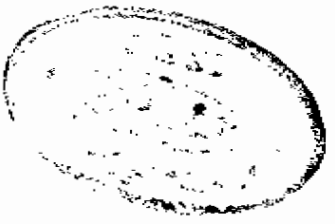
PHOTOTHERAPY AND ITS COMPLICATIONS

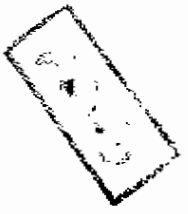
ESSAY

SUBMITTED IN PARTIAL FULFILLMENT OF

THE REQUIREMENTS FOR THE DEGREE OF

MASTER in PAEDIATRICS





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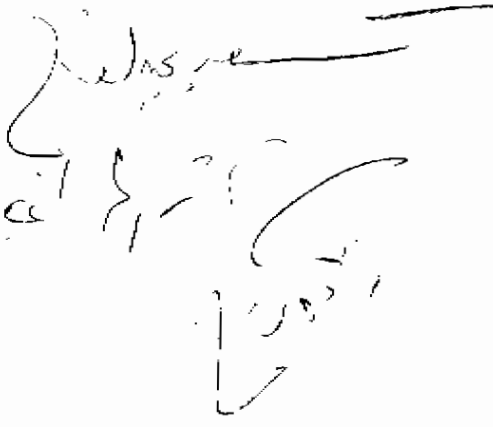


Faculty of Medicine

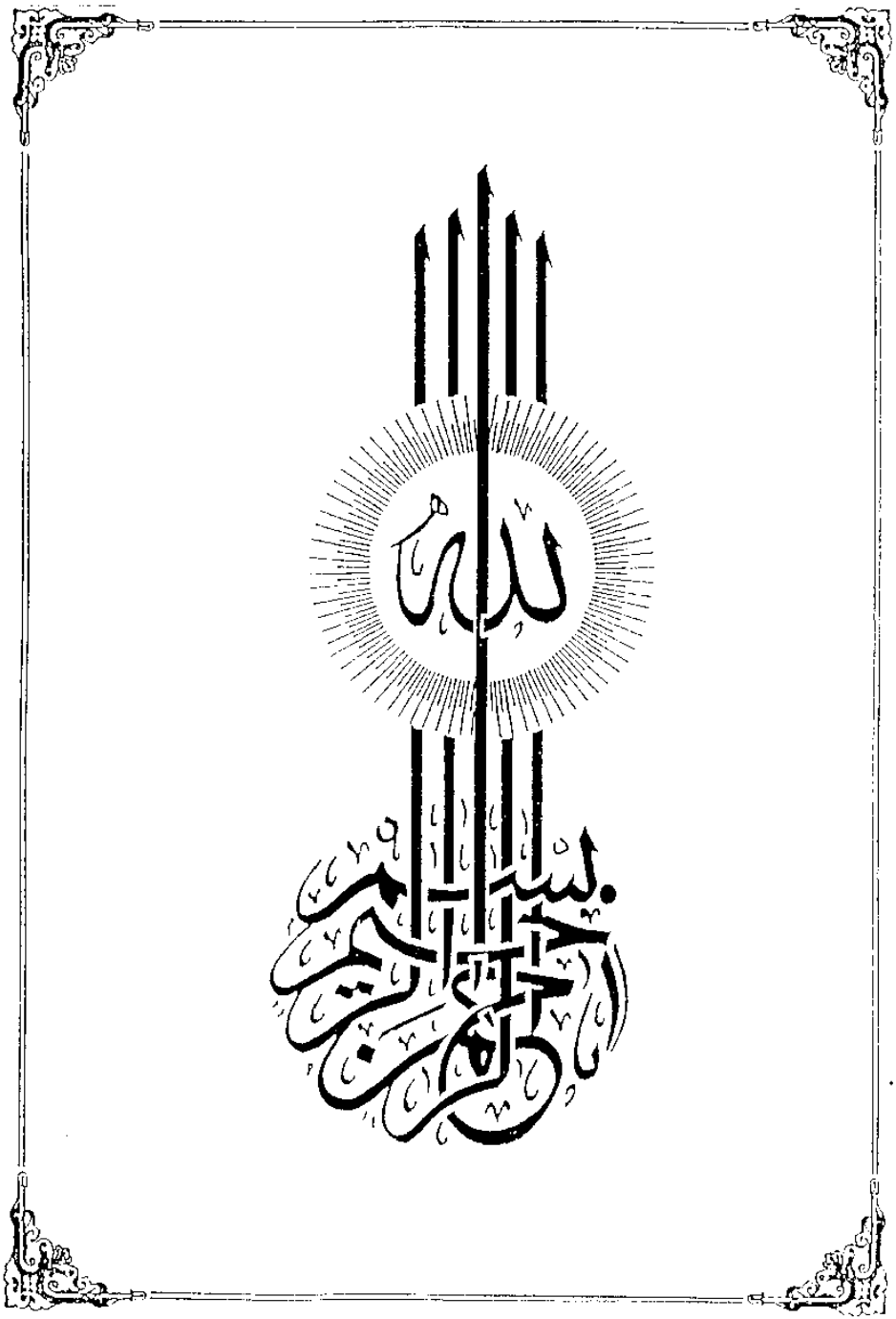
AIN SHAMS UNIVERSITY

1986

Dedication

To

my parents



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C O N T E N T S

Introduction and Aim of the Work

phototherapy usage per se. Because of these findings, it is suggested that phototherapy should not be used indiscriminately for hyperbilirubinaemia until the results of further long-term studies are available (Drew et al., 1976).

REVIEW OF LITERATURE

watts/cm^2 over a particular wavelength interval. The illuminance is expressed in foot-candles, standard units of illumination. The effective wavelengths for isomerization of bilirubin are those having a high-energy output near the maximum absorption peak of bilirubin 400-500 nanometers (Avery, 1981).

The blue lamps emit most strongly in violet and blue wavelengths from 400-500 nanometers and are most effective in rapidly photodecomposition bilirubin from 420-470 nanometers. At 440 nanometers, a very rapid response can be achieved with an energy from a light source of 90 microwatts per square centimeter per nanometer.

The cool white lamps emit green and yellow wavelengths between 500 and 600 nanometers. The retina is more sensitive to the yellow-green than the blue violet portions of the spectrum. Thus, the risk of retinal damage might be less with the blue light, which has little yellow or red and no ultraviolet wavelengths.

The daylight lamps are balanced between the blue and yellow. It can be argued that since very little is known about the spectral or intensity characteristics of the irradiation that produces the direct or indirect biologic effect of light, the lamp used for phototherapy should be as similar to sunlight as possible. Blue wavelengths are

MECHANISM OF ACTION OF PHOTOTHERAPY

The complete mechanism of action of phototherapy is still unknown, but many interesting bits of information have been unfolded over the last few years.

It was shown that phototherapy led to accelerated bilirubin turnover via two mechanisms. The first mechanism is the increased appearance of unconjugated bilirubin per se in bile and the second is the increased secretion of polar derivatives of bilirubin in bile and urine (Ostrow, 1971).

Lund and Jacobson (1974) confirmed these findings in neonates undergoing phototherapy.

McDonagh (1971) then presented evidence that the major in vitro pathway of bilirubin photooxidation involved auto-sensitized addition of singlet oxygen to the bridge methene groups of unconjugated bilirubin and showed that the administration of singlet oxygen sensitizers (rose bengal, hematoporphyrin) to Gunn rats dramatically augmented the effect of phototherapy on hyperbilirubinaemia. The author, therefore, proposed that the generation and addition of singlet oxygen was the major mechanism of phototherapy.

Three observations were incompatible with this report: the first one is that the singlet oxygen mechanism would yield 1 mole 5,5 diformyl dipyrromethene and 2 moles of

methylvinyl-maleimide as the major products, yet these products were undetectable or present only in minor amounts in bile excreted during phototherapy.

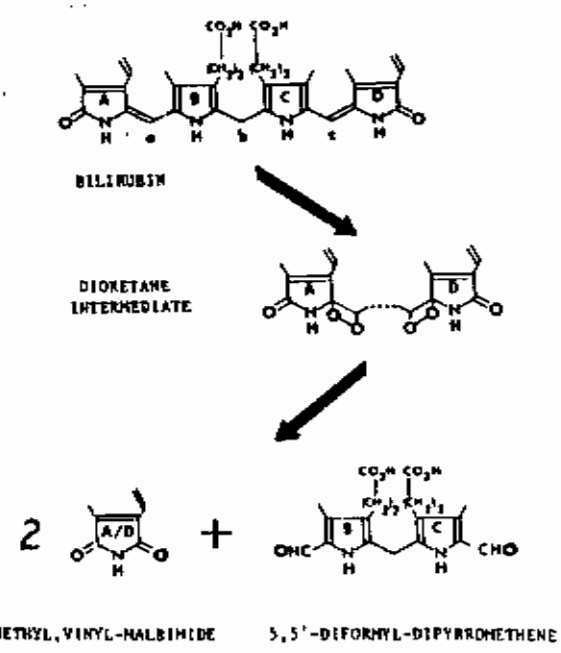

Fig. 1: Pathways of bilirubin photodegradation by the singlet oxygen mechanism (Ostrow et al., 1974)

The second observation is that the dihydroxyl and monohydroxyl derivatives of bilirubin that were identified in Gunn rat bile during phototherapy were difficult to explain by singlet oxygen reactions and constituted only a minority of the photoproducts. The third observation is that the major two pigments excreted during phototherapy, unconjugated bilirubin itself and a yellow-diazopositive-acid labile pigment were not reproduced by photochemical singlet oxygen reaction (Ostrow et al., 1974).

The next major advance was by McDonagh and Ramonas (1978) in their continuous spectrophotometric monitoring of the bile excreted by the Gunn rat during phototherapy, which revealed excretion of photoproducts within minutes of the start of phototherapy. Such a rapid process suggested the possibility of photoisomerization as the main mechanism.

Stoll et al. (1979) produced two pairs of polar photoisomers by irradiation of unconjugated bilirubin in chloroform under anaerobic conditions to preclude oxidation reactions. The authors then showed that these labeled photobilirubins, produced in vitro illumination of unconjugated bilirubin, were rapidly excreted in bile ofter intravenous administration to Gunn rats kept in the dark.

It was documented that photoisomerization was virtually instantaneous, preceded the photooxygenation reactions and could proceed in virtually any medium, even with oxygen present, though singlet oxygen attack was not involved in their formation (Lightner et al., 1979).

The combined evidence from these investigations indicated that the two pairs of photoisomers were formed from unconjugated bilirubin. Isomer IA (the major one 6.4%), isomer IB (1.4%), isomer IIA and isomer IIB (2.8%) and these two pairs were readily separated by chromatography on

silica gel or polyamide. These two pairs of photoisomers account for the major mechanism of bilirubin photocatabolism during phototherapy. The photoisomerization was thus rapidly reversible, so that within minutes, an equilibrium developed in which less than 10% of the pigment was in the isomeric forms. Both pairs of photoisomers are presumably formed rapidly in the skin, subcutaneous tissue and their capillaries, which are the limit of significant penetration of light during phototherapy (Sisson et al., 1973). Being more polar, these pigments partition into the plasma, continuously shifting the equilibrium to promote more photoisomer formation. In the plasma, the isomers are likely stabilized by binding to albumin, from which they are rapidly extracted by the hepatocytes and transported into bile. Isomers I destabilized by bile acids, rapidly revert to the native unconjugated bilirubin, accounted for the augmented excretion of unconjugated bilirubin during phototherapy. The more stable isomers II remain mostly intact to constitute the major polar photoproduct found in bile, but in part hydroxylated at the methene bridges to yield the other minor photoproducts (Arnold and Donald, 1980).

DOUBLE SURFACE VERSUS SINGLE SURFACE PHOTOTHERAPY

Single surface phototherapy unit provides light on the exposed body surface of the neonate from above only, while double surface unit provides light from the top as well as from the bottom simultaneously on the ventral and dorsal body surfaces of the neonates placed naked on a glass table (Srivastava et al., 1980).

In double surface phototherapy, nearly double quantum of bilirubin is exposed at one time to the effect of photons in contrast to single surface exposure (Kasha, 1960). Isenberg and Fusch (1973) also showed the superiority of double light phototherapy over single light and attributed it to an enhancement in the photodegradation of bilirubin as a result of exposure of the greatest possible area of skin surface.

In intensive phototherapy (blue double light), the infant is exposed to blue light from above and below, which is more effective in reducing serum bilirubin concentration per hour than ordinary phototherapy. It is also concluded that double surface phototherapy is expected to be specially useful in neonates with rapidly rising bilirubin levels and also with moderate to severe hyperbilirubinaemia (Ebbesen et al., 1980).

On the other hand, Tan (1975) did not find the effect of multidirectional exposure to be any different from that of single directional irradiation. The author related the effect of phototherapy to the amount of energy output in the effective range and not to its effect on the skin area exposed.

INTERMITTENT VERSUS CONTINUOUS PHOTOTHERAPY

Clinical studies comparing intermittent versus continuous phototherapy have produced conflicting results. Rubattelli et al. (1978) have found continuous phototherapy to be more effective than the intermittent use of light whereas others have not (Vogl et al., 1978). They reported that 15 minutes of illumination followed by 60 minutes with the lights off was found to be as effective as continuous illumination. An irradiance of 350 micro W/cm^2, a regimen of one hour of phototherapy and three hours off is as effective as continuous exposure in term infants with physiological jaundice (Lau and Fung, 1984).

The total dose of light can be considered equal to the total number of photons in the blue spectrum that strike the infant's skin during a specific time interval. Based on this assumption, an infant receiving a flux of 60 photons per second, administered continuously for 24 hours