Column: Products
Tyndall Effect: What, Why, and How?

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Epigraph:
An apple fell on Newton’s head, the Chinese admired dewdrops on a lotus leaf, while John Tyndall must have been walking in a forest when noticed a light cone. Is it a fairytale? Maybe. But one of the most splendid phenomena is called after him, the Tyndall effect...[1]

Heading
All the cosmetology textbooks mention the Tyndall Effect. Authors do not usually move further than mentioning in a couple of phrases that when injected superficially hyaluronic acid fillers may show through the skin with a blue glow. However, you can hardly find out why it happens and whether it is possible to work always in such a way that you avoid this effect. And on the top of that - what should be done if a filler colors skin with white and blue and causes concerns among patients. There are just a few references related to this issue. We have prepared a brief theoretical overview and a detailed description of two cases to highlight the causes of the Tyndall effect in the injection cosmetology and ways to correct it.

Physical Background
Let us remember our physics classes at school to understand what happens in our skin. How do we perceive colors and what determines the color of an object? Key factor: no light, no color. A small note: speaking about the light, we mean visible rays. Visible range of the spectrum is perceived thanks to retinal receptors that are capable of reacting to electromagnetic oscillations of a specific wavelength. So, light is an electromagnetic wave emitted by a heated or excited substance. The sun, light bus, LED flashlight, fire flame as well as different chemical reactions may be sources of light. Visible radiation or white light consists of a spectrum of different colors (figure 1) with the wavelength of 380 to 780 nm, and this is only a minor part of the entire spectrum of electromagnetic waves. The white color is the strongest of all the colors we perceive and it represents the sum thereof. The opposite of white is black. Black is a total absence of light.

Figure 1. Electromagnetic spectrum.
The color of an object for us is defined by our visual perception which reflects specific objective features of the object. Such an object can be only seen if it reflects or absorbs light. If an object completely absorbs light, it looks black. While it seems white, when reflects almost all the incident light. So, the color of an object is determined by the amount of absorbed, transmitted or reflected light which illuminates the object. Molecular composition and structure of a substance determine its ability to reflect, transmit or absorb light. We see grass as green because being illuminated by the white light it absorbs the red and blue waves of the spectrum and reflects the green one (figure 2). A lab white coat looks white because its tissue reflects all the components of the spectrum. We perceive bodies which completely reflect or absorb light waves as non-transparent, while those which transmit a certain amount of light are perceived as transparent (glass). Hence, the color of an object is the color of a reflected spectral wave. That is how we can perceive colors of objects.

Figure 2. Green spectrum reflection.

What determines our skin color?
Based on the theory, the color of an object depends on which rays are absorbed and which are reflected. Alongside with the main factors which determine the color of surfaces of nontransparent objects, the color also depends on the homogeneity of the upper layer, its thickness, and transparency as well as condition of the surface, light nature, and observing conditions. If the light absorbing medium consists of optically-inhomogeneous substances, the penetrating light is partially absorbed and partially reflected from the surface boundary of the media, so you can see light fluxes reflected from different depths.

Our skin consists of different tissues and its final color is determined by the presence of blood in the vessels of the dermis, dark pigment of melanin in the epidermis as well as by other pigments, melanoids and carotin [2]. The color of the pigments is defined by chromophoric groups in their molecules as they cause selective absorption of light of the visual solar spectrum. The most important pigment of them is melanin, a dark brown substance. All healthy people have melanin in their skin; white-skin ones have less and dark-skin ones have more.

Similarly to melanin, carotin is present in the skin of all people, but due to its bright color, it is not so well seen - melanin hides it. Among people with less melanin, some have more carotin, others have less. East Asian people with the largest amount of carotin have yellowish skin.

Skin color differences serve as a basis for the traditional division of the human beings into three races: Negroid with a high content of melanin; Mongoloid with a low content of melanin but high content of carotin, and Caucasoid with low content of both melanin and carotin.
Naturally, the third pigment, hemoglobin, which makes our blood red, is present in all people. However, hemoglobin is in our blood vessels under the skin, hence, it is almost invisible. Its color is almost completely hidden by the sufficient amount of both melanin and carotin available in the skin. Hemoglobin can only be noticed in the skin of white people, especially
those with fair complexion. It is hemoglobin which colors our cheeks pink and makes them blush.

**TEXT BOX**
The molecule of hemoglobin is a hemeprotein which makes erythrocytes red. There are three physiological forms of hemoglobin: oxyhemoglobin, deoxyhemoglobin, and carbaminohemoglobin.

Oxyhemoglobin (hemoglobin with oxygen) is bright scarlet. Many factors impact the capability of hemoglobin to retain oxygen (affinity) as well as its dissociation property (detaching oxygen molecules from oxyhemoglobin). Thus, hemoglobin oxygen affinity increases with the higher partial pressure of oxygen ($P_{O_2}$) and with the lower partial pressure of carbon dioxide ($P_{CO_2}$). When changed contrariwise, these parameters will decrease the hemoglobin oxygen affinity and simplify the dissociation as oxygen is easily delivered to the tissues. By releasing oxygen, hemoglobin becomes reduced, and this state is called deoxyhemoglobin. When hemoglobin binds with carbon dioxide (carbaminohemoglobin), its color changes to dark cherry-red which is characteristic for venous blood.

In case of a slow venous blood flow with superficially located vessels and deficiency of subcutaneous fat (which is best seen in the infraorbital area), the skin may become cyan due to translucent muscle and vessels full of venous blood. This phenomenon may be one of the causes of such aesthetic defect as dark under-eye circles.

**END OF THE TEXT BOX**

Thus, a relative count of the three main pigments determines the skin color. The pigments reflect waves of different length which finally interfere. However, this is how skin color is formed under normal conditions. But what happens with a hyaluronic acid gel (HA) injection when it is translucent through the skin and a blue glow occurs (Tyndall effect)? We inject a transparent gel, don't we? Indeed, our syringe is full with a transparent substance, and it would be reasonable to expect it to let the light go through. Moreover, the occurrence rate of the Tyndall effect is not high even among the patients who get their fillers injected superficially into the areas with thin skin and subcutaneous fat. So, why do we observe the Tyndall effect in some cases and in some we see nothing?

**Mechanism of the Effect**

To answer the question, let us learn better the physics of the Tyndall effect. According to the definition, it is glowing of an optically inhomogeneous medium due to scattering of the light going therethrough. It is caused by diffraction (deviation from the rectilinear prorogation) of light on certain particles or elements of a structurally inhomogeneous medium whose dimensions are much smaller than the scattered light wavelength. The more inhomogeneous is the medium, the larger is the diffraction effect. It commonly occurs when the light goes through disperse systems*.

**Footnote 1** *A disperse system represents formations of two or more phases (matters) which scarcely mix and chemically react with each other. In a typical two-phase system, the first substance (dispersed phase) is finely distributed in the second one (dispersion medium). If
there are several phases, they can be physically detached (centrifuged, separated, etc.). Disperse systems are usually colloid solutions, sols. A solid disperse medium with another dispersed phase is one of the disperse systems.

Light scattering is one of the common features of highly dispersed systems. When laterally illuminated, a disperse system has an indicative and usually bluish glowing which is best seen against a dark background. This feature of light scattering by dispersed phase particles is called opalescence because of opal (from Lat. *opalus*) which is a bluish or yellowish white translucent mineral. In 1868 John Tyndall discovered that when a colloid solution is laterally illuminated by a beam of light from a strong light source, a bright and evenly glowing cone is observed, i.e. Tyndall cone or Tyndall effect, while in case of a low molecular solution the liquid seems to be optically empty, in other words, the beam trace is invisible. Tyndall also showed that this effect is typical for colloid systems (for example, hydrosols, tobacco smoke) with low concentrations of dispersed phase particles with a refraction index different from that of the dispersed medium. The short-wave component of the white light (heterogeneous light) is scattered better by colloid particles than the long-wave component, therefore, Tyndall cone is bluish.

The Tyndall effect occurs in case of scattering of suspended particulate matters which are several times larger than atoms. When the suspended particles get larger, up to 1/20 of the light wavelength (from 25 nm and larger), scattering becomes polychromic, so that light disperses evenly in all the visible range of colors, from purple to red. As a result, the Tyndall effect fades [1]. Thus, the intensity of the Tyndall effect depends on concentrations of dispersed particles and their size, in other words, on the formula of the injected product and number of particles of stabilized HA per a unit volume. Skin color changes (blue and pink lines on the skin) due to post-traumatic damages of minor skin vessels are frequently treated as related to this effect. Although those are different undesirable effects.

Text Box 2

John Tyndall (1820—1893)

He was an Irish physicist and engineer. He was born in Leighlinbrige, County Carlow. After finishing school, he worked as a draftsman in military institutions and railway construction companies. While working, he graduated from the Mechanics Institute of Preston. He was fired from the military land surveying service for his protests against poor working conditions. He worked as a teacher at Queenwood College (Hampshire) while continuing his self-education. In the period of 1848—1851 he attended lectures at the Universities of Marburg and Berlin. He returned to England and became a lecturer and then a professor of the Royal Institution in London. His main scientific works are dedicated to magnetism, acoustics, radiant heat absorption by gases and steam, light scattering in turbid media. He worked under Faraday and dedicated a book to him, "Faraday as a Discoverer" (1870).

He studied glaciers and glacier motion in the Alps. Tyndall Glacier in Torres del Paine National Park in Chile was named after him. Tyndall was a passionate science popularizer. He regularly gave public lectures, quite often they were free for everybody: for plant workers during lunch breaks, Christmas lectures for kids in the Royal Institution. Tyndall became such
a famous science popularizer that the American edition of his "Fragments of Science" (1871) was completely sold out in just one day. His death in 1893 was absurd: when cooking, his wife (outlived him by 47 years) used by mistake one of the chemical agents stored in their kitchen instead of salt.

End of text box 2

How to Avoid?

Clinical implications of the Tyndall effect are almost the same among all the patients. This undesirable effect is seen after stabilized HA was injected in any area of the face, predominantly, in the areas with thin skin (inner eye canthus, neck). The highest risk of the Tyndall effect occurrence is when there is an excessive or superficial injection of fillers (often dense and poorly flexible ones). Clinically, the Tyndall effect is expressed by bluish skin in the place of the filler injection and around (figures 3, 4). Blue papulae and lines formed due to such superficial injection are highly resistant to isovolumic degradation which is natural for hydrogels, and they may remain for a period much longer than a normal term of biodegradation of the same filler [3]. It should be stated that the Tyndall effect is not followed by inflammations and other processes hazardous for our skin.

Figure 3. Hypercorrection and the Tyndall effect. Authors' photo archive.

Figure 4. The Tyndall effect in the infraorbital area. Authors' photo archive.

Preventive treatment?

The first condition is to inject fillers which are recommended for specific areas, inject them to the right depth, and use proper techniques. Some specialists suggest as a way out to mix fillers with an ex tempore one-to-one or two-to-one lidocaine solution. No doubts, by changing rheological properties of the filler you can decrease the probability of the Tyndall effect. But this approach has certain disadvantages (decreased time of the clinical effect, increased risk of anaphylaxis, augmented post-treatment edema).

What shall we do in case of the effect?

Today, the most efficient and effective as well as practically single way to restore the skin color is a hyaluronidase injection. It is a family of enzymes that catalyze the degradation of HA to oligomers (figure 5). The medicine mainly applies hyaluronidase made from bovine testes. In the USA they use human recombinant hyaluronidase, however, the product has not been registered in Russia yet [7]. Glycosaminoglycans (HA, chondroitin, chondroitin sulfate) are a specific substrate for hyaluronidase, they serve as a basis for the intercellular matrix. Hyaluronidase is commonly used in ophthalmology. As for the aesthetic medicine, hyaluronidase there is mainly used to treat undesirable phenomena and complications after contouring plastics procedures when an injected product must be quickly removed.

Figure 5. Specificity of hyaluronidase
There are the following contraindications for hyaluronidase injection - individual hypersensitivity, acute inflammatory and infectious diseases, pregnancy, and breastfeeding. It should be noted that the majority of these conditions are at the same time a contraindication for the injection contouring plastic treatment. So, the first and foremost concern is individual intolerance. The data provided by Nelly Gauthier in her report at the recent international AMWC Congress ("Complications associated with injectable fillers") evidence that hypersensitivity to hyaluronidase (figure 6) is witnessed in less than 5% cases and the data also confirm that the reaction acuteness depends on a dose (figure 7). The extensive use of hyaluronidase in different areas of medicine (surgery, gynecology, urology, dermatology, pulmonology, orthopedics, ophthalmology) as a product to prevent and treat hyperplasia of connective tissues speaks for a high safety level of this product [8]. In case of unfavorable allergy anamnesis, the procedure may be performed under the cover of antihistaminic or even steroidal agents.

Figure 6. Hypersensitivity reaction to a hyaluronidase injection [9].
Figure 7. Dose dependency of hypersensitivity to a hyaluronidase injection [9].

One should be cautious when prescribing hyaluronidase with other medical products injected intradermally or intramuscularly because it may lead to their higher absorption. Patients taking large doses of salicylates, cortisone, adrenocorticotropic hormone, estrogens or antihistaminic products may experience the reduced efficiency of hyaluronidase.

Hyaluronidase application rules

Today, a commonly used product is Longidase [international non-proprietary name (INN): Bovhyaluronidase azoxymer] which is not only an enzyme but a conjugate of hyaluronidase and biologically active carrier. As a result of this conjugation, the enzyme activity becomes 1.5 folds higher as compared to the native enzyme; resistance to inhibitors and body temperature increases and this ensures a long-term effect. Moreover, the product can mitigate the acute phase of inflammations by regulating the synthesis of inflammatory mediators (interleukin-1 and tumor necrosis factor-alpha).

It is produced in a lyophilized form, before application, it should be diluted with the isotonic sodium chloride solution (normal saline). When 1500 IU of hyaluronidase dilute with 4 ml of the solution, the concentration of the active substance is 375 IU per 1 ml. For such injections, it is convenient to use insulin fixed needle syringes. In a 1.0 ml orange syringe there will be 7.5 IU hyaluronidase per line. Hyaluronidase is injected into the areas that need corrections. In particular, in the case of the Tyndall effect, the product is injected into the bluish skin areas to the depth of the filler in a dose compared with the volume of the filler injected before. On average, about 15 IU are injected into the area of about 1 cm². Hyaluronidase immediately effects, however, to assess the final result you need to wait until the post-treatment edema resolves. The solution prepared is non-storable.

Clinical case 1
A female patient of 27 addressed a cosmetologist to improve the result of her previous unsuccessful lip correction. A filler was injected 2 months before the visit. When examining,
the doctor found an asymmetry, resistant blue and gray skin color by the upper lip contour line and that color did not change when being pressed (figure 8). Skin condensing was found in the area where the lip contour had changed color, and that was characteristic for a filler injected superficially. The phenomenon was considered to be the Tyndall effect, the patient was suggested to have a correction treatment with hyaluronidase and probable further filler correction. Under aseptic conditions and with the patient being unanesthetized, 12 IU of hyaluronidase were injected into the upper right contour line of the lip. The palpation proved that the lip became softer and the skin turned back to its normal color in several minutes. Figure 9 shows the patient in a week after the treatment. The Tyndall effect was eliminated, and it also influenced the symmetry of the lips. The patient said she was completely satisfied with the form of her lips and there was no need to correct it.

Figure 8. The Tyndall effect in the upper left part of the lip.
Figure 9. The patient after the corrective hyaluronidase treatment.

Clinical case 2
A female patient of 48. Patient-reported information: 3 months before the visit she had been invited to a workshop as a model. During the master class, she had her mid-face and infraorbital area corrected with a mono-phase HA filler with the cannula technique. In the course of 3 days, the patient had been observing an acute edema which she considered then as a post-treatment one. Later, the edema localized in the tear trough and malar festoon areas. Clinical observation confirmed an acute edema in the infraorbital area, the Tyndall effect in the tear trough projection which evidence that the filler had been injected superficially and the injection procedure had been compromised (figure 10). Under palpation, the superficial position of the filler was felt. After the application anesthesia was provided, the patient received hyaluronidase injections into the edema and color changed areas of the skin. The injections were made in the infiltration technique with the depth of up to 6 mm from the skin surface. The total dose of hyaluronidase was 100 IU.

Figure 10. Hypercorrection and the Tyndall effect in the infraorbital area.
Figure 11. Right after the hyaluronidase injection.
Figure 12. Three days after the corrective treatment.

Conclusion
The Tyndall effect is a specific adverse effect which occurs after HA-based fillers are injected. Timely understanding of the situation ensures that the problem is solved quite quickly because you treat it with the hyaluronidase enzyme which gives you the effect you need just on the tip of the needle. Off-label use hampers doctors’ work with this product as well as the absence of surveys to confirm that the procedure is of a high safety profile.

References
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