu Y, Liang W, Liu L, & Li L. (No Title). New England Journal of Medicine 2020 18 1708–1728. (doi:10.1056/NEJMoa2002032)
2. Wu Z & McGoogan JM. Characteristics of and Important Lessons from the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases from the Chinese Center for Disease Control and Prevention. JAMA - Journal of the American Medical Association2020. pp 1239–1242. . (doi:10.1001/jama.2020.2648)
3. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, Cereda D, Coluccello A, Foti G, Fumagalli R, Iotti G, Latronico N, Lorini L, Merler S, Natalini G, Piatti A, Ranieri MV, Scandroglio AM, Storti E, Cecconi M, & Pesenti A. Baseline Characteristics and Outcomes of 1591 Patients Infected with SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. JAMA - Journal of the American Medical Association 2020 323 1574–1581. (doi:10.1001/jama.2020.5394)
4. Petrakis V, Panagopoulos P, Papazoglou D, & Papanas N. Diabetes Mellitus and Hypertension as Major Risk Factors of Mortality From Covid-19 Pneumonia. Exp Clin Endocrinol Diabetes.
5. Guan W jie, Ni Z yi, Hu Y, Liang W hua, Ou C quan, He J xing, Liu L, Shan H, Lei C liang, Hui DSC, Du B, Li L juan, Zeng G, Yuen KY, Chen R chong, Tang C li, Wang T, Chen P yan, Xiang J, Li S yue, Wang J lin, Liang Z jing, Peng Y xiang, Wei L, Liu Y, Hu Y hua, Peng P, Wang J ming, Liu J yang, … Zhong N shan. Clinical Characteristics of Coronavirus Disease 2019 in China. New England Journal of Medicine 2020 382 1708–1720. (doi:10.1056/nejmoa2002032)

6. Wu L, Girgis CM, & Cheung NW. COVID-19 and diabetes: Insulin requirements parallel illness severity in critically unwell patients. Clinical Endocrinology 2020 93 390–393. (doi:10.1111/cen.14288)
7. Codo AC, Davanzo GG, Monteiro L de B, Souza GF de, Muraro SP, Virgilio-da-Silva JV, Prodonoff JS, Carregari VC, Biagi Junior CAO de, Crunfli F, Jimenez Restrepo JL, Vendramini PH, Reis-de-Oliveira G, Bispo dos Santos K, Toledo-Teixeira DA, Parise PL, Martini MC, Marques RE, Carmo HR, Borin A, Coimbra LD, Boldrini VO, Brunetti NS, Vieira AS, Mansour E, Ulaf RG, Bernardes AF, Nunes TA, Ribeiro LC, … Moraes-Vieira PM. Elevated Glucose Levels Favor SARS-CoV-2 Infection and Monocyte Response through a HIF-1α/Glycolysis-Dependent Axis. Cell Metabolism 2020 32 437-446.e5. (doi:10.1016/j.cmet.2020.07.007)
8. Lim S, Bae JH, Kwon HS, & Nauck MA. COVID-19 and diabetes mellitus: from pathophysiology to clinical management. Nature Reviews Endocrinology2020. p 1. . (doi:10.1038/s41574-020-00435-4)
9. Šestan M, Marinović S, Kavazović I, Cekinović Đ, Wueest S, Turk Wensveen T, Brizić I, Jonjić S, Konrad D, Wensveen FM, & Polić B. Virus-Induced Interferon-γ Causes Insulin Resistance in Skeletal Muscle and Derails Glycemic Control in Obesity. Immunity 2018 49 164-177.e6. (doi:10.1016/j.immuni.2018.05.005)
10. Groop LC, Bonadonna RC, DelPrato S, Ratheiser K, Zyck K, Ferrannini E, & DeFronzo RA. Glucose and free fatty acid metabolism in non-insulin-dependent diabetes mellitus. Evidence for multiple sites of insulin resistance. Journal of Clinical Investigation 1989 84 205–213. (doi:10.1172/JCI114142)
11. Jose RJ & Manuel A. COVID-19 cytokine storm: the interplay between inflammation and coagulation. The Lancet Respiratory Medicine2020. pp e46–e47. . (doi:10.1016/S2213-2600(20)30216-2)
12. Xu H, Zhong L, Deng J, Peng J, Dan H, Zeng X, Li T, & Chen Q. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. International Journal of Oral Science 2020 12 . (doi:10.1038/s41368-020-0074-x)
13. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, Schiergens TS, Herrler G, Wu NH, Nitsche A, Müller MA, Drosten C, & Pöhlmann S. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. Cell 2020 181 271-280.e8. (doi:10.1016/j.cell.2020.02.052)
14. Zou X, Chen K, Zou J, Han P, Hao J, & Han Z. Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. Frontiers of Medicine 2020 14 185–192. (doi:10.1007/s11684-020-0754-0)
15. Rabi FA, Zoubi MS Al, Al-Nasser AD, Kasasbeh GA, & Salameh DM. Sars-cov-2 and coronavirus disease 2019: What we know so far. Pathogens2020. (doi:10.3390/pathogens9030231)
16. Shestakova M V., Mokrysheva NG, & Dedov II. Course and treatment of diabetes mellitus in the context of COVID-19. Diabetes Mellitus 2020 23 132–139. (doi:10.14341/DM12418)
17. Roca-Ho H, Riera M, Palau V, Pascual J, & Soler MJ. Characterization of ACE and ACE2 expression within different organs of the NOD mouse. International Journal of Molecular Sciences 2017 18 . (doi:10.3390/ijms18030563)

18. Brufsky A. Hyperglycemia, hydroxychloroquine, and the COVID-19 pandemic. Journal of Medical Virology2020. pp 770–775. . (doi:10.1002/jmv.25887)
19. Lin L, Lu L, Cao W, & Li T. Hypothesis for potential pathogenesis of SARS-CoV-2 infection–a review of immune changes in patients with viral pneumonia. Emerging Microbes and Infections2020. pp 727–732. . (doi:10.1080/22221751.2020.1746199)
20. Bode B, Garrett V, Messler J, McFarland R, Crowe J, Booth R, & Klonoff DC. Glycemic Characteristics and Clinical Outcomes of COVID-19 Patients Hospitalized in the United States. Journal of Diabetes Science and Technology 2020 14 813–821. (doi:10.1177/1932296820924469)
21. Guo W, Li M, Dong Y, Zhou H, Zhang Z, Tian C, Qin R, Wang H, Shen Y, Du K, Zhao L, Fan H, Luo S, & Hu D. Diabetes is a risk factor for the progression and prognosis of COVID-19. Diabetes/Metabolism Research and Reviews 2020 36 . (doi:10.1002/dmrr.3319)
22. Garg S, Kim L, Whitaker M, O'Halloran A, Cummings C, Holstein R, Prill M, Chai SJ, Kirley PD, Alden NB, Kawasaki B, Yousey-Hindes K, Niccolai L, Anderson EJ, Openo KP, Weigel A, Monroe ML, Ryan P, Henderson J, Kim S, Como-Sabetti K, Lynfield R, Sosin D, Torres S, Muse A, Bennett NM, Billing L, Sutton M, West N, … Fry A. Hospitalization Rates and Characteristics of Patients Hospitalized with Laboratory-Confirmed Coronavirus Disease 2019 — COVID-NET, 14 States, March 1–30, 2020. MMWR. Morbidity and Mortality Weekly Report 2020 69 458–464. (doi:10.15585/mmwr.mm6915e3)
23. Simonnet A, Chetboun M, Poissy J, Raverdy V, Noulette J, Duhamel A, Labreuche J, Mathieu D, Pattou F, Jourdain M, Caizzo R, Caplan M, Cousin N, Duburcq T, Durand A, kalioubie A El, Favory R, Garcia B, Girardie P, Goutay J, Houard M, Jaillette E, Kostuj N, Ledoux G, Mathieu D, Moreau AS, Niles C, Nseir S, Onimus T, … Verkindt H. High Prevalence of Obesity in Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) Requiring Invasive Mechanical Ventilation. Obesity 2020 28 1195–1199. (doi:10.1002/oby.22831)
24. Horby P, Lim WS, Emberson J, Mafham M, Bell J, Linsell L, Staplin N, Brightling C, Ustianowski A, Elmahi E, Prudon B, Green C, Felton T, Chadwick D, Rege K, Fegan C, Chappell L, Faust S, Jaki T, Jeffery K, Montgomery A, Rowan K, Juszczak E, Baillie JK, Haynes R, & Landray M. Effect of Dexamethasone in Hospitalized Patients with COVID-19: Preliminary Report. New England Journal of Medicine 2020 2020.06.22.20137273. (doi:10.1101/2020.06.22.20137273)
25. Sterne JAC, Murthy S, Diaz J V., Slutsky AS, Villar J, Angus DC, Annane D, Azevedo LCP, Berwanger O, Cavalcanti AB, Dequin PF, Du B, Emberson J, Fisher D, Giraudeau B, Gordon AC, Granholm A, Green C, Haynes R, Heming N, Higgins JPT, Horby P, Jüni P, Landray MJ, Gouge A Le, Leclerc M, Lim WS, Machado FR, McArthur C, … Marshall JC. Association between Administration of Systemic Corticosteroids and Mortality among Critically Ill Patients with COVID-19: A Meta-analysis. JAMA - Journal of the American Medical Association 2020 324 1330–1341. (doi:10.1001/jama.2020.17023)
26. Fadel R, Morrison AR, Vahia A, Smith ZR, Chaudhry Z, Bhargava P, Miller J, Alangaden G, Ramesh MS, & Ford COVID- H. Title: Early Short Course Corticosteroids in Hospitalized Patients with COVID-19 2 Running Title: Early short corticosteroids COVID-19 3. medRxiv 2020 2020.05.04.20074609. (doi:10.1101/2020.05.04.20074609)
27. JP Z, Y H, RH D, ZS C, Y J, M Z, J Z, JM Q, & B C. [Expert consensus on the use of corticosteroid in patients with 2019-nCoV pneumonia]. Zhonghua jie he he hu xi za zhi =

Zhonghua jiehe he huxi zazhi = Chinese journal of tuberculosis and respiratory diseases 2020 43 . (doi:10.3760/CMA.J.ISSN.1001-0939.2020.0007)
28. Lam CWK, Chan MHM, & Wong CK. Severe acute respiratory syndrome: clinical and laboratory manifestations. The Clinical biochemist. Reviews 2004 25 121–132.
29. Sterne JAC, Murthy S, Diaz J V., Slutsky AS, Villar J, Angus DC, Annane D, Azevedo LCP, Berwanger O, Cavalcanti AB, Dequin PF, Du B, Emberson J, Fisher D, Giraudeau B, Gordon AC, Granholm A, Green C, Haynes R, Heming N, Higgins JPT, Horby P, Jüni P, Landray MJ, Gouge A Le, Leclerc M, Lim WS, Machado FR, McArthur C, … Marshall JC. Association between Administration of Systemic Corticosteroids and Mortality among Critically Ill Patients with COVID-19: A Meta-analysis. JAMA - Journal of the American Medical Association 2020 324 1330–1341. (doi:10.1001/jama.2020.17023)
30. Hasan SS, Capstick T, Ahmed R, Kow CS, Mazhar F, Merchant H a., & Zaidi STR. Mortality in COVID-19 patients with acute respiratory distress syndrome and corticosteroids use a systematic review and meta-analysis. Expert Review of Respiratory Medicine 2020 14 1149–1163. (doi:10.1080/17476348.2020.1804365)
31. Mattos-Silva P, Felix NS, Silva PL, Robba C, Battaglini D, Pelosi P, Rocco PRM, & Cruz FF. Pros and cons of corticosteroid therapy for COVID-19 patients. Respiratory Physiology and Neurobiology 2020 280 103492. (doi:10.1016/j.resp.2020.103492)
32. Singh AK, Majumdar S, Singh R, & Misra A. Role of corticosteroid in the management of COVID-19: A systemic review and a Clinician's perspective. Diabetes and Metabolic Syndrome: Clinical Research and Reviews 2020 14 971–978. (doi:10.1016/j.dsx.2020.06.054)
33. Zaitsev AA, Golukhova EZ, Mamalyga ML, Chernov SA, Rybka MM, Kryukov EV, Klyuchnikov IV, Semyonov VY, & Orlov IN. Efficacy of methylprednisolone pulse therapy in patients with COVID-19. Clinical Microbiology and Antimicrobial Chemotherapy 2020 22 88–91. (doi:10.36488/cmac.2020.2.88-91) Article in Russian
34. Normand SLT. The RECOVERY Platform. New England Journal of Medicine 2020 . (doi:10.1056/nejme2025674)
35. Ni YN, Chen G, Sun J, Liang BM, & Liang ZA. The effect of corticosteroids on mortality of patients with influenza pneumonia: A systematic review and meta-analysis. Critical Care 2019 23 . (doi:10.1186/s13054-019-2395-8)
36. Perez A, Jansen-Chaparro S, Saigi I, Bernal-Lopez MR, Miñambres I, & Gomez-Huelgas R. Glucocorticoid-induced hyperglycemia (糖皮质激素诱导的高血糖). Journal of Diabetes 2014 6 9–20. (doi:10.1111/1753-0407.12090)
37. Rayman G, Lumb AN, Kennon B, Cottrell C, Nagi D, Page E, Voigt D, Courtney HC, Atkins H, Higgins K, Platts J, Dhatariya K, Patel M, Newland-Jones P, Narendran P, Kar P, Burr O, Thomas S, & Stewart R. Dexamethasone therapy in COVID-19 patients: implications and guidance for the management of blood glucose in people with and without diabetes. Diabetic Medicine 2021 38 1–5. (doi:10.1111/dme.14378)
38. Bain SC, Czernichow S, Bøgelund M, Madsen ME, Yssing C, McMillan AC, Hvid C, Hettiarachchige N, & Panton UH. Costs of COVID-19 pandemic associated with diabetes in Europe: a health care cost model. Current Medical Research and Opinion 2020 1–16. (doi:10.1080/03007995.2020.1862775)
39. Bornstein SR, Rubino F, Khunti K, Mingrone G, Hopkins D, Birkenfeld AL, Boehm B, Amiel S, Holt RI, Skyler JS, DeVries JH, Renard E, Eckel RH, Zimmet P, Alberti KG, Vidal

J, Geloneze B, Chan JC, Ji L, & Ludwig B. Practical recommendations for the management of diabetes in patients with COVID-19. The Lancet Diabetes and Endocrinology 2020 8 546–550. (doi:10.1016/S2213-8587(20)30152-2)
40. Babenko Y & Laevskaya MY. Diabetes mellitus and COVID-19. How are they connected? The current strategy of fight. Arterial Hypertension (Russian Federation) 2020 26 304–311. (doi:10.18705/1607-419X-2020-26-3-304-311) Article in Russian
41. Rayman G, Lumb A, Kennon B, Cottrell C, Nagi D, Page E, Voigt D, Courtney H, Atkins H, Platts J, Higgins K, Dhatariya K, Patel M, Narendran P, Kar P, Newland-Jones P, Stewart R, Burr O, & Thomas S. New Guidance on Managing Inpatient Hyperglycaemia during the COVID-19 Pandemic. Diabetic Medicine2020. pp 1210–1213. . (doi:10.1111/dme.14327)
42. Klypa T V., Orehova MS, & Zabrosaeva LI. Hyperglycaemia in criticaly ill patients. Diabetes Mellitus 2015 18 33–41. (doi:10.14341/DM2015133-41) Article in Russian
43. Association AD. 15. Diabetes care in the hospital: Standards of medical care in diabetesd2019. Diabetes Care 2019 42 S173–S181. (doi:10.2337/dc19-S015)
44. Pérez A, Ramos A, & Carreras G. Insulin Therapy in Hospitalized Patients. American Journal of Therapeutics 2020 27 e71–e78. (doi:10.1097/MJT.0000000000001078)
45. Willms A, Schumm-Draeger PM, & Siegmund T. Glucocorticoids and diabetes. Diabetologe 2016 12 127–138. (doi:10.1007/s11428-016-0070-0) Article in German
46. Clinical Guidelines of Management Diabetes mellitus in Georgien. 2010 Tbilisi Article in Georgian
47. Raalte DH Van, Ouwens DM, & Diamant M. Novel insights into glucocorticoid-mediated diabetogenic effects: Towards expansion of therapeutic options? European Journal of Clinical Investigation2009. pp 81–93. . (doi:10.1111/j.1365-2362.2008.02067.x)
48. Wise JK, Hendler R, & Felig P. Influence of glucocorticoids on glucagon secretion and plasma amino acid concentrations in man. Journal of Clinical Investigation 1973 52 2774–2782. (doi:10.1172/JCI107473)
49. Ruzzin J, Wagman AS, & Jensen J. Glucocorticoid-induced insulin resistance in skeletal muscles: Defects in insulin signaling and the effects of a selective glycogen synthase kinase-3 inhibitor. Diabetologia 2005 48 2119–2130. (doi:10.1007/s00125-005-1886-0)
50. Weinstein SP, Wilson CM, Pritsker A, & Cushman SW. Dexamethasone inhibits insulin-stimulated recruitment of GLUT4 to the cell surface in rat skeletal muscle. Metabolism: Clinical and Experimental 1998 47 3–6. (doi:10.1016/S0026-0495(98)90184-6)
51. Barthel, A. Scherbaum, WA. Bornstein, SR. Neue Aspekte zur insulin- und steroidvermittelten Regulation der hepatischen Glukoseproduktion und zu Mechanismen des Steroiddiabetes. Med Klin 2003 98 282–286. Article in German
52. Siegmund T. Stoffwechselentgleisung bei Steroiddiabetes: Müssen die glukokortikoide jetzt abgesetzt Werden? MMW-Fortschritte der Medizin 2014 156 90–93. (doi:10.1007/s15006-014-3692-4) Article in German
53. Beise U. Steroidtherapie führt oft zu diabetischer Entgleisung. Rheumatologie2014. pp 1–2. . Article in German
54. Clore JN & Thurby-Hay L. Glucocorticoid-induced hyperglycemia. Endocrine Practice2009. pp 469–474. . (doi:10.4158/EP08331.RAR)
55. Magee MH, Blum RA, Lates CD, & Jusko WJ. Prednisolone pharmacokinetics and pharmacodynamics in relation to sex and race. Journal of Clinical Pharmacology 2001 41 1180–1194. (doi:10.1177/00912700122012733)

56. Lobnig BM. Sekundäre diabetesformen. Diabetologe 2011 7 425–438. (doi:10.1007/s11428-011-0772-2) Article in German
57. Capraro J & Wiesli P. Steroid-induzierter Diabetes. Schweiz Med Forum 2012 12 562–565. Article in German
58. Jungmann E. Steroidinduzierter Diabetes mellitus: Wie erkennen - wie behandeln? Diabetes Aktuell 2019 17 189–196. (doi:10.1055/a-0970-6865) Article in German
59. Oyer DS, Shah A, & Bettenhausen S. How to manage steroid diabetes in the patient with cancer. The journal of supportive oncology 2006 4 479–483.
60. Lobnig BM. Individuelle therapieziele bei glukokortikoid-induziertem diabetes mellitus - 'Steroiddiabetes'. Diabetologe 2012 8 123–126. (doi:10.1007/s11428-011-0819-4) Article in German
61. Yuen KCJ, McDaniel PA, & Riddle MC. Twenty-four-hour profiles of plasma glucose, insulin, C-peptide, and free fatty acid in subjects with varying degrees of glucose tolerance following short-term, medium-dose prednisone (20 mg/day) treatment: evidence for differing effects on insulin secretion. Clinical Endocrinology 2012 77 224–232. (doi:10.1111/j.1365-2265.2011.04242.x)
62. Umpierrez GE, Hellman R, Korytkowski MT, Kosiborod M, Maynard GA, Montori VM, Seley JJ, & Berghe G Van Den. Management of hyperglycemia in hospitalized patients in a non-critical care setting: An endocrine society clinical practice guideline. Journal of Clinical Endocrinology and Metabolism2012. pp 16–38. . (doi:10.1210/jc.2011-2098)
63. Dhital SM, Shenker Y, Meredith M, & Davis DB. A retrospective study comparing neutral protamine Hagedorn insulin with glargine as basal therapy in prednisone-associated diabetes mellitus in hospitalized patients. Endocrine Practice2012. pp 712–719. . (doi:10.4158/EP11371.OR)
64. Grommesh B, Lausch MJ, Vannelli AJ, Mullen DM, Bergenstal RM, Richter SA, & Fish LH. Hospital insulin protocol aims for glucose control in glucocorticoid-induced hyperglycemia. Endocrine Practice 2016 22 180–189. (doi:10.4158/EP15818.OR)
65. Dedov II, Shestakova M V., & Mayorov AY. Standards of specialized diabetes care. Diabetes Mellitus2019. pp 1–143. . (doi:10.14341/DM221S1) Article in Russian
66. Waldmann E. Glucocorticoid-induced diabetes — A case report. MMW-Fortschritte der Medizin2019. pp 51–54. . (doi:10.1007/s15006-019-0513-9) Article in German

PROCEEDINGS
THE SOUTHERN CAUCASUS INTERNATIONAL ACADEMY
E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

SIMILAR FEATURES OF TWO VARIOUS DISEASES. CASE REPORT

Guliko Kiliptari[1], Grigol Nemsadze[2], Miranda Kokhreidze[3]
[1]Head of critical care department of university clinic after acad. Kipshidze, Professor of TSMU. Georgia.
[2]Head of radiology department of university clinic after acad. Kipshidze, Professor of TSMU. Georgia.
[3]Doctor of university clinic after acad. Kipshidze, Georgia.
Email: gulikiliptari@yahoo.com

ABSTRACT

COVID-19 pneumonia manifests with chest CT imaging abnormalities, bilateral, subpleural, ground-glass opacities with air bronchograms. Different radiological patterns are observed at different times throughout the disease course. Diffuse bilateral ground-glass opacities co-exists or progresses with consolidations and fibrosis. Evaluation of imaging features, clinical and laboratory findings could to diagnosis of COVID-19 pneumonia and assessment of prognostic values.
We presented cases to analyses the chest CT imaging features in patients with COVID-19 pneumonia, to compare the imaging and laboratory data to across the disease course and to other severe infection , like pneumocyst pneumonia.
Conclusion: Evaluation of blood tests and comparison of clinical data made it possible to diagnose a similare in the course of and CT findings, but an absolutely different disease. This comparison allow distinguish similar characteristics of different diseases and make prognostic conclusions during the course and treatment.
Keywards: Covid-19, HIV, Respiratory distress-syndrom

Introduction: COVID-19 pneumonia manifests with chest CT imaging abnormalities, bilateral, subpleural, ground-glass opacities with air bronchograms. Different radiological patterns are observed at different times throughout the disease course. Diffuse bilateral ground-glass opacities co-existes or progresses with consolidations and fibrosis. Evaluation of imaging features, clinical and laboratory findings could to diagnosis of COVID-19 pneumonia and assessment of prognostic values.
We presented cases to analyse the chest CT imaging features in patients with COVID-19 pneumonia, to compare the imaging and laboratory data to across the disease course and to other severe infection, like pneumocyst pneumonia. This comparison allow distinguish similar characteristics of different diseases and make prognostic conclusions during the course and treatment.

Case presentation

Patient 1: A 50 old man was admitted to our hospital with one week history of fever, dry cough, he reported to reduced appetite and altrered sens of taste. chest radiography displays -Breast contour without deformation. Lymphadenopathy is not expressed. The main bronchi recede. The size of the heart is not enlarged. The amount of fluid in the pericardial cavity is not increased.
Infiltrative changes in bilateral lung parenchyma are reflected in subtotal infiltrative changes of the ground glass type, the density of which is higher in the lower extremities, where areas of consolidation and thicker areas in adults are revealed. Relatively small volume consolidations are also reflected in the upper rates. The intervertebral pleura is thickened.

In the bilateral pleural cavity, a small amount of separated, free air was not found.
Semi-quantitative methodological analysis of computed tomography data, index of lung damage - 21 points (0-24).
Angiographic examination showed no filling defect of the pulmonary trunk and bilateral main, parietal arteries.
Aggravation of respiratory parameters despite NIV and HFNC, has lead to mechanical ventilation. Severe respiratory distress syndrom was treated with suitable strategy of ventilation and patient state was managed with foreseeing of all clinical and laboratory parameters.
Laboratory studies showed increased level of leuvocytes, CRP, IL_6, Liver enzymes.

Humoral immunity and cell-mediated immunity

Table 1.

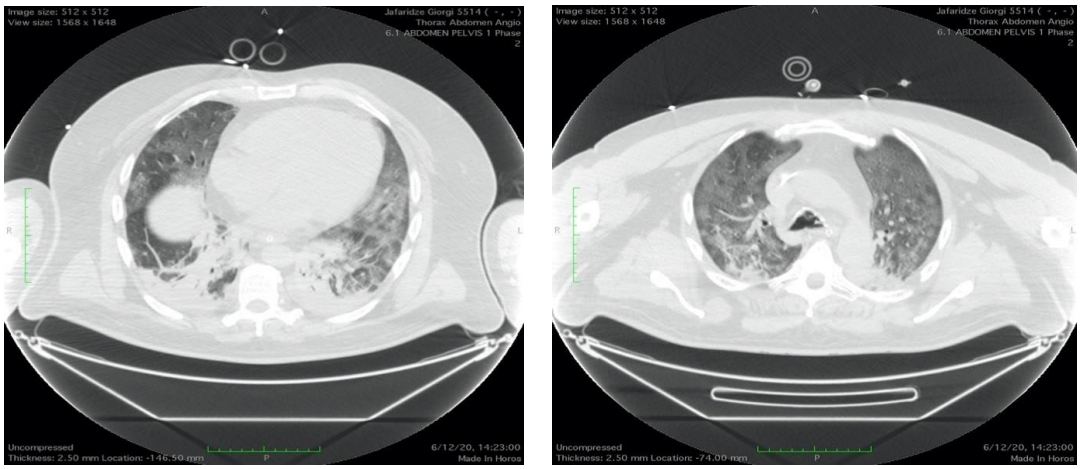
CD3 %/ 10^9 /l	62	59	IgG g/l	11	13.3
CD3 abs . number	366	207	IgA g/l	2.93	2.33
CD4 %/ 10^9 /l	36	32	IGM g/l	1.82	2.83
CD4 abs . number	212	112			
CD8 %/ 10^9 /l	25	25			
CD8 abs . number	148	88			
CD4/CD8 1.29	1.43	1.29			
B abs number	214	98			
NK cells abs number	37	25			

CD3, CD4, CD8 absolute number has been decreased and more decreased after 10 day of symptom onset (Table 1, Table 3)
PCT, CRP, D dimer and IL-6 level was increased in appliance of deterioration patient state (Table 2, Table 3)

Table 2

Day after symptom onset									
PCT (ng/ml)	0.362	0.432	0.168	2,45	3.2	2.35	2.19	1.02	0.864
D dimer (mkg/ml)	0.48	0.5	0.47	3.13	19.76	3.31	3.95	2.11	1.89
CRP (mg/l)	17	39	62	99.8	121,25	62.3	30.4	29.8	16.1
IL-6 (pg/ml)	21				69.7		60		24

E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021



Picture 1 A Subtotal ground glass infiltrative changes are reflected on the bilateral lung parenchyma b. In which the density is higher in the lower parts, where areas of consolidation of adults and thick areas are revealed. Relatively small volume consolidations are also reflected in the upper rates. Semi-quantitative methodological analysis of computed tomography data, index of lung damage - 21 points

On the picture is presented tipical radiology sighns of covid pneumonia, subtotal ground glass infiltration, with consolidation in upper parts an interlobal pleura thickening. A small amount of secretion is released into the bilateral pleural cavity, no free air was found. With Semi-quantitative methodological analysis of computed tomography data, lung damage index was high -21 points.

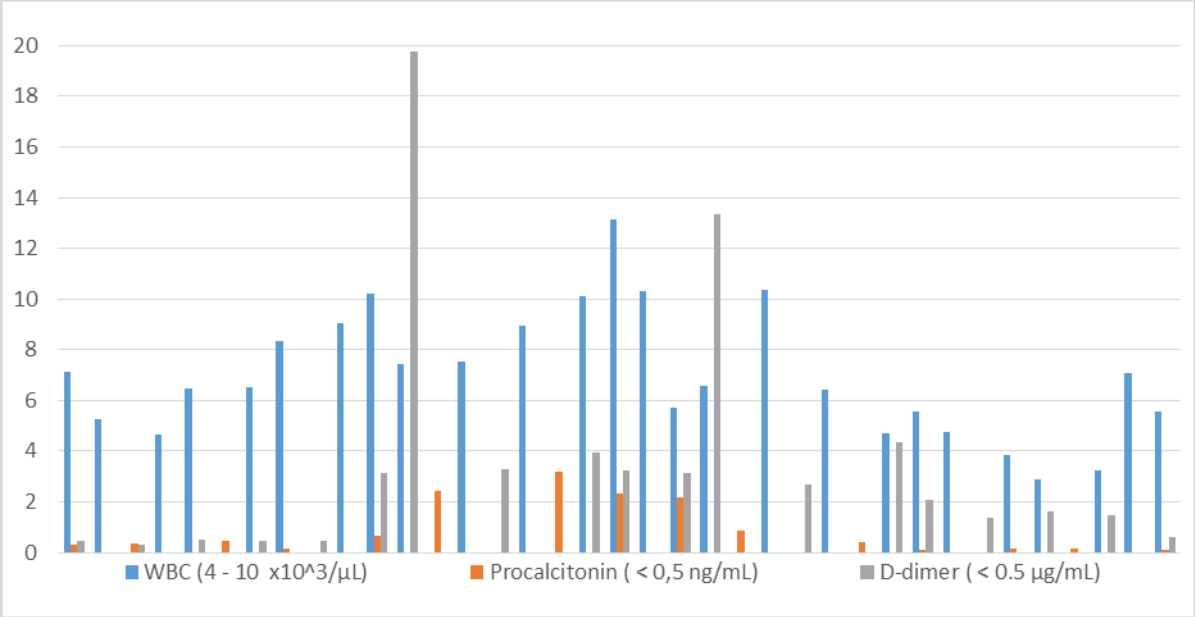
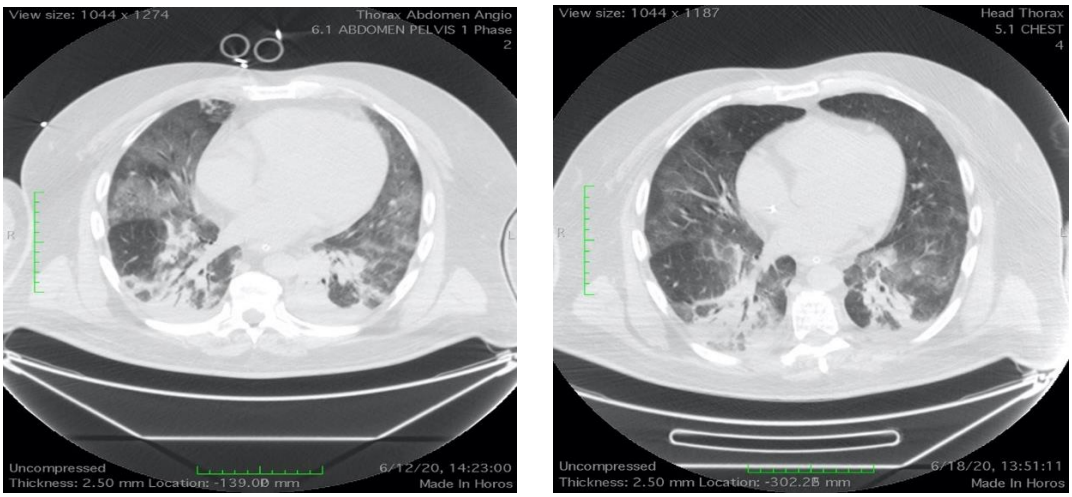


Table 3



Picture 2

The intensity of subtotal ground glass infiltrative changes in the bilateral lung parenchyma is significantly reduced, although the process volume is not reduced.

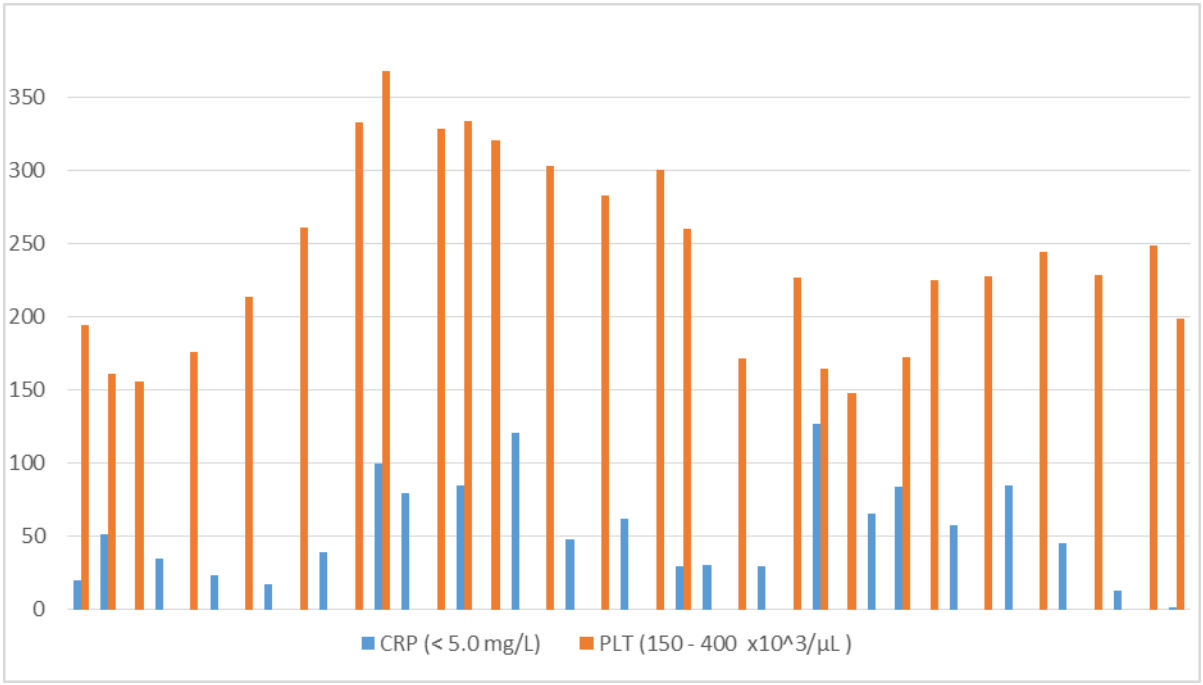
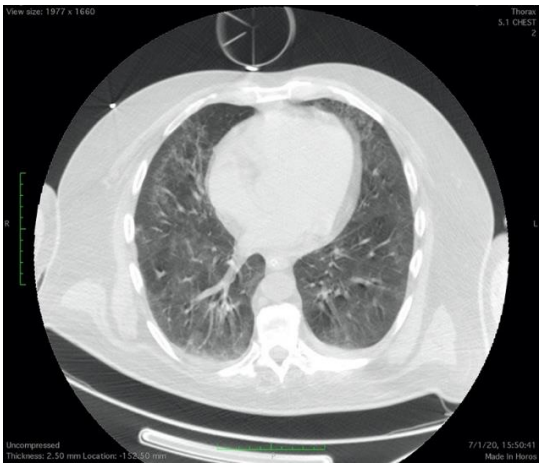


Table 4

E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021



Picture 3
The severity of ground-glass infiltrative changes in the bilateral lung parenchyma is somewhat reduced, consolidation at the level of the basal segments without significant dynamics. Against the background of the compaction on the right, a single bronchiectasis is reflected.

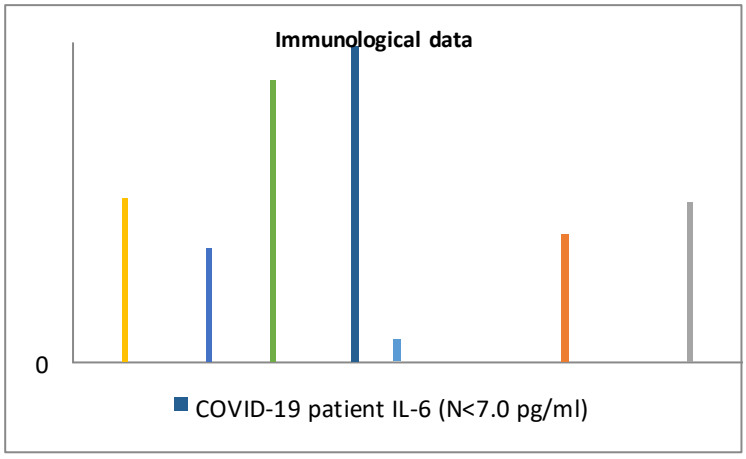
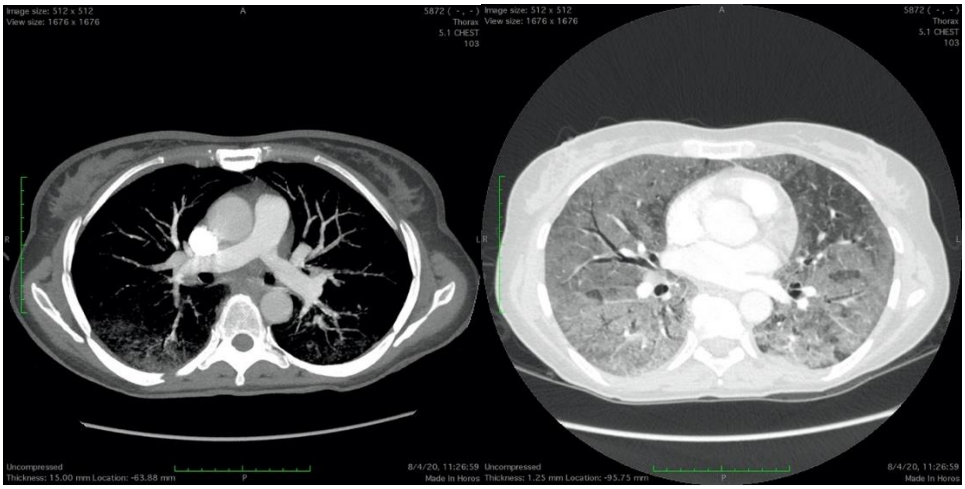


Table 5

Patient was extubated on 29 day of illness and discharge from clinic after 48 days of admission

Case 2: Patient, women was admetted in emergency departament with fever , dry cough, dispnoea Chest computed tomography revealed bilateral pneumonia and (with Semi-quantitative methodological analysis) lung demage index --18 point . After 5 day , patient with worsened respiratory failure and dispnoea, was admetted in ICU.
Dispnoea worsened beside HFNC and NIV. CT of the chest revealed bilateral irregular infiltrates with varying density, neither emphysema, not pulmonary embolism was detected (Picture 4)

Patient was intubated and started mechanical ventilation . PaO_2/FiO_2 was < 200. Sputem was RT-PCR negative for SARS-COV-2 . Laboratory studies showed normal leucocyte count and CRP, PCT, D dimer level. Despite the fact that RT-PCR on SARS-COV-2 was negative, we started the treatment like a respiratory distress –syndrom of covid-19.



A B

Picture 4 Computed tomography of the chest with contrast enhancement 08/04/2020.
Angiographic examination does not reveal a defect in filling the pulmonary trunk, bilateral main, parietal and segmental arteries, reliable signs of thrombosis. The aorta is not enlarged (picture 4A)
Inflammatory changes in the phenomenon of diffuse ground glass are reflected at all levels (except for peaks) in the bilateral lung with a small basal consolidation and foci of subpleural fibrosis. Free fluid and air are not reflected in the bilateral pleural cavity (picture 4,B)
D dimer,CRP and PCT level was increased gradually (Table 6 ,Table 7)

D dimer	0.2	0.32	0.35	0.22	3.1	5,2	3.01	3.15		3.13	3.01
PCT	0.3	0.36	0.43	0.16	2.45	3.2	2.35	2.19		1.1	0.8
CRP	30,5	32.5			118.6	147.2	41.6	34		15.7	

Table 6

E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

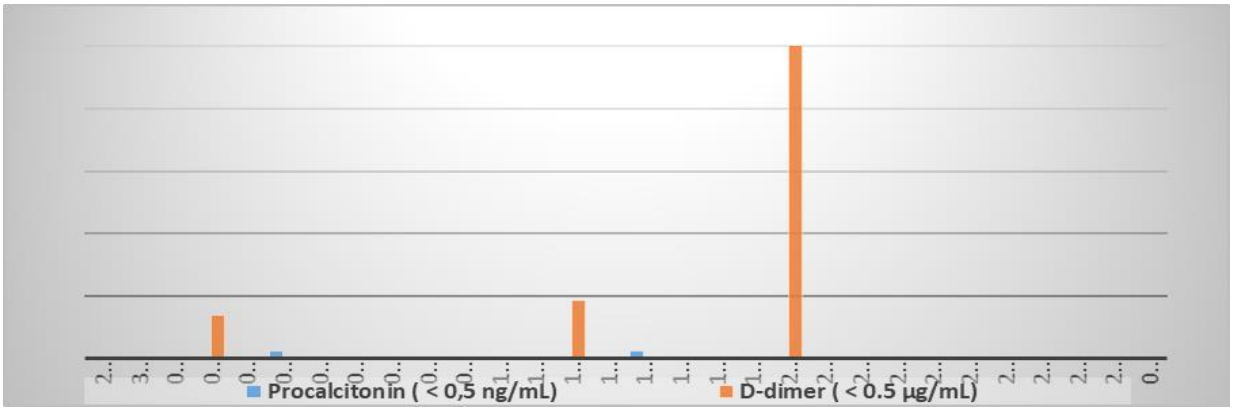
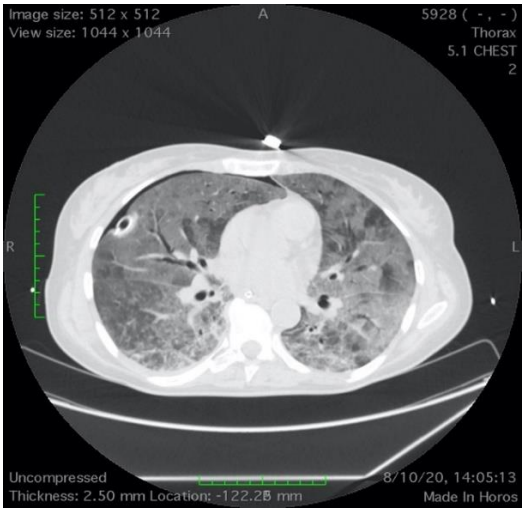


Table 7

On computed tomography of chest infiltrative changes in the diffuse ground glass phenomenon are still reflected in the bilateral lung. At the base, there are small seals and foci of subpleural fibrosis. There is little air in the right pleural space. Free fluid are not reflected in the left pleural cavity (Picture 5).



Picture 5 Computed tomography of the axial section of the lung window 08/10/2020.

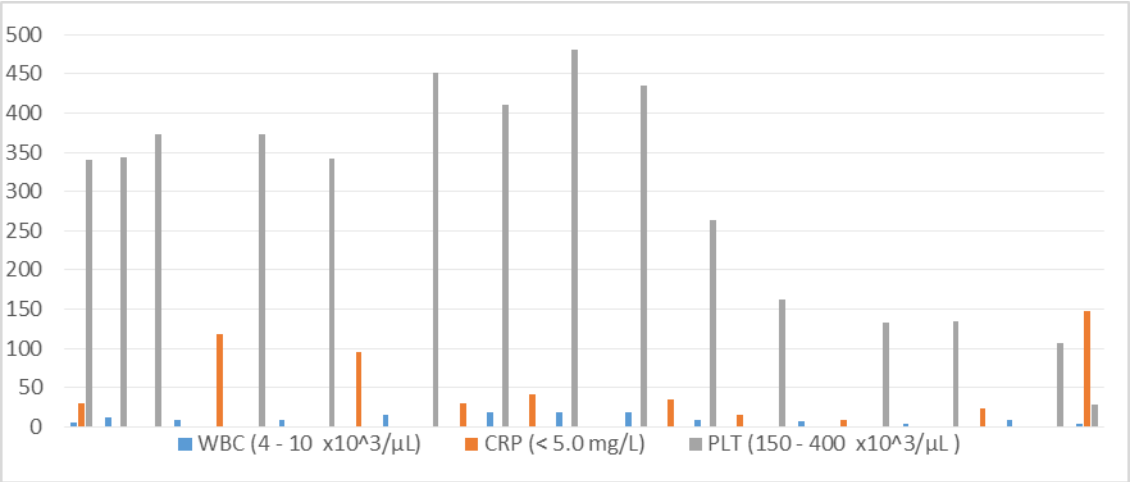
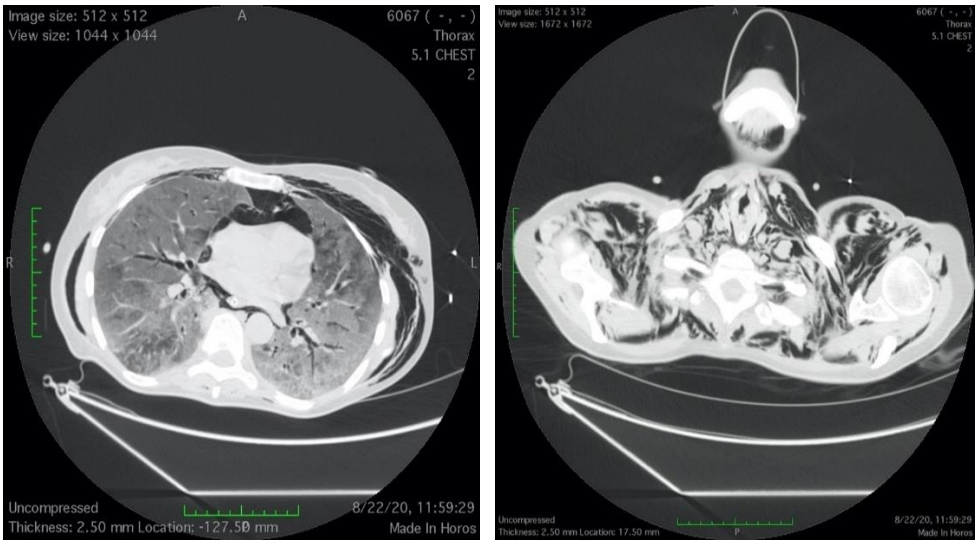


Table 8

Patient state was aggravated. Blood analyses on Anti HBs,HBsAg, Anti HCV, was negative HSV-1 or HSV-2 IgG --0.5Iu/ml, herpes-zoster IgG-80g/l, toxoplasma IgG -1000g/l, Cryptococcal antigen was negative. Blood analyses on Anti-HIV antibody test was positive, CD4 abs. count- 5, CD3 abs. count –35, CD-8 abs. count—28
The human immunodeficiency virus type 1 (HIV-1) Western blotting (immunoblotting) band patterns and the sensitivity of an HIV-1 DNA PCR assay have been determined by testing the blood of patient with AIDS.



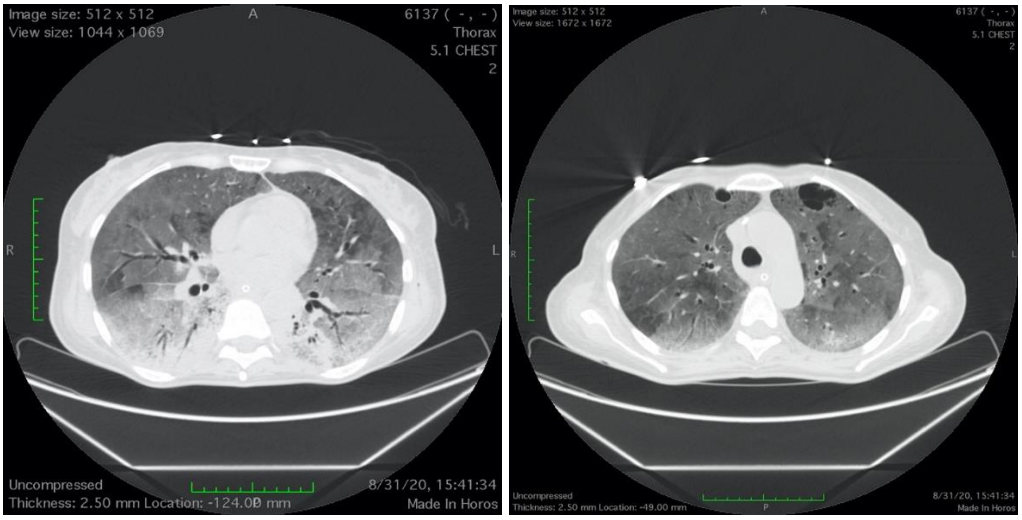
A B

Picture 6. Computed tomography of the axial section of the lung window 08/22/2020.

On computed tomography A-large amount of gas, pneumomediastinum - is found in the mediastinum at almost all levels. B. Massive emphysema of the subcutaneous soft tissue manifests

E-ISSN: XXXX-XXXX
VOLUME 01 ISSUE 01 2021

itself in both the chest and neck. In the bilateral lungs at all levels, infiltrative changes such as the phenomenon of diffuse ground glass are again reflected. Free fluid and air are not reflected in the bilateral pleural cavity(pict 6.)



A B

Picture 7. Computed tomography of the axial section of the lung window 08/31/2020.

A. Air is no longer reflected on the mediastinum and soft tissues of the chest. In the bilateral lungs, infiltrative changes such as the phenomenon of diffuse ground glass are again reflected at all levels.
B. In the ventral-subpleural areas of both upper extremities, cavities with air were formed, around one of them on the right fibrous-infiltrative changes are visible - a destructive process is possible. Free fluid and air are not reflected in the bilateral pleural space (Picture 7).
The patient's condition, the onset of the disease and the course of the disease in both cases were similar and clinically consistent with the course of respiratory distress syndrome caused by Covid infection. The appearance of antibodies from the human immunodeficiency virus and the confirmation of this disease, pneumocyst pneumonia, made changes in the patient's treatment, improved the condition and the patient was transferred to the intensive care unit of the central infectious diseases hospital.
COVID-19 pneumonia was diverse, ranging from normal appearance to diffuse changes in the lungs. In addition, different radiological patterns was observed at different times throughout the disease course in both patient , also the time between onset of symptoms and the development of acute respiratory distress syndrome was short, ct scan obtained on day 7- 9 after symptom onset showed extensive ground glass opacities in both lungs.

Conclusion: Evaluation of blood tests and comparison of clinical data made it possible to diagnose a similare in the course of and CT findings, but an absolutely different disease. This comparison allow distinguish similar characteristics of different diseases and make prognostic conclusions during the course and treatment**.**

REFERENCES

1. Centers for Disease Control and Prevention. Coronavirus Disease 2019 (Covid-19): Cases and Latest Updates, 2020.
2. Pan F, Ye T, Sun P, Gui S, Liang B, Li L, Zheng D, Wang J, Hesketh RL, Yang L, Zheng C. Time Course of Lung Changes at Chest CT during Recovery from Coronavirus Disease 2019 (COVID-19) Radiology. 2020;295:715–721. [PMC free article] [PubMed] [Google Scholar]
3. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW and the Northwell COVID-19 Research Consortium, Barnaby DP, Becker LB, Chelico JD, Cohen SL, Cookingham J, Coppa K, Diefenbach MA, Dominello AJ, Duer-Hefele J, Falzon L, Gitlin J, Hajizadeh N, Harvin TG, Hirschwerk DA, Kim EJ, Kozel ZM, Marrast LM, Mogavero JN, Osorio GA, Qiu M, Zanos TP. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA. 2020 [PMC free article] [PubMed] [Google Scholar]
4. Tisoncik JR, Korth MJ, Simmons CP, Farrar J, Martin TR, Katze MG. Into the eye of the cytokine storm. Microbiol Mol Biol Rev. 2012;76:16–32. [PMC free article] [PubMed] [Google Scholar]
5. Radiology: Cardiothoracic Imaging. **Ng MY,** Lee EY, Yang J, Yang F, Li X, Wang H, Lui MM-s, Lo CS-Y, Leung B, Khong P-L, Hui CK-M, Yuen K-y, Kuo MD. Imaging Profile of the COVID-19 Infection: Radiologic Findings and Literature Review. 2020; 2: e200034. [Google Scholar]

6. Zhao W, Zhong Z, Xie X, Yu Q, Liu J. Relation Between Chest CT Findings and Clinical Conditions of Coronavirus Disease (COVID-19) Pneumonia: A Multicenter Study. AJR Am J Roentgenol. 2020;214:1072–1077. [PubMed] [Google Scholar]
7. Li W, Cui H, Li K, Fang Y, Li S. Chest computed tomography in children with COVID-19 respiratory infection. Pediatr Radiol. 2020;50:796–799. [PMC free article] [PubMed] [Google Scholar]
8. Kim H. Outbreak of novel coronavirus (COVID-19): What is the role of radiologists? Eur Radiol. 2020;30:3266–3267. [PMC free article] [PubMed] [Google Scholar]
9. Dennie C, Hague C, Lim RS, Manos D, Memauri BF, Nguyen ET, Taylor J. Canadian Society of Thoracic Radiology/Canadian Association of Radiologists Consensus Statement Regarding Chest Imaging in Suspected and Confirmed COVID-19. Can Assoc Radiol J. 2020:846537120924606. [PubMed] [Google Scholar]
10. Castiglioni I, Ippolito D, Interlenghi M, Monti CB, Salvatore C, Schiaffino S, Polidori A, Gandola D, Messa C, Sardanelli F. Artificial intelligence applied on chest X-ray can aid in the diagnosis of COVID-19 infection: a first experience from Lombardy, Italy. [Preprint]. In press 2020. [Google Scholar]
11. Abbas A, Abdelsamea M, Gaber M. Classification of COVID-19 in chest X-ray images using DeTraC deep convolutional neural network. [Preprint]. In press 2020. [Google Scholar]
12. Detection of human immunodeficiency virus type 1 (HIV-1) antibody by western blotting and HIV-1 DNA by PCR in patients with AIDS. J B Jackson, J S Parsons, L S Nichols, N Knoble, S Kennedy, and E M Piwowar, J Clin Microbiol. 1997 May; 35(5): 1118–1121.
13. Song F, Shi N, Shan F, Zhang Z, Shen J, Lu H, et al. Emerging 2019 Novel Coronavirus (2019-nCoV) Pneumonia. [published online ahead of print, 2020 Feb 6]. Radiology. 2020:200274. doi: 10.1148/radiol.2020200274 https://doi.org/10.1148/radiol.2020200274 [Links]

14. COVID-19 pneumonia: Diagnostic and prognostic role of CT based on a retrospective analysis of 214 consecutive patients from Paris, France Enora Guillo a , Ines Bedmar Gomez a , Severine Dangeard a , Souhail Bennani a , Ines Saab a,b , Mickael Tordjman a , Lea Jilet c , Guillaume Chassagnon a,b , Marie-Pierre Rev, European Journal of Radiology
15. Clinical presentation and diagnosis of Pneumocystis pulmonary infection in patients with HIV Paul E Sax, MD, UP TO DATE
16. Recent Advances in the Diagnosis and Management of Pneumocystis Pneumonia, Sadatomo Tasaka, M.D. Tuberc Respir Dis (Seoul). 2020 Apr; 83(2): 132–140. Published online 2020 Mar 10. doi: 10.4046/trd.2020.0015
17. Reid AB, Chen SC, Worth LJ. *Pneumocystis jirovecii pneumonia* in non-HIV-infected patients: new risks and diagnostic tools. Curr Opin Infect Dis. 2011;24:534–544. [PubMed] [Google Scholar]
18. Onishi A, Sugiyama D, Kogata Y, Saegusa J, Sugimoto T, Kawano S, et al. Diagnostic accuracy of serum 1,3-beta-D-glucan for pneumocystis jiroveci pneumonia, invasive candidiasis, and invasive aspergillosis: systematic review and meta-analysis. J Clin Microbiol. 2012;50:7–19. [PMC free article] [PubMed] [Google Scholar]

LTD The Southern Caucasus International Academy of Modern Sciences (UK, London) is publishing scientific papers of scientists on Website and in Refereed Journals with subjects:

PSCIAMS-Proceedings of The Southern Caucasus International Academy of Modern Sciences.
ISSN: XXXX-XXXX (Print), E-ISSN: XXXX-XXXX (Online), UDC: ; DOI prefix: 10.36962 / PSCIA

Applied Social Research & Behavioral Sciences

TOPICS OF JOURNAL

International Economics
Financial Economics
Business studies
Public Economics
Labor and Demographic Economics
Law and Economics
Industrial Organization
Business Administration and Business Economics, Marketing, Accounting.
Economic History
Economic Development, Innovation, Technological Change, and Growth
Economic Systems
Agricultural and Natural Resource Economics, Environmental and Ecological Economics.
Urban, Rural, Regional, Real Estate, and Transportation Economics
Tourism Economics
Anthropology
Area studies
Civics
Criminology
Demography
Development studies
Education
Environmental studies
Gender studies
Geography
History
Industrial relations
Information science
International relations
Law
Library science
Linguistics
Political science
Psychology
Public administration
Sociology
Social work
Sustainable development
Health, Education, and Welfare

LTD The Southern Caucasus İnternational Academy of Modern Sciences.

AIMS AND SCOPE

SCİAMS LTD Scientific Journals publishes peer-reviewed, original research and review articles in an open access format. Accepted articles span the full extent of the social and behavioral sciences and the humanities.
SCİAMS LTD Scientific Journals seeks to be the world's premier open access outlet for academic research. As such, unlike traditional journals, SCİAMS LTD Scientific Journals does not limit content due to page budgets or thematic significance. Rather, SCİAMS LTD Scientific Journals evaluates the scientific and research methods of each article for validity and accepts articles solely on the basis of the research. Likewise, by not restricting papers to a narrow discipline, SCİAMS LTD Scientific Journals facilitates the discovery of the connections between papers, whether within or between disciplines.
SCİAMS LTD Scientific Journals offers authors quick review and decision times; a continuous-publication format; and global distribution for their research via SCİAMS LTD Scientific Journals Online. All articles are professionally copyedited and typeset to ensure quality.
Those who should submit to SCİAMS LTD Scientific Journals include:
Authors who want their articles to receive quality reviews and efficient production, ensuring the quickest publication time.
Authors who want their articles to receive free, broad, and global distribution on a powerful, highly discoverable publishing platform.
Authors who want their articles branded and marketed by a world-leading social science publisher.
Authors who want or need their articles to be open access because of university or government mandates.

E-ISSN: XXXX-XXXX; UDC:
DOI PREFIX: 10.36962/PSCİA
PSCIA-Proceedings of The Southern Caucasus İnternational Academy of Modern Sciences.

E-ISSN: XXXX-XXXX; DOI: 10.36962/PSCIA

VOLUME 01, ISSUE 01, 2021

PROCEEDINGS

Proceedings of The Southern Caucasus İnternational Academy of Modern Sciences

MULTIDISCIPLINARY JOURNAL
REFEREED SCIENTIFIC JOURNAL

Applied Social Research & Behavioral Sciences