IMPA JOURNAL

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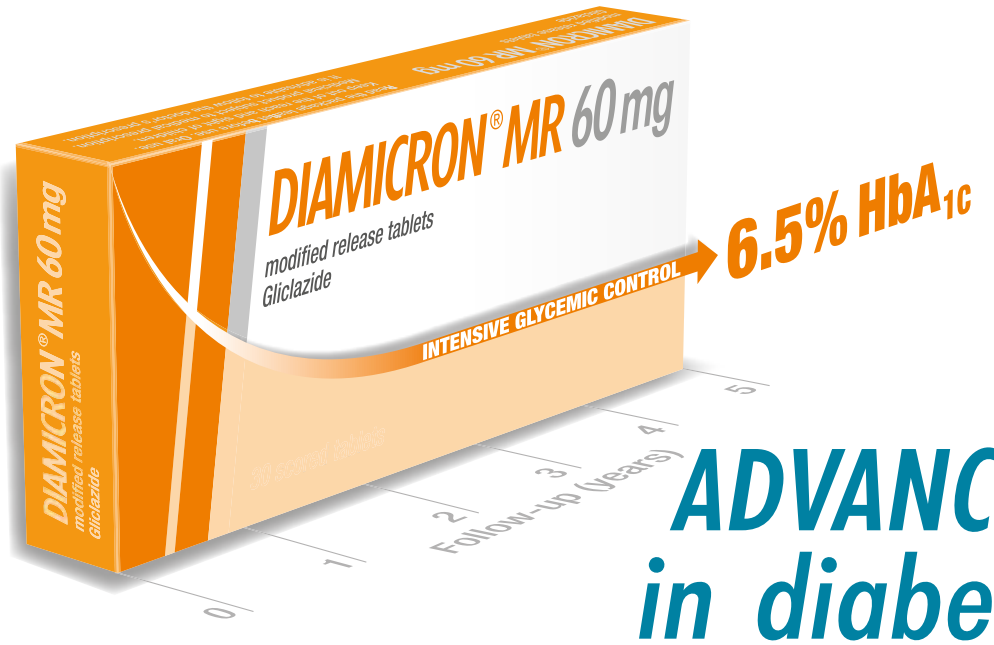
December 2020 | Volume 14

NEW

DIAMICRON® MR 60

Gliclazide

Scored Tablets



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1. The ADVANCE Collaborative Group. *N Engl J Med.* 2008;358:2560-2572. **2.** The GUIDE Study. *Eur J Clin Invest.* 2004;34:535-542. **3.** The STENO 2 Group Study. *N Engl J Med.* 2008;358:580-591. **4.** The CONTROL Study. *Diabetologia.* 2009;52:2288-2298. **5.** Khalangot M, Tronko M, Kravchenko V et al. *Diabetes Res Clin Pract.* 2009;20(6):611-615. **6.** Diamicron MR 60 mg. *Product Monograph.* **7.** Drouin P. and the Diamicron MR Study Group. *J Diabetes Complications.* 2000;14:185-191. **8.** Sawada F, Inoguchi T, Tsubouchi H, et al. *Metabolism.* 2008;57(8):1038–1045. **9.** Del Guerra S, D'Aleo V, Lupi R, et al. *Diabetes Metab.* 2009;35(4):293-298. **10.** Katakami N, Yamasaki Y, Hayaishi-Okano R, et al. *Diabetologia.* 2004;47:1906-1913.

Composition: Each modified-release tablet contains 60 mg of gliclazide. **Indication:** Type 2 diabetes. **Dosage:** One half to 2 tablets per day, ie, 30 to 120 mg as a single daily intake at breakfast time, including in elderly patients and those with mild to moderate renal failure. One DIAMICRON 60 mg modified release tablet is equivalent to two DIAMICRON 30 mg modified release tablets. The breakability of the DIAMICRON 60 mg modified release tablet enables flexibility of dosing to be achieved. **Properties:** Diamicron MR 60 mg is a sulfonylurea lowering blood glucose levels by stimulating insulin secretion thereby restoring the first peak of insulin secretion and increasing the second phase of insulin secretion in response to a meal or intake of glucose. Independent hemovascular properties. No active circulating metabolite. **Contraindications:** Hypersensitivity to sulfonylureas or sulfonamides, type 1 diabetes, diabetic precoma and coma, diabetic ketoacidosis, severe renal or hepatic insufficiency, treatment with miconazole, breast-feeding. **Interactions:** Increased risk of hypoglycemia with miconazole, phenylbutazone, alcohol, other antidiabetics, β-blockers, fluconazole, ACE inhibitors, H_2-receptor antagonists, MAOIs, sulfonamides, NSAIDs. Risk of hyperglycemia with danazol, chlorpromazine, glucocorticoids, β_2 agonists, ritodrine, salbutamol, terbutaline, anticoagulants. **Adverse effects:** Hypoglycemia, gastrointestinal disturbance; more rarely: skin and subcutaneous reactions, hematological disorders, hepato-biliary disorders, visual disorders. **Overdosage:** Possible severe hypoglycemia requiring urgent IV glucose and monitoring. Please refer to the complete summary of product characteristics for your country as variations may exist.

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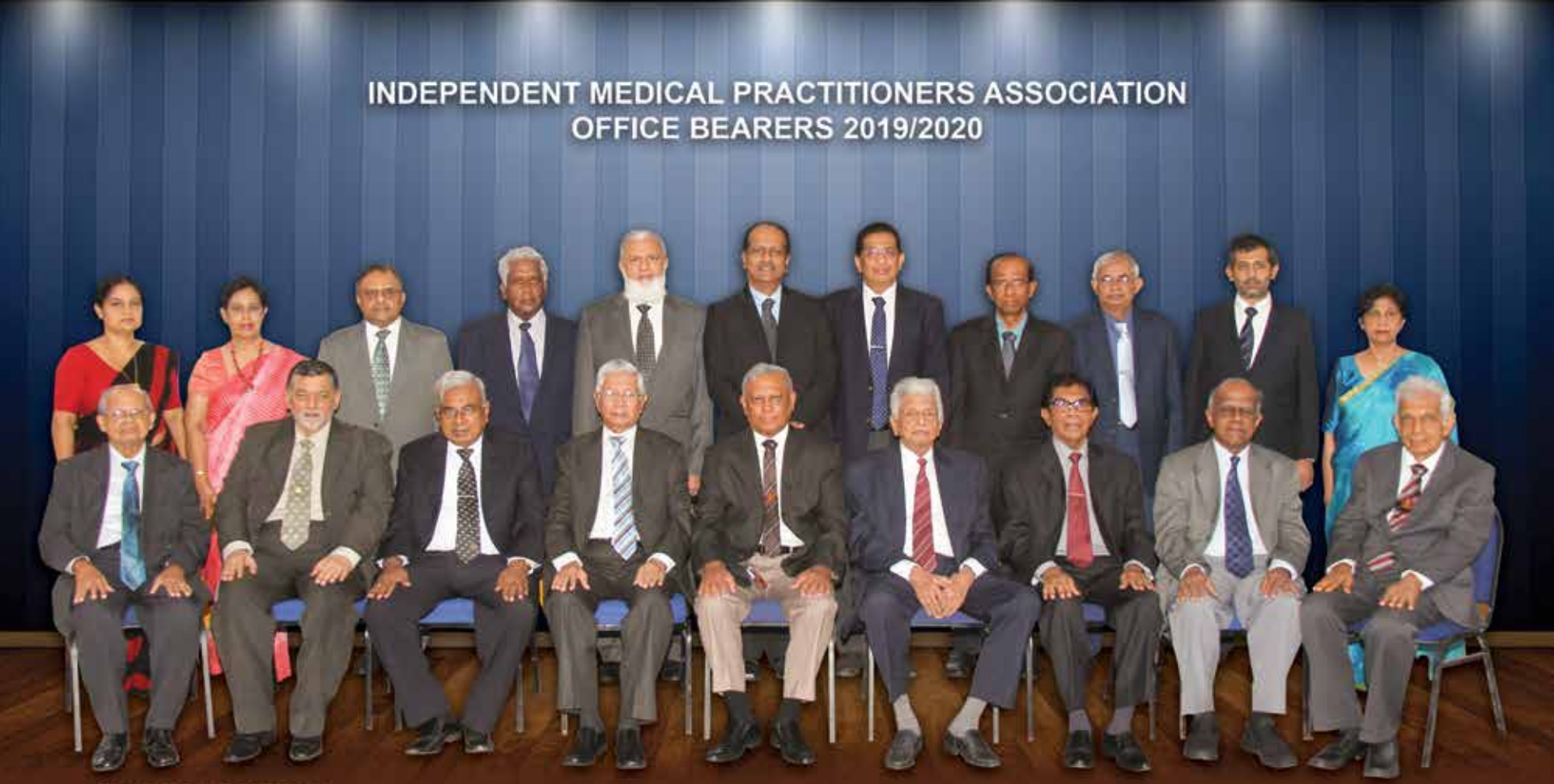

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President's Message 2020

It is with great pleasure that I pen this message for the current year's journal. The editors, authors and our IMPA administrative secretary should be congratulated for the yeomen task they have successfully completed.

This year 2020 had been a year of adopting a NEW NORMAL in the face of dire circumstances impelled by the corona pandemic. Many traditional rituals and beliefs had to be discarded. For instance face to face meetings were replaced with video-conferencing modalities. Many of our members had to adopt new styles of consultations. Patients too in turn would have difficult times in managing their day to day health problems while in the midst of fast spreading SARS-COV-2 pandemic.

If nothing else had been taught to us this pandemic has taught us that NO ONE IS SAFE UNLESS EVERY ONE IS SAFE. In addition it has also taught us that sometimes in the face of adversity when science has to bow down to an unknown and lowly microorganism all that is left to us to protect ourselves are nothing but so called primitive methods of hand washing, distancing, masking, avoiding confined areas, crowds and gatherings. Is this some eerie reminder of George Santayana's, "those who forget the past may have to live it again"?

This year also has been an active and productive year for the IMPA. We have completed two important and related tasks this year. First the IMPA new website which is responsive - thus accessible through your smartphones, dynamic and interactive - is now complete. Second the Sri Lanka Drug Index (SLDI) 2020 is now completed.

The website needs to be promoted and used for income generating activities. While a website is a showcase of an institute it can also be leveraged to accomplish many services to be rendered to the membership. This is the reason why the new IMPA website includes MOODLE integration which will help the IMPA to commercialize the site and generate some income. Already negotiations are currently on the way to rent the site for continuous professional development activities and to conduct courses for other colleges.

The other product SLDI 2020 also needs to be promoted. A new business model has to be discussed by the membership. While there are many beneficiaries for the SLDI 2020 we may as well give access to the drug companies and to pharmacists on a subscription basis and the income could be credited to the IMPA accounts directly.

Over and above all these our usual CPD activities had been conducted as usual despite CORONA thanks to our energetic CPD coordinator Dr. A.H.A. Hazari.

We thank the Ministry of Health for providing us the annual grant for CME activities. We appreciate the services of Dr. Joe Fernando our patron in facilitating the receipt of this grant.

I wish IMPA success and financial viability in the years to come.

Dr Ananda Perera
President
IMPA

Content

NEW

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Editorial

Prof I Joel Fernando

Continuing Education

Understanding the concept of continuing education and its application in one's own practice is of crucial importance to the professional in shaping his role to meet the needs of the community. A group of family physicians from East and West Europe met in Leeuwenhorst and identified four aims for continuing education[1]. These aims modified appropriately to apply to professionals in general read as follows:

1. To review knowledge, skills and attitudes already acquired in professional training, eliminating those which are obsolete while retaining those which are still valuable.
2. To help the professional to discover his deficiencies and to deal with the difficulties which he already recognizes in his own work by sharing experience with his colleagues both professional and non-professional.
3. To help professionals recognize and apply new evidence and ideas, using the experience of professional practice as a basis for their evaluation and application. By giving as well as receiving training in this way he will be enabled to develop new competences and learn new roles effectively.
4. To help the professional's capacity to think creatively and to appraise his own work critically, by means of education and research activities.

Evaluating what is new in the light of practice experience takes place within the context of the professional - client relationship. Self-critical thinking and decisions on eliminating the obsolete take place within the professional, according to his individual learning capacity. Learning through sharing is group learning in professional peer groups and non-professional community groups.

Most professionals continue to learn through the individual learning process, and their experience, in relating to clients. This type of learning is dominated by self. Therefore, any role change that may result from such learning will be self-centred, domineering (over the client), and overriding client interests.

For example prescribing drugs for patients is a common professional practice among doctors. Doctors read medical journals, gather information on correct prescribing and believe that they prescribe rationally. Contrary to this commonly held belief among doctors, studies in USA[2] and UK[3] have suggested that doctors' prescribing was more influenced by promotional activities of the drug industry rather than scientific literature in medical journals. Perhaps this explains why a recent study of 630 patients attending government medical institutions reported irrational prescribing for 24% of inpatients and 27% of outpatients in the Colombo group of hospital, where undergraduate and postgraduate medical education take place[4].

Continuing education demands that

individual learning be combined with group learning to ensure role changes that could satisfy both the needs of the professionals as a group and the needs of society at large. Kurt Lewin[5] an early worker who investigated the dynamics of group interaction discovered the efficiency of the group in achieving a change of behavior. He realized the great pressures towards change which the group could exert on the individual. He attributed success with the group method firstly to the high degree of involvement of the participants and secondly to the fact that after a group discussion it was easier for an individual to make a decision to change his behaviour.

Successful use of group learning by family physicians in Sri Lanka through the IMPA continuing education programme has been reported by Fernando 1981[6], 1984[7]. In one such group learning exercise family physicians were able to construct a detail protocol on how to provide information to patients on drug use when drugs were prescribed[8]. This exercise developed the doctor's role in providing correct drug-use information for the patient, thereby indirectly promoting better drug use in the community which is a priority national need.

Investing in your continuing education by taking advanced training courses and gaining new certifications for is more important now than ever before. Continuing education should go beyond the sheer acquisition of knowledge, and also seek changes in practice, attitudes and behaviours of physicians.

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Indicated for the treatment of moderate to severe acne related to androgen-sensitivity (with or without seborrhea) and/or hirsutism, in women of reproductive age[3]

References: 1. Aydinlik S, et al. Clinical Trials Journal 1990;27:392–402. 2. Aydinlik, S, Lachnit-Fixson U, Lehnert J. Fortschr Med 1986;104:547–50. 3. Diane-35® Current Product Information Leaflet.

DIANE 35 Abridged prescribing information:

COMPOSITION: Each coated tablet contains 0.035 mg ethinylestradiol, 2.0 mg cyproterone acetate **INDICATIONS:**Treatment of moderate to severe acne related to androgen-sensitivity (with or without seborrhoea) and/or hirsutism in women of reproductive age. This includes patients with polycystic ovary syndrome requiring treatment of these symptoms. For the treatment of acne, Diane-35 should be used when topical therapy or systemic antibiotic treatments are not considered appropriate. Since Diane-35 is also a hormonal contraceptive, it should not be used in combination with other hormonal contraceptives **DOSAGE & ADMINISTRATION:**Tablets must be taken in the order directed on the package every day at about the same time with some liquid as needed. One tablet is to be taken daily for 21 consecutive days. Each subsequent pack is started after a 7-day tablet-free interval, during which time a withdrawal bleed usually occurs. This usually starts on day 2-3 after the last coated tablet and may not have finished before the next pack is started. How to start Diane-35 No preceding hormonal contraceptive use (in the past month) Tablet-taking has to start on day 1 of the woman's natural cycle (i.e. the first day of her menstrual bleeding). Starting on days 2-5 is allowed, but during the first cycle a barrier method is recommended in addition for the first 7 days of tablet-taking. Changing from a combined hormonal contraceptive (combined oral contraceptive /COC), vaginal ring, or transdermal patch The woman should start with Diane-35 preferably on the day after the last hormone–containing tablet of her previous COC, but at the latest on the day following the usual tablet-free or hormone-free tablet interval of her previous COC. In case a vaginal ring or transdermal patch has been used, the woman should start using Diane-35 preferably on the day of removal of the last ring or patch of a cycle pack, but at the latest when the next application would have been due. Changing from a progestogen–only-method (minipill, injection, implant) or from a progestogen-releasing intrauterine system (IUS) The woman may switch any day from the minipill (from an implant or the IUS on the day of its removal, from an injectable when the next injection would be due), but should in all of these cases be advised to additionally use a barrier method for the first 7 days of tablet-taking. Following first-trimester abortion The woman may start immediately. When doing so, she does not need additional contraceptive measures. Women should be advised to start at day 21 to 28 after delivery or second-trimester abortion. When starting later, the woman should be advised to additionally use a barrier method for the first 7 days of tablet-taking. However, if intercourse has already occurred, pregnancy should be excluded before the actual start of Diane-35 use or the woman has to wait for her first menstrual period. Management of missed tablets If the user is less than 12 hours late in taking any tablet, contraceptive protection is not reduced. The woman should take the tablet as soon as she remembers and should take further tablets at the usual time. If she is more than 12 hours late in taking any tablet, contraceptive protection may be reduced. The management of missed tablets can be guided by the following two basic rules: 1. tablet-taking must never be discontinued for longer than 7 days. 2. 7 days of uninterrupted tablet-taking are required to attain adequate suppression of the hypothalamic-pituitary-ovarian-axis. **CONTRAINDICATIONS:** Presence or a history of venous or arterial thrombotic/thromboembolic events (e.g. deep venous thrombosis, pulmonary embolism, myocardial infarction) or of a cerebrovascular accident., Presence or a history of prodromi of a thrombosis (e.g. transient ischaemic attack, angina pectoris). A high risk of venous or arterial,History of migraine with focal neurological symptoms, Diabetes mellitus with vascular involvement. Severe hepatic disease as long as liver function values have not returned to normal, Presence or history of liver tumors (benign or malignant), Known or suspected sex-steroid influenced malignancies (e.g. of the genital organs or the breasts), Undiagnosed vaginal bleeding, Concomitant use with another hormonal contraceptive, , Hypersensitivity to the active substances or to any of the excipients. Diane-35 is not for use in men **PRECAUTIONS:** The risk of venous or arterial thrombotic/thromboembolic events or of a cerebrovascular accident,The user group of Diane-35 is likely to include patients that may have an inherently increased cardiovascular risk such as that associated with polycystic ovary syndrome,An increase in frequency or severity of migraine during Diane-35 use, In women with hereditary angioedema exogenous estrogens may induce or exacerbate symptoms of angioedema. Crohn's disease and ulcerative colitis have been associated with COC use. Chloasma may occasionally occur, especially in women with a history of chloasma gravidarum. Women with a tendency to chloasma should avoid exposure to the sun or ultraviolet radiation whilst taking COCs. With estrogen/progestogen combinations, irregular bleeding (spotting or breakthrough bleeding) may occur, especially during the first months of use. **INTERACTIONS:** Some Substances increase the clearance of Diane-35 (diminished efficacy of Diane-35 by enzyme-induction), e.g.: Phenytoin, barbiturates, primidone, carbamazepine, rifampicin, and possibly also oxcarbazepine, topiramate, felbamate, griseofulvin and products containing St. John's wort. Some Substances have variable effects on the clearance of Diane-35, e.g.: when co-administered with Diane-35, many HIV/HCV protease inhibitors and nonnucleoside reverse transcriptase inhibitors can increase or decrease plasma concentrations of estrogen or progestin. Estrogen/progestogen combinations like Diane-35 may affect the metabolism of certain other drugs. Accordingly, plasma and tissue concentrations may either increase (e.g. cyclosporin) or decrease (e.g. lamotrigine). **PREGNANCY AND LACTATION:** Use of Diane 35 is contraindicated in pregnancy and lactation ADVERSE EFFECTS: In rare cases, headaches, gastric upsets, nausea, feeling of tension in the breasts, changes in body weight and libido or depressive moods can occur. Long term use of tablets can cause brownish patches of face which can be made worse by long exposure to sun. Poor tolerance of contact lenses has been reported. **PRESENTATIONS:** Memo pack of 21 tablets

DIN API v2, 04 February 2014 (CCDS version 16- 7 Oct 2013)

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Free Education and Freedom for Free Medical Education in Sri Lanka

Prof Sanath P Lamabadusuriya

Since Sri Lanka became independent in 1948, education up to tertiary level and health services have been provided free of charge by successive governments.

Dr C W W Kannangara

The late Dr C W W Kannangara who was born on the 13th of October 1884 could be considered as the father of free education in Sri Lanka. He had his early education in Wesleyan College, Ambalangoda and later at Richmond College, Galle. During a prize giving at Wesleyan College, Reverend Father J H Darrel, Principal of Richmond College had been the chief guest. When the young Kannangara carried away most of the prizes, Reverend Darrel had jokingly remarked that he would need a bullock cart to carry away all the prizes! He had also invited him to sit for the scholarship examination to enter Richmond College. After admission as a hosteller, he had noticed that the fee-levying students were served food of a superior quality. Perhaps the seeds of free education would have been sown in his mind at that time. He had been a brilliant student who excelled in sports as well. Later he had passed the Cambridge Senior examination as well as the university entrance examination.

In his professional life, he had taught at Richmond College and later practised law. He had been a member of the Legislative Assembly and later the State Council from 1931 to 1947. Then he became the Minister of Education in the first Cabinet of Ceylon and chaired a sub-committee on education. In spite of intense opposition (even from some of his cabinet colleagues), he introduced revolutionary reforms and paved the way for free education in Ceylon. He passed away on the 29th of September 1969 as a forgotten person.

His vision for education was to have a single education system in all schools, free of tuition fees and promote upward social mobility through acquisition of knowledge, skills and attitudes. He was not against private schools but wanted these to be strictly regulated.

History of State Medical Education in Sri Lanka

In Table 1 the establishment of medical schools in Si Lanka is listed in chronological order.

Table 1A. History of medical education in Sri Lanka

- 1840 Manipai - Dr. Samuel Green
- 1870 Colombo Medical School
- 1942 University of Ceylon MBBS
- 1962 Faculty of Medicine Peradeniya
- 1978 Jaffna and Ruhuna
- 1992 Kelaniya and Sri Jayawardhapura
- 2005 Rajarata and Eastern
- 2009 Kotelawala Defence University
- 2018 Sabaragamuwa and Wayamba

Table 1B.

State Medical Schools in Sri Lanka

Total Admissions - 1470

1. Colombo	- 1870	6. Sri Jayawardhanapura	- 1992
2. Peradeniya	- 1962	7. Eastern	- 2005
3. Ruhuna	- 1978	8. Rajarata	- 2005
4. Jaffna	- 1978	9. KDU	- 2009
5. Kelaniya	- 1992		

In 2018 - Sabaragamuwa
Wayamba
Later Moratuwa

Total Admissions to Universities in 2018	-	30,510
Total Admissions to Medical Faculties	-	1470
Total Admissions to Sabaragamuwa Medical Faculty	-	70

North Colombo Medical College (NCMC)

NCMC was the first private medical school to be established in Sri Lanka and functioned between 1981 and 1991. It was established by the Sri Lanka College of General Practitioners. During this period it produced about 850 graduates inclusive of about 100 consultants including professors. As it tried to award the MBBS (Colombo) degree through the back door, due to intense political pressure it was forced to close down. It was acquired by the government and converted to the Faculty of Medicine, University of Kelaniya.

South Asian Institute for Technology and Medicine (SAITM)

In 2009 Dr. Neville Fernando established SAITM in order to fill an existing vital need and cater to the growing demand for Private Medical Education (PME) in Sri Lanka. Three batches of students graduated from SAITM in 2015, 2016 and 2017. About one thousand more students were also admitted. The course fee charged was Rs.9.8 million and scholarships worth Rs.550 million were offered for deserving less privileged students. All students had 'A' level grades higher than the minimum mark set by the University Grants Commission (UGC) for admission to state medical schools for that particular year. For political reasons SAITM had to be closed down and the students admitted to the Faculty of Medicine of the KDU to continue their training. After a decision delivered by the Supreme Court, the Sri Lanka Medical Council (SLMC) was compelled to register the first three batches of SAITM graduates and they commenced their internship together with the state graduates in September 2019.

Faculty of Medicine, Kotelawala Defence University (KDU)

This faculty was established in 2009, initially to provide medical officers for the armed forces. Later about 30-40 fee levying foreign students were admitted and charged six million rupees for the entire course. After the closure of SAITM, their students were also admitted paying lesser fees. With the admission of SAITM students the numbers of foreign students had to be reduced.

The Global Scene

Table 2 illustrates the distribution of state and private medical schools in different continents and countries. In some

countries such as Chile, Nepal, Bangladesh and India, there are more private than state medical schools.

Table 2. Distribution of State and Private Medical Schools.

Country	Public	Private	Total	
USA	69	62	131	Chile 35/60
UK	43	01	44	Caribbean 56/60
Germany	35	01	36	Nigeria 02/34
France	07	00	07	Sudan 08
Nepal	11	11	22	Gulf 08/32
Bangladesh	30	60+60	96	China, Canada
Spain	26	02	28	France, South Africa
Australia	17	02	19	Greece, Netherands
New Zealand	02	00	02	Malaysia 11/29
Japan	50	29	79	Thailand +
India	134	137	271(348)	Philippine +

Medical Education in China

China is a popular destination for our students to study medicine abroad. However, the average time taken by these graduates to pass the Examination for Registration to Pratcise Medicine (ERPM) examination was 18 months to two years. There were 3-4 attempts at the ERPM examination by 90% of graduates and 10% had more attempts. In China there are several medical schools and in the Tianjian Medical School there are over a hundred Sri Lankan students in each batch. Sri Lankan doctors visit this school to conduct classes for our students to prepare for the ERPM examination when they eventually return. The course fee is about Rs.10 million and the medium of instruction is English.

Medical Education in the Russian Federation

In Russia the fee structure is based on a quota system. The first quota is only for Russian students who are admitted on merit and no fees are charged. The second quota is for Russian students who failed to enter on merit and 50% of the fee is charged. The third quota is for foreign students who pay 100% of the fee. In 2009 the free quota: paying quota was 70:30 and it gradually changed to 60:40 in 2019.

Medical Education in Nepal

The first medical school was established in 1980 and presently there are 4 state and 12 private medical schools. Many Sri Lankan students study medicine in Nepal draining massive amounts of foreign exchange. Generally, the educational standards are satisfactory because Sri Lankans students who later appear for the ERPM examination pass it without much difficulty.

Medical Education in IMU Malaysia.

The IMU is another popular destination for Sri Lankan students who pay heavy fees to be taught by Sri Lankan academics employed by the IMU!

Current Status of Education

In our country only a minority of students eventually enter a university to pursue higher education. The statistics are shown in Table 3.

Table 3. Primary and Secondary Education

300,000 students enter Grade 1 annually
30,510 students entered the universities in 2018
70,000 students travel abroad for education
About Rs. 231 billion drained out of the country annually for education

Doctor - Patient Ratios

The doctor-patient ratios in different countries are shown in Table 4. It is estimated that about 1480 medical graduates qualify from the state medical schools each year. Of these about 200 doctors leave the country annually facilitated by the absence of a compulsory period of service. In 2019 there were 29,954 medical officers registered with the SLMC. The WHO recommends a total of 40,000 doctors for Sri Lanka. Therefore, there is a shortage of about 10,000 doctors at present. It is estimated that for every student who enters a state medical school, about two others travel abroad for medical studies.

Table 4.
Doctor Patient Ratios

Total number of doctors in Sri Lanka - 29,954

Sri Lanka	1 for 728 in 2019
U.K.	1 for 357 in 2013
Australia	1 for 350
Cuba	1 for 350
India	1 for 1700
Spain	1 for 208
Germany	1 for 257
France	1 for 312
Pakistan	1 for 1400

Situation analysis in Sri Lanka

The current status of medical officers in Sri Lanka is shown in Table 5. The output of medical graduates by the state universities are shown in Table 6. As could be seen in Table 5, our country is short of all categories of doctors. At the current rate of production of medical graduates by state medical schools, it would take more than 10 years to fill the gap. If PME is allowed, this discrepancy could be rectified within a shorter time frame. There is valuable time wasted between qualifying at the 'A' level examination and entering medical schools. There is a further delay between graduation and commencement of internship because all graduates commence their internship after a common list is provided by the UGC. As the different universities conduct the Final MBBS examination in a staggered manner, the UGC is compelled to do so. This procedure could be changed by offering internship to those who have qualified, for two batches, on two fixed days of the year such as 1st of March and 1st of September. This would also discourage students from resorting to industrial action in individual faculties.

Table 5. Current status of Medical Officers in Sri Lanka

Service Provider	Number	Dual Employment	Contribution	50%	Total
Medical Officers	7960	60%	10800	5400	23360
Consultants	2100	93%	1953	977	2077
University staff	625	72%	450	225	850
Full time GPs	3090			3090	3090
Defence forces	320	60%	192	96	416
Total	24095		13395	9788	29793

Source : Dr Dilip de Silva Consultant in Health Economics and Consultant in Community Dentistry

Table 6. Graduate output by Year and Universtiy

Country	2012	2013	2014	2015	2016	2017
UOC	205	188	189	202	198	164
UOP	192	192	204	199	208	160
SJU	175	150	155	153	152	123
UOK	189	157	173	182	162	120
UOJ	71	67	88	108	96	65
UOR	152	126	129	137	146	92
EUSL	27	37	33	58	49	35
RUSL	163	176	172	174	182	148
Total	1173	1093	1143	1216	1195	907

Selection of students for state medical schools

Currently students are selected for state medical schools based on the performance at the 'A' level examination a quota basis. 40% are selected on merit, 55% on a district quota basis (DSQ), determined by the population in each district and 5% from educationally under privileged areas. At the time the present quota system was introduced, it was planned to increase the merit quota at the expense of the district quota, over the years as the standards in rural schools improved. However, for political reasons the DSQ remains unchanged.

Table 7. Missing out with 3 'A's

NUMBER OF STUDENTS OBTAINED "3A" AND **NOT SELECTED** FOR THE COURSE OF STUDY IN MEDICINE

	DISTRICT	A/L YEAR				
		2016	2015	2014	2013	2012
1	COLOMBO	7	7	4	-	-
2	GAMPAHA	1			-	-
3	KALUTARA				-	-
4	MATALE				-	-
5	KANDY				-	-
6	NUWARA ELIYA				-	-
7	GALLE	6			-	-
8	MATARA	6			-	-
9	HAMBANTHOTA				-	-
10	JAFFNA				-	-
11	KILINOCHCHI				-	-
12	MANNAR				-	-
13	MULAITIVU				-	-
14	VAVUNIYA				-	-
15	TRINCOMALEE				-	-

16	BATTICALOA				-	-
17	AMPARA				-	-
18	PUTTALAM				-	-
19	KURUNEGALA	1			-	-
20	ANURADHAPURA				-	-
21	POLONNARUWA				-	-
22	BADULLA				-	-
23	MONARAGALA				-	-
24	KEGALLE				-	-
25	RATHNAPURA				-	-
	TOTAL	**21**	**7**	**4**	**0**	**0**

As depicted in Table 7, there was a total of 38 students who obtained 3 'A's, in 2014, 2015, 2016 and 2017. As shown in Table 8, there was a total of 1518 students, during the period 2010 to 2016, who obtained two 'A's and one 'B', but failed to gain entry to the state medical schools.

Table 8. Missing out Medicine with 2A / 1B

University Admission
No. of students missing Course of study Medicine after obtaining "2A" and "1B"

District Code	District	2009	2010	2011	2012	2013	2014	2015	2016
1	Colombo	28	69	70	58	47	73	116	131
2	Gampaha		5	1	11		5	17	24
3	Kalutara	1	8	3	13	1	7	8	24
4	Matale		3		1				1
5	Kandy	2	7	15	9	13	22	14	39
6	Nuwara Eliya								
7	Galle	3	24	8	12	22	17	30	3
8	Matara	13	26	15	10	12	15	23	43
9	Hambanthota	8	5	3	5	3	7	10	14
10	Jaffna		1	2	1	1	12	9	23
11	Kilinochchi								1
12	Mannar								
13	Mulaitivu								
14	Vavuniya						1		1
15	Trincomalee								
16	Batticaloa							1	8
17	Ampara							2	2
18	Puttalam						1		2
19	Kurunegala		12	5	10	1	13	19	23
20	Anuradhapura								4
21	Polonnaruwa							1	

22	Badulla				2				4
23	Monaragala								
24	Kegalle	2	14	2	2		1	9	9
25	Rathnapura	2		1			1	10	21
	TOTAL	**59**	**174**	**125**	**134**	**100**	**175**	**269**	**432**

2009—59, 2010---174, 2011---125, 2012---134, 2013---100, 2014---175, 2015---269, 2016---432

This is totally unacceptable and is a severe indictment on the prevailing DSQ. Some of these students whose parents were affluent may have proceeded abroad for higher studies at great cost. These students and their parents were compelled to be separated for at least five years and some of them may not have returned to Sri Lanka after graduation thereby worsening the brain drain. Those students who were not affluent would have remained at home pursuing a career with less job prospects.

The need and justification for Private Medical Education (PME) in Sri Lanka

There are several reasons for having PME in Sri Lanka.

a) The country is short of doctors and the resources of the government are stretched. If there is a surplus in the future, they could travel abroad and earn valuable foreign exchange. As our standards of medical education has an excellent reputation abroad, there would not be a problem for them to find suitable employment. It is much more dignified to export doctors rather than housemaids!

b) The massive loss of foreign exchange amounting to billions of rupees could be drastically reduced.

c) Students from other countries would be attracted to study medicine in Sri Lanka, bringing in valuable foreign exchange.

d) The local students would have to compete with foreign students to obtain higher grades thereby promoting healthy rivalry.

e) There are other fields of university education in the private sector such as for law, architecture, accountancy, management, business studies and Information technology (IT).

Safeguards in establishing PME

a) The admission criteria should be determined by the UGC and the minimum mark for admission should be higher than the minimum mark for admission to a state medical school for that year.

b) Scholarships should be offered to less privileged students.

c) The training and teaching facilities within the faculties, teaching hospitals and the community, should be closely monitored by the SLMC.

d) Preferably new private schools should be established in provinces and districts away from the big cities so as to minimize the internal brain drain. It would also lead to economic development of these rural areas.

e) All evaluations should be conducted together with the participation of academic staff from other state universities as visiting examiners so as to ensure transparency.

The Opposing Forces

There are two main opposing forces for the establishment of PME in Sri Lanka. Firstly, the agencies which find placements for students to study medicine abroad, because they would lose out on a massive income if less students proceed abroad.

Secondly, the doctors (majority of whom are members of a powerful trade union) who conduct courses for foreign graduates who are preparing to appear for the ERPM examination.

Sri Lanka Medical Council (SLMC)

The current SLMC was established under the medical ordinance of 1927. The chief function of the SLMC is to safeguard the health of the community. At present the composition of the SLMC is dominated by the medical profession and the community is not represented. It should be restructured immediately with representatives from sectors such as education, law, accountancy, clergy etc., as in the General Medical Council (GMC) of the UK, where the majority are lay members.

The UGC and SLMC must agree on a common set of medical standards for admission to local and foreign medical schools both in the state and private sectors, which should then be gazetted. The SLMC should visit the state medical schools regularly and monitor the staff/student ratios and facilities available for training within the faculty premises, hospital sector and in the community. If there are deficiencies, these should be highlighted and if not rectified in due course, such schools should be derecognized.

The need for a National Health Commission (NHC)

A NHC should be established by the government which is responsible to parliament. It should be funded through the national budget, be an independent institution with specific terms of reference, have a representative membership, monitor implementation of policies and funding and submit regular reports to the parliament and public.

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PCR Testing for COVID-19: Basic Principles

Dr Nafeesa Noordeen

Today the world faces a situation like none in living memory. Heart-rending images abound on TV and social media, as the new coronavirus SARS-CoV-2 burns its way across the world. Whilst we watch in shock and horror, doctors and scientists from far flung corners of the earth are racing to find a cure or a vaccine. Identifying individuals who have been infected with SARS-CoV-2 as well as those who have recovered from COVID-19, through diagnostic testing, is paramount if we are to resume a sense of normalcy in our lives, until an effective vaccine is produced. People who test positive for the virus can quarantine themselves, thus preventing the virus from spreading. In the case of COVID-19, some infected persons have no symptoms (asymptomatic), and can therefore spread the virus without even knowing they have it. Furthermore, the hope is (though not proven yet) that people who have recovered from COVID-19 will be immune to the deadly virus and thus can help re-start the economy. To this end, two main types of molecular tests are available to diagnose and manage COVID-19. These techniques are well-known to medical scientists and doctors familiar with nucleic acid amplification tests (such as PCR) and antibody assays, but unknown to the public. This article describes the basic principles of the PCR diagnostic test that is being used globally to diagnose COVID-19.

The PCR Test

What is PCR? PCR (Polymerase Chain Reaction) is a well-established scientific technique, that has been widely used for about 25 years in molecular diagnostics field. PCR is fundamentally a nucleic acid (DNA) amplification method. To detect the novel SARS-CoV-2 virus, a special version of PCR is used, namely real-time RT-PCR. This type of test has frequently been used as a frontline test for COVID-19 as it directly tests for the presence of the virus genetic material, RNA. RT-PCR tests are sensitive and accurate and produce results in 6-8 hours on average. The technology is widely available, and many diagnostic and companies produce RT-PCR products, test kits and machines. Some RT-PCR tests are developed as an `all in one' kit, reducing laboratory handling and potential for contamination. For SARS-CoV-2 RT-PCR testing, the FDA recommends test kits produced by certain companies only (for example Integrated DNA Technologies and Roche).

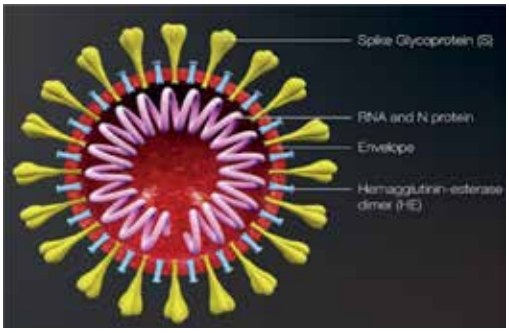
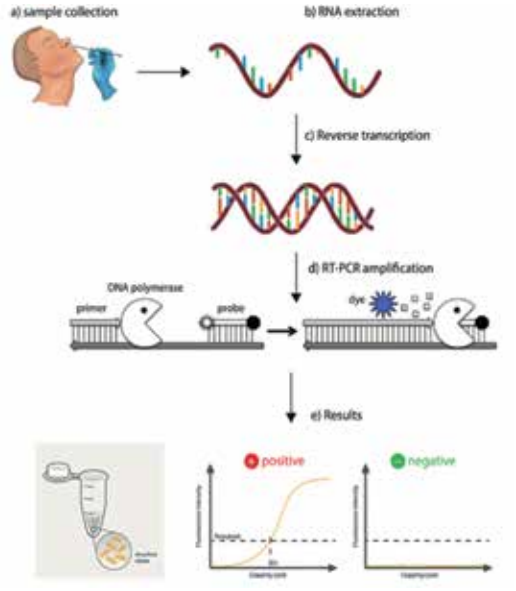


Figure 1. A virus contains the genetic material (either DNA or RNA) contained within an envelope made of fat and protein molecules. Certain viruses such as the coronavirus (SARS-Cov2) only contain RNA. This means that they rely on a hosts' healthy cells to multiply and survive. Once inside the host cell, the virus uses its own genetic material to take control of and 're-programme' the hosts cells to make them become virus-making factories.

A nose or throat sample is taken using a swab – if the sample is collected from where the virus is shedding or multiplying, the accuracy of the test is improved. Chemicals are used to purify the viral RNA from other contaminants in the sample. Then, an enzyme (a molecule that speeds up chemical reactions), called Reverse Transcriptase, is used to copy the viral RNA to DNA. The DNA is then amplified using another enzyme DNA polymerase, which required short DNA molecules called primers to copy the viral DNA. The reaction is done in a PCR machine, which cycles the temperature (repeated heating and cooling cycles). This results in billions of copies of viral DNA being made for each viral RNA strand that was originally present in the sample. In real-time PCR method, fluorescent probes (molecules which give out light when they absorb energy) are added to the mixture, which bind very specifically to a part of the viral genetic material. These probes emit fluorescent light at each PCR cycle. The fluorescence signal increases as more copies of DNA is produced. This fluorescence light can be read (quantified) by the PCR machine to produce the test result. If the light produced reaches a certain threshold fluorescence (which is set above background levels), it is a positive test. If the virus were not present in the sample, the PCR test would not have made copies, so the fluorescence threshold is not reached - the test is then negative. The number of PCR temperature cycles that are required to reach fluorescence threshold is recorded and gives an estimate of how much virus was present originally in the patient sample.

Quality control procedures are extremely important to monitor the test performance and is crucial for the interpreting test results, as well as ensuring that the test kit components and all reagents (chemical substances) are working properly. The inclusion of both positive and negative controls with every batch of patient samples is a must. For example, for a negative control that has no genetic material in it should provide no amplification, whereas the positive control (a sample which is known to be positive for SARS-CoV-2 genetic material) should be amplified in the expected manner for a test to be valid.



Converts viral RNA to DNA

Amplification of DNA and in increase in fluorescent light

Figure 2. Steps in the RT-PCR test: a) Specimen is taken from the nose or throat of patient; b) RNA is extracted and; c) is converted into DNA; d) An enzyme, DNA polymerase, amplifies the DNA. The fluorescence increases as more and more copies of the virus DNA are made; (e) If the fluorescence level crosses the threshold, the test is positive.

What do the test results mean?

A positive PCR result means that the person the sample was taken from is currently infected by the virus. A negative PCR result could mean that the person is not currently infected by this virus, the virus is not present at the site the sample was taken from, the sample taken was of poor quality, or that it is too early, or too late in the infection to detect replicating virus. The RT-PCR test cannot detect if a person has had the virus and then cleared it after the disease ended, i.e. whether a person had the disease, as it only detects when active virus is present. Therefore, for a negative test result, if the patient has clinical symptoms of COVID-19, and/ or contact with a confirmed positive case, re-testing a few days later is a must. The test can also give false positives, if for example, specimens are contaminated, or the protocol is not followed appropriately.

What are the advantages of this test?

RT-PCR is accepted by medical researchers as a robust and well documented technique. It is highly sensitive and reliable if performed on a sample from an infected part of the body whilst an active infection is occurring. The disadvantages are that RT-PCR relies on detecting the virus itself and so it is possible to miss patients who have cleared virus and recovered from disease. RT-PCR for COVID-19 can only tell if a person is currently infected with SARS-CoV-2. A bottleneck in using this test for high-throughput COVID-19 testing is the major demand of testing kits and ancillary ingredients needed for sample preparation and testing.

Ultimately, scientific knowledge and research leading to a vaccine or cure could be the saviour of this dreaded disease that has shaken the very edifice of life as we know it. Science could pave the way to a COVID-19 free world, and maybe we shall awake once more every morning with renewed strength and hope.

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Is it safe to use antihistamines in early respiratory tract viral infections like Covid 19?

Dr Sanath Hettige and Dr Minaka Hettige

Antibodies in nasal secretions are the first line defense against viral infections and induced cough and sneezing will reduce the viral load reaching the lungs. Antihistamines will reduce nasal secretions, cough and sneezing thus increasing the possibility of a larger viral load reaching the bronchioles and alveoli resulting in complications like viral pneumonia in infections of viruses, potentially capable of infecting alveolar epithelium like Covid 19.

Introduction

Antihistamines are generally classified as first or second generation. Sedation results from the ability of first-generation antihistamines to cross the blood-brain barrier and to block central histamine one receptors. In contrast, second-generation antihistamines are commonly described as non-sedating as they cross blood brain barrier to a significantly less extent. Another difference between first and second-generation antihistamines is their effect on non-histamine receptors. First-generation antihistamines block cholinergic and serotonergic receptors in addition to histamine receptors, resulting in the potential for dry mouth, urinary retention, increased heart rate and increased appetite[1].

A 2015 Cochrane review assessed the effects of antihistamines on the common cold, evaluating data from 18 randomized controlled trials, including 4,342 participants, 212 (<5%), of whom were pediatric patients and concluded that no evidence supports the efficacy of antihistamines for cough and cold. Authors of a 2015 review on the effectiveness of treatments for the common cold concluded that there is no evidence to support the effectiveness of decongestant or antihistamine formulations in children[2]. Studies have not been done to evaluate the adverse outcomes of early antihistamine treatment in potentially lethal respiratory tract infections caused by coronaviruses.

It is rare to see a primary care physician or a pediatrician who does not prescribe antihistamines or cough syrup containing antihistamine to patients having upper respiratory tract infections although there is no research evidence of their benefit.

In a study done to evaluate the prescription practice of antihistamines for acute upper respiratory tract infections in paediatric patients in a local emergency department in Hong Kong, among the 162 cases, 141 (87%) patients were prescribed one antihistamine of any group. Sixty (37%) patients were prescribed two or more antihistamines[3].

The reason behind these prescriptions could be that there is simply no other medicine to offer at primary care level for viral upper respiratory tract infections. Even though few antiviral drugs are available they are expensive and are not freely available in many third world countries.

Hypothesis and evaluation

Antihistamines may interfere with the first line defence mechanism against respiratory tract infections like corona virus worsening the clinical outcome.

Like other respiratory tract viruses Corona virus enters the upper respiratory tract invading nasal and pharyngeal mucosa. Then it gradually spreads to the lower respiratory tract invading the alveolar epithelial cells[4].

Host first line defence mechanism for viral infections is nasal secretions containing non-specific anti bodies which will neutralise the invading viruses and induce cough and sneezing taking the viruses out of the respiratory tract with the nasal secretions[5].

When a patient takes antihistamines with early symptoms of rhinorrhoea the nasal secretions, cough and the sneezing will be reduced[5]. This can increase the viral population in the upper respiratory tract and also prevent the natural mechanism by which the body prevents viruses reaching the lower respiratory tract.

This may enhance the spread of virus to the lower respiratory tract epithelium covering the bronchia and alveoli inducing type two pneumocystis, resulting in initiating the disease process[6,7].

Therefore, it is important to review the early use of antihistamine in viral respiratory tract infections that have a potential ability to invade alveolar epithelium.

Testing the Hypothesis

Retrospective cohort studies could be carried out in the current Covid 19 pandemic comparing the clinical outcomes of patients who have been treated or taken antihistamines in early illness and who have not taken antihistamines. Alternatively a randomised control clinical study could be performed by treating patients with or without antihistamines in early upper respiratory tract infections and following them up to the end point. RT-PCR or rapid IGM test could be performed to determine the type of viral infection that the participants are been infected.

Conflict of Interest

The author declares no conflict of interest

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Increasing your life span is not rocket science : A prescription for long life

Dr Ananda Perera

Summary

The purpose of this thesis is very simple. Rather than attempting to increase the genetic life span why not increase the genetically available life span to the fullest extent possible using already available simple facts and evidence? Premature mortality has been extensively researched by the medical scientists and there is now very clear cut evidence to unerringly guide the journey towards wellness. In fact 2019 has been a year with many megatrials publishing their results in the medical journals. As avoiding premature death is practically possible, feasible, implementable and modifiable by the individual person without any extrinsic support we should strive for this target. This article deals with 12 facts unearthed so far by the clinical epidemiologists on premature mortality. Finally, I will develop a model of a long living professional for all of us to emulate. This will help us the professionals who in the pursuit of money, status, transient states of joy and family upliftment forget the life's end. Further a set of professionals living according to this model will provide an inestimable role model to the rest of the society who are not so scientifically empowered.

1. Introduction

Despite the certainty of the death and uncertainty of the life at the next moment humankind has never been satisfied with the life span available to them by virtue of biology. End of life beliefs run the entire spectrum from one end having the beliefs like "I wish I could ask God why the good die young" to "bad and the ugly lives forever" at the other end.

Why is this Knowledge Important?

A. Unawareness prevents seeking information and thus making use of strategies available for prevention of death. Among older persons who fall, only one-third seek medical care, and thus, two-thirds of those who have fallen at least once are unlikely to seek and take advantage of fall prevention services. One explanation for not seeking medical care for fall prevention is likely insufficient public awareness regarding the importance of fall prevention and the availability of fall prevention programs and also the complications of the falls in the elderly.

B. To advocate the policy of reimbursing the wellness programs more in comparison to the disease insurance which is currently in vogue. This is already happening in US where several big insurance companies already are moving towards wellness and disease prevention rather than reimbursements for disease, death and hospitalizations. The cost efficacy of insurance against wellness as opposed to insurance against disease is certainly going to be a very viable business proposition.

C. The most cost effective and efficacious approach for longevity is wellness promotion than treatment or

management of the diseases.

D. Wellness programs do not need medical attention nor any physician intervention. They are available for those who seek them. While most of them are focused on populations as a whole, for a given individual the principles applicable are same.

2. Evidence

American Heart Association LS7 score or Life's Simple 7 risk factors study done in 2019 found in an ideal person with normal blood pressure, normal cholesterol levels, normal blood sugar who is a non-smoker, active and of normal weight and consuming an ideal diet is probably very much less likely to die of cancer when compared with a normal average adult in the community. Indeed, very few people in the community meet this ideal profile (STUDY 1).

Another study carried out in US in 2017 found that a substantial proportion of the deaths in a community from heart disease, stroke, and type 2 diabetes is attributed to dietary factors. Important dietary factors identified as preventing deaths were: fruits (more), nuts (more), whole grains (more), unprocessed red meats (minimal), processed meats (none), sweetened sugary beverages (none), polyunsaturated fats (minimal), sea food enriched with omega 3 fatty acids (more), sodium (minimal) and saturated fats (minimal) (STUDY 2)

In 2019 a group of 5 researchers found that number of steps taken in the course of a day too has an important effect on the length of life. It was thought sometime back a value of 10,000 steps is required to get the health benefits. But this research calculated that even at low levels of 3000 steps will help get the health benefits and the benefits increase in proportion to the number of steps. But they found at the level of 7500 steps per day the health benefits stopped. (STUDY 3)

In another study conducted in 2019 medical researchers found that older adults who did home based muscle strengthening exercises and balancing exercises had very few falls. The falls are an extremely common event in community. Also falls in the elderly are potentially catastrophic not only because of the injury but also as the fall can cause This was simply because falls are very common in the elderly and a fall in an elderly person can cause disability, institutionalization, complications of immobility which together can increase the death rates. In fact, in US the commonest cause of death in the elderly is traumatic injury. (STUDY 4)

In 2019 yet another landmark study concluded that stronger purpose in life was associated with decreased mortality. This is a modifiable risk factor for premature deaths. Having a purpose in life means: goal directed life, sense of directedness in even daily trivia, a meaningful past and a present, live activities and personal role functions have aims and objectives for living. A similar study in the same year found optimism is also a positive attribute for living. The optimism is associated with cardiovascular benefits and pessimism is associated with cardiovascular risk. It is also notable effects of these psychological variables are as strong as other well known factors like smoking, alcohol, high fat etc. (STUDY 5 AND 6)

A Japanese study published in the year 2019 found that higher intake of plant-based proteins may contribute to long-term health and longevity. The deaths were avoided mostly by avoiding the heart diseases. But a direct effect on allcause mortality was also explored. It also

found that there was no effect of animal protein intake on the premature deaths. But increasing the plant-based proteins will invariably reduce the animal protein consumption. This is because the protein energy contribution is usually kept around 15% of the total estimated daily energy requirements. (STUDY 7)

Group of European and American researchers in 2019 reported the value of avoiding sedentariness in our day to day life. This was a massive multinational study of data synthesis from many epidemiological studies reported in the public health literature. They found not only more of exercise at any intensity but also less time spent sedentary are associated with substantially reduced risk for premature death. In addition they were able to show that there was dose response in the effect. Therefore the current guidelines are de-emphasized in terms of arbitrary level of intensity of exercise. Specifically, they found maximal risk reduction of death rate was seen at about 375 min/day of light intensity physical activity or 24 min/day of moderate-to-vigorous intensity physical activity. Further a higher risk of death was observed from 9.5 or more hours per day for time spent sedentary. (STUDY 8)

Skipping breakfast has been found in a study reported in 2019 to increase the premature deaths from heart diseases. Thus, it seems breakfast is proving to be very heart friendly. While the reasons for this association are mostly theoretical yet it is well known in the field of nutritional epidemiology that breakfast has enduring effects on the hormonal milieu of the body all throughout the day. In fact, this is the reason why in the management of uncontrolled diabetes sometimes more focus is given to the breakfast than to other meals of the day. (STUDY 9)

Yet another study on dietary factors and premature death reported from Europe in 2019 found that consumption of total sugar-sweetened, and artificially sweetened soft drinks were positively associated with all-cause deaths. This means that your death from multiple common causes are hastened by consumption of these soft drinks. Is there a safe limit to these commonly available foods? This study results are based on a comparison between 2 or more glasses per day with 1 glass per month. A glass was defined as 250 ml in this study. The soft drinks included low calorie or diet fizzy soft drinks, fizzy soft drinks and fruit squash or cordial. (STUDY 10)

Red meat has long been known to cause heart diseases, diabetes, cancers particularly GUT cancers. Processed red meat in hot dogs, sausages and bacon in addition may cause respiratory diseases, heart failure and high blood pressure. Contents of red and processed meats like saturated fat, polycyclic aromatic hydrocarbons, sodium and preservatives as well as a trimethylamine N-oxide or TMAO are thought to mediate the health risks. Therefore, that red and processed meat may cause premature deaths is not difficult to understand. Several recent epidemiological studies have extended these findings with more detailed analysis showing the dose response effects. Thus, not only increasing consumption may augment the risk of dying prematurely but also that decreasing or avoiding the consumption may in fact diminish the risk substantially. (STUDY 11)

Yet several more studies published in 2019 came out with the ill effects of ultra-processed foods we consume. Ultra processed foods usually contain substances which are rarely used in kitchens like high-fructose corn syrup, hydrogenated or inter-

esterified oils, and hydrolyzed proteins, classes of additives designed to make the final product palatable or more appealing such as flavors, flavor enhancers, colors, emulsifiers, emulsifying salts, sweeteners, thickeners, and anti-foaming, bulking, carbonating, foaming, gelling and glazing agents. With such a list probably it is not surprising that there is risk of premature death from consuming these substances. Most of the studies published in 2019 on ultra-processed foods found that they increase your chance of dying from multiple common causes. Again, not only due to the high risk but also, the dose response effect. That is the more one consumes the higher the chance of death and also the reverse that if consumption is reduced the chance of premature death is also proportionately reduced. (STUDY 12)

3. Synthesis

Altogether 12 important clinical variables have been harvested by medical researchers in the year 2019 to prevent premature death. Unfortunately, none of these studies was done on Sri Lankans. Therefore, the question of applicability of the mostly US and European data arises naturally. Obviously, there are many differences. For instance, level of development, socio-economic status, cultural and religious differences are too obvious to be ignored. The opinion of medical scientists are divided on this matter. There is a group who suggests that these findings can never be extrapolated to our population. But there is also a group which vociferously argue for the possibility of extrapolation of inferences to our population. The author is in the latter group and the discussion on this matter is out of scope for this paper. But in the final analysis all of us are humans and coming down from the same evolutionary lines and just happened to be drifted into various continents. The DNA is same, metabolism is same, body systems are same, and physiology is also overwhelmingly same. It is just that environment required so drastic adaptations that finally resulted in so much of ethnic and racial diversity.

There is yet another argument in favor of accepting the Western research findings. The personal clinical experience of the Sri Lankan physicians is in agreement with most of the expectations and context of the Western research. For instance, frequency of falls, increasing trends for sedentariness, pathological eating patterns causing non communicable diseases are not significantly different from those that reported in the West. In addition, an argument which is very strong in supporting the applicability of the Western research is the applicability of research on drugs. While the research on drug development is virtually nonexistent in Sri Lanka we are consuming 6000 million rupees worth of drugs annually mostly researched and developed in the West (2007 figures).

Therefore, it is expected that the facts teased out from the Western literature which are only the basic environmental variables which are going to act on the same physiology and anatomy of the human. It could not be so very different indeed!

4. Creation of the Profile of an ideal Long Living Professional

Therefore the ideal long living professional will look something like this: He or she has normal blood pressure (treated or untreated), normal cholesterol levels (treated or untreated), normal blood sugar (treated or untreated), a non-smoker (or a quitter more than 2 yrs), physically active and of normal weight and consuming an optimal diet. That person does not skip breakfast and also avoids sugar sweetened beverages and avoids ultra-processed foods.

He or she is also engaged in the prescribed amount of exercise and also actively avoids sedentariness. This professional is highly optimistic and engaged in the routine of daily life with a sense of purpose in life.

Conclusions

Despite all the clear current evidence available the wellness research and the preventive care service in Sri Lanka is given step motherly treatment in the policy making, funding of research projects and the creation of public awareness regarding wellness. Wellness is given scanty attention in the medical school curricula. While a standard medical school curriculum teaches you everything about diseases, pathology, illness and psychology it does not teach you wellness. In fact, the problem with us physicians is that we do not know the normal. We do not know wellness. In fact, we are never taught the features of wellness. Nor for that matter of death. This is one of the reasons why we physicians are ordering investigation after investigation and scan after yet more complicated scan in persons who are consulting us in our day to day clinical work. We are in pursuit of a mirage of a so called medical diagnosis when in fact the person concerned is in all probability normal and well. Substantial improvements in mortality rates and thus the life span can be achieved with the available scientific evidence with minimal cost and effort. Focusing on life and wellness is million times more efficient and efficacious.

Ayu - Bowan.

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1. A list of all the references for this paper is available on request from the author.

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Anticoagulation - an overview

Dr Bernadene Fernandopulle

Introduction

An anticoagulant is a drug which inhibits the action or reduces formation of clotting factors necessary for blood coagulation. Anticoagulants will cause blood to be less coagulable and in other countries the clinicians use phrases such as "we will give you a drug to make your blood thinner" when referring to them. The injectable anticoagulants are unfractionated Heparin and Low Molecular Weight Heparins. Other new direct oral anticoagulants include drugs such as Rivoroxaban, Dabigatrin, Apixaban etc and these are registered for use in Sri Lanka.

Warfarin is an age old anticoagulant which has been in use since 1954. It inhibits the gamma carboxylation of Vitamin K dependant clotting factors 11, V11, 1X and X. Since the factors that are already formed are in the circulation of the patient and need to decay it takes about 72 hours after the initiation or change in dose of warfarin for the maximum effect to be seen. Thus a patient who is started on warfarin will have the full expected effect in 72 hours (3 days).

INR (International Normalised Ratio) is a laboratory test that is used to measure the effect of the action of Warfarin . The common coagulation test Prothrombin Time (PT) of the patient is taken to derive INR by the following formula. (PT of patient/ PT of control) * ISI , where control plasma is pooled normal plasma and ISI is the International Sensitivity Index given to the warfarin reagent used. The expected INR is usually given as a target INR however it can be expressed as a range of +/- 0.5. For example target INR of 2.5 is usually target range of 2-3.

Indications for anticoagulation

First episodes of Venous thrombotic events (Deep vein thrombosis (DVT) or Pulmonary embolism (PE)) are treated with an INR target of 2·5. However, if there are recurrent episodes while on treatment a higher INR is usually targeted.

Patients with Atrial fibrillation (AF) require warfarin for the prevention of cardio-embolic phenomena and once again target INR is 2·5.

Presence of mitral stenosis or regurgitation alone is not a reason to commence anticoagulation, however concomitant atrial fibrillation, history of systemic embolism, left atrial thrombus or an enlargement of the left atrium are indications for Warfarin.

Patients with bioprosthetic heart valves need anticoagulation for only 3 months after surgery. However mechanical heart valves need long term anticoagulation and the target INR is ranges from 2.5 to 3.5 depending on the type of valve thrombogenicity and patient risk factors.

Sometimes anticoagulation with warfarin may be initiated following myocardial

infarction with an INR target of 2·5. Patients with dilated cardiomyopathy are anticoagulated to prevent systemic embolism and again target INR is 2·5. Patients undergoing elective cardioversion should be anticoagulated with warfarin for at least 3 weeks before and 4 weeks after cardioversion.

Monitoring Warfarin therapy

Although a loading dose regime of 10 mg, 10mg 5mg was practiced previously at warfarin initiation there is no evidence to suggest a 10 mg loading dose is superior to a 5 mg loading dose. Therefore lower dose warfarin initiation is now practiced with dose escalation if appropriate INR has not been achieved.

The target range for INR for different clinical conditions varies but is usually between 2-3 or 2.5-3.5. The expected target range will be documented in the patients clinical notes by the cardiologist, physician or haematologist who follows up the patient. If high INR of over 4.0 are seen the patient is over anticoagulated and is at risk of bleeding. Inquire of any bleeding manifestations - haematuria, bleeding from gums, purpura and examine the patient for any skin bleeding.

Ask about any drug or food interactions in the few days before that may have led to the increase in INR.

Major bleeding, defined as limb or life-threatening bleeding requires complete warfarin reversal within 6–8 and is treated with 5 mg intravenous vitamin K and 25-50 u/kg four-factor prothrombin complex concentrate. Fresh frozen plasma should only be used if prothrombin complex concentrate is not available.

1-3 mg intravenous vitamin K is used for anticoagulation reversal for non-major bleeding.

Patients who are not bleeding but with an INR >5·0 should have 1–2 doses of warfarin withheld and their maintenance dose should be reduced.

Patients with an INR >8 and not bleeding should be given 1-5mg of oral vitamin K.

Drugs and food that cause increase/ decrease in INR

The drugs and food that potentiate and inhibit the action of Warfarin are many it is not possible to include a comprehensive list. The highly probable drugs /foods listed in literature are short listed below.

Warfarin's anticoagulant effect was potentiated by antibiotics (cotrimoxazole, erythromycin, fluconazole, isoniazid, metronidazole, and miconazole); cardiac drugs (amiodarone, clofibrate, propafenone, propranolol, and sulfinpyrazone); phenylbutazone; piroxicam; alcohol cimetidine and omeprazole.

Warfarin's anticoagulant effect was inhibited by antibiotics (griseofulvin, rifampin, and nafcillin); drugs acting on the CNS (barbiturates, carbamazepine, and chlordiazepoxide); cholestyramine and sucralfate.

Foods high in Vitamin K perpetuated to inhibit warfarin effect include green leaves (spinach) green vegetables (broccoli, lettuce) fruits (avocado, kiwi fruit) and soya beans.

If the INR is subtherapeutic then factors that have to be looked into include,

Drug /food interactions - (usually increase in the intake of green leaves and other vit K containing foods), compliance and tablet strengths.

If no cause is found the warfarin dose is increased and INR is checked in 3 days to assess the effect.

If the patient is in stable INR range the INR can be checked every 6 weeks but any dose adjustments need to be followed up by more frequent INR tests to assess the effect of the change.

Duration of treatment

Patients with unprovoked proximal DVT or PE should be treated with long-term anticoagulation. However individualised decisions need to be made taking into consideration patient preference , risk factors for thrombosis /bleeding etc. If anticoagulation is to be discontinued it can be considered after 3-6 months . Repeat imaging , D dimers and thrombophilia screening is indicated when stopping.

In patients where the VTE was provoked by a trigger such as surgery, immobilization, use of oral contraceptives etc. long term anticoagulation is not indicated and 3-6 months of treatment is adequate.

In isolated calf vein thrombosis where the thrombus does not extend to popliteal vein anticoagulation of 6 weeks is adequate.

Cancer-associated VTE is best treated with therapeutic dose LMWH rather than warfarin in the initial 6 months.

Anticoagulation in procedures/surgery

Warfarin need not be stopped for procedures such as joint injections, simple cataracts, endoscopic procedures including mucosal biopsies, bone marrow examinations.

Warfarin can be stopped five days prior to the procedure and procedure done, if INR is less than 1.5 without bridging with heparin for low thrombotic risk patients (low risk AF , bileaflet aortic Mechanical heart valve, more than 3 months after DVT)

For high risk patients (VTE less than 3 months ago, AF with previous stroke or multiple other risk factors, Mitral mechanical heart valve) "Bridging with LMWH" is indicated.

Bridging with LMWH

Warfarin is omitted 5 days prior to procedure and the patient in commenced on therapeutic dose of LMWH (ex. enoxaparin 1mg/kg bd). The INR can be checked on day of surgery or procedure and procedure can be done if INR is less than 1.5. LMWH needs to be stopped 24 hours before procedure (omit evening dose if procedure is in the morning)

Warfarin can be commenced at the dose he was on previously, on the evening of the procedure if haemostasis is satisfactory. INR is monitored and Warfarin continued daily until therapeutic range is reached. LMWH at therapeutic dose is continued till INR is in range INR for two consecutive days.

Heparin and LMW Heparins

Heparin is a Large mucopolysaccharide which acts by binding and activating antithrombin. Low Molecular Weight Heparins are small fragment heparins and include dalteparin, enoxaparin etc. Administration of unfractionated Heparin needs to be monitored by APTT. LMWH are administered subcutaneously. The

advantages are that they do not need regular monitoring and are not affected by drug and food interactions. In certain instances such as renal failure, obesity and pregnancy monitoring is necessary and is done by measuring anti-factor Xa (anti-FXa) levels.

Direct Oral Anticoagulants

Several new oral anticoagulants have been developed (Dabigatran, rivaroxaban, apixaban) and most act by inhibiting thrombin or activated factor X (factor Xa). They have advantages over Warfarin such as rapid onset and off set of action, absence of an effect of dietary vitamin K intake on their activity, fewer drug interactions, absence of requirement for routine monitoring. The oral route of administration is a definite advantage over heparin and it's low molecular weight forms.

Research suggests that direct oral anti coagulants are at least as safe and effective as warfarin. Some guidelines recommend direct oral anticoagulants over Vitamin K antagonist therapy in treating VTE, however the lack of availability and cost factor remain a restrain for wider use in Sri Lanka.

Warfarin and antiplatelets

Since patients already on Warfarin for above indications may also sometimes require antiplatelet drugs for acute coronary syndrome (ACS) and following coronary artery stenting there is an increasing population of patients on combined treatment (both warfarin and antiplatelets). The risk of bleeding is higher for these patients. Bleeding admission rate (% per year) for patients were documented in literature as follows s Aspirin alone 2.6, Clopidogrel alone 4.6, Warfarin alone 4.3, clopidogrel+Aspirin 3.7, warfarin + Aspirin 5.1, warfarin + Clopidogrel 12.3, warfarin + clopidogrel + Aspirin 12.0). Discontinuation of antiplatelet agents for surgical procedures needs to be done in consultation with cardiologists.

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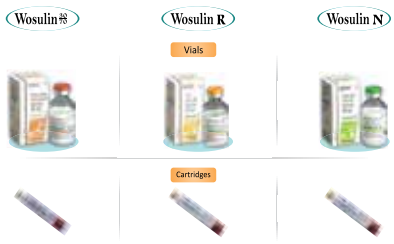

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Childhood Headache: A Concise Overview

Dr Anuruddha Padeniya and Dr Clement Perera

Introduction

Headache, defined as pain located above the orbito-meatal line is the most common neurological symptom in the world[1]. It is the most common manifestation of pain in childhood and it is the most frequent reason for referral to a child neurologist[2]. An increased prevalence of headache in children and adolescents is being reported lately[3].

The prevalence of headache ranges from 37 to 51% in seven-year-old children, gradually increasing to 57-82% by age 15. Before puberty, boys are affected more frequently than girls, but after puberty, headaches occur more frequently in girls[4,5].

Several factors are postulated to contribute to the increasing trend of incidence of childhood headache. Unhealthy lifestyle owing to increasing academic demands and high parental expectations, introduction of various afterschool clubs and extra-curricular activities and reduced and abnormal sleep patterns are among them[6].

Childhood headache is overlooked most of the time[7]. This affects not only the child but also the parents, the siblings and the society. It results in a significant impact on the lives of children resulting in absence from school, decreased participation in extracurricular activities, and poor academic achievement.

Parents suffer additional expenses and lose valuable productive time as they seek medical assistance. This negatively affects the whole family by unintentional neglect of the other siblings and their own work. The impact on the society is related to the financial burden and loss of productivity of the parents which is augmented by poor academic performance of the child[8].

Difference from adult headache

Children can get similar types of headache to that of adults. Criteria for diagnosis of headache in children are yet to be developed. Hence, diagnostic criteria used for adult headache is being used for children at present.

As children cannot adequately describe the symptoms, the criteria of specific types of headaches cannot be applied for them. The symptoms they describe evolve over time. Hence, the term "immature headaches" is more appropriate when describing childhood headaches.

Classification of headache

The International Headache Society (IHS) has introduced a classification for headache in 2013. Primary headaches are classified as,

1. Migraine
2. Tension-type headache (TTH)
3. Trigeminal autonomic cephalalgias (TACs)
4. Other primary headache disorders

Secondary headaches are,

5. Headache attributed to trauma or injury to the head and/or neck

6. Headache attributed to cranial or cervical vascular disorder
7. Headache attributed to non-vascular intracranial disorder
8. Headache attributed to a substance or its withdrawal
9. Headache attributed to infection
10. Headache attributed to disorder of homoeostasis
11. Headache or facial pain attributed to disorder of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth or other facial or cervical structure
12. Headache attributed to psychiatric disorder

Neuropathies & Facial Pains and other headaches

13. Painful lesions of the cranial nerves and other facial pain
14. Other headache disorders

Tension headache

The pathophysiology of tension type headache is complex and multifactorial and is not due to abnormal muscle contraction as it was previously believed to be. It is now thought to be due to abnormal neuronal sensitivity and pain facilitation (sensitization of nociceptive second order neurons) with contributions from central and peripheral factors[10].

The IHS diagnostic criteria[10] for tension-type headaches states that two of the following characteristics must be present for the diagnosis.

The typical tension type headache is described as a continuous constricting or band-like pain involving the neck and the occiput which is dull or aching in nature (not pulsatile) and occurring during obvious times of stress. It is not associated with nausea, vomiting or abdominal pain and it is usually relieved by sleep or rest. This, and the fact that they are not paroxysmal, distinguishes tension type headaches from migraines. Tension type headache is also not aggravated by physical activities and a family history of migraine is less likely.

Some patients may have obvious symptoms of depression, in this subgroup; headaches are relieved when depression is treated.

Diagnostic criteria: Frequent episodic TTH

A. At least 10 episodes of headache occurring on 114 days/month on average for >3 months 12 and <180 days/year) and fulfilling criteria B-D
B. Lasting from 30 minutes to seven days
C. At least two of the following four characteristics:
    1. Bilateral location
    2. Pressing or tightening (non-pulsating) quality
    3. Mild or moderate intensity
    4. Not aggravated by routine physical activity such as walking or climbing stairs
D. Both of the following:
    1. No nausea or vomiting
    2. No more than one of photophobia or phonophobia
E. Not better accounted for by another ICHD-3 diagnosis.

Diagnostic criteria: Infrequent episodic TTH

A. At least 10 episodes of headache occurring on <1 day/month on average (<12 days/year) and fulfilling criteria B-D
B. Lasting from 30 minutes to seven days
C. At least two of the following four characteristics:
    1. Bilateral location
    2. Pressing or tightening (non-pulsating) quality
    3. Mild or moderate intensity
    4. Not aggravated by routine physical activity such as walking or climbing stairs
D. Both of the following:
    1. No nausea or vomiting
    2. No more than one of photophobia or phonophobia
E. Not better accounted for by another ICHD-3 diagnosis.

Migraine

Two major hypotheses exist for the pathogenesis of migraines[11].

The vascular hypothesis states that cranial vasoconstriction causes auras or focal neurological signs. These prodromic episodes are followed by painful vasodilation of cranial vasculature.

The neurogenic hypothesis claims afferent inputs to the brainstem result in a slowly spreading cortical neuronal depression. This depression is followed by painful dilation and inflammation of brain vasculature

The headache in migraine is commonly described as throbbing, pulsatile pain which commonly occurs as periodic attacks with intervals with absence of symptoms in between. It is commonly associated with irritability, nausea, vomiting, constipation or diarrhea and often photophobia and there is often a family history of migraine.

Migraine can be simple or may be complicated with a variety of unusual associations. Migraine variants include migraine with aura, migraine without aura, complicated migraine, hemiplegic migraine, and basilar migraine. Neurological signs or symptoms may accompany before, during or after the attack of migraine. These can be described in 4 stages: prodrome, aura, headache and postdrome.

Symptoms of prodrome may occur days before the actual headache. Roughly half of all migraineurs experience this stage which is identified by light and sound sensitivity, depression, irritability and lack of appetite. Auras are present in some and usually occur up to one hour prior to the onset of the headache. The symptoms of aura include changes in visual perception (such as seeing spots, blurring, flashing lights, geometric patterns, temporary loss of half of the visual range) and weakness (such as stumbling, unsteadiness, muscle weakness) as well as cyclical vomiting and sensation of spinning (paroxysmal vertigo) and smelling a certain odour.

The next is the headache phase which can be moderate to severe in intensity and may last up to 3 days. During this phase, photophobia, phonophobia, nausea, vomiting, sensitivity to movement and speech difficulties are characteristic.

Most migraineurs may be irritable and fatigued during the postdrome phase and find it difficult to concentrate. This is described as a "migraine hang-over". Their scalp may also be very tender.

According to the diagnostic criteria established by the International Headache Society (IHS), 10 it is very supportive to diagnosed migraine in primary care level.

Diagnostic criteria: Migraine without aura

A. At least five attacks fulfilling criteria B-D
B. Headache attacks lasting 4-72 hours (when untreated or unsuccessfully treated)
C. Headache has at least two of the following four characteristics:
    1. Unilateral location
    2. Pulsating quality
    3. Moderate or severe pain intensity
    4. Aggravation by or causing avoidance of routine physical activity (e.g. walking or climbing stairs)

Diagnostic criteria: Migraine with aura

A. At least two attacks fulfilling criteria B and C
B. One or more of the following fully reversible aura symptoms:
    1. Visual
    2. Sensory
    3. Speech and/or language
    4. Motor
    5. Brainstem
    6. Retinal
C. At least three of the following six characteristics:
    1. At least one aura symptom spreads gradually over 5 minutes
    2. Two or more aura symptoms occur in

D. During headache at least one of the following:
   1. Nausea and/or vomiting
   2. Photophobia and phonophobia
E. Not better accounted for by another ICHD-3 diagnosis.

succession
3. Each individual aura symptom lasts 5-60 minutes
4. At least one aura symptom is unilateral2
5. At least one aura symptom is positive3
6. The aura is accompanied, or followed within 60 minutes, by headache

D. Not better accounted for by another ICHD-3 diagnosis.

Other Types of Headaches

According to ICHD-3 important types of childhood headaches with ICHD-3 diagnostic criteria10 include:

• Cluster headache

Diagnostic criteria: Cluster headache

A. At least five attacks fulfilling criteria B-D
B. Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15-180 minutes (when untreated)
C. Either or both of the following:
   1. At least one of the following symptoms or signs, ipsilateral to the headache:
      a) Conjunctival injection and/or lacrimation
      b) Nasal congestion and/or rhinorrhoea
      c) Eyelid oedema
      d) Forehead and facial sweating
      e) Miosis and/or ptosis
   2. A sense of restlessness or agitation
D. Occurring with a frequency between one every other day and eight per day
E. Not better accounted for by another ICHD-3 diagnosis.

• Sinus headache

Diagnostic criteria: Sinus headache

A. Any headache fulfilling criterion C
B. Clinical, nasal endoscopic and/or imaging evidence of acute rhinosinusitis
C. Evidence of causation demonstrated by at least two of the following:
   1. Headache has developed in temporal relation to the onset of rhinosinusitis
   2. Either or both of the following:
      a) Headache has significantly worsened in parallel with worsening of the rhinosinusitis
      b) Headache has significantly improved or resolved in parallel with improvement in or resolution of the rhinosinusitis
   3. Headache is exacerbated by pressure applied over the paranasal sinuses
   4. In the case of a unilateral rhinosinusitis, headache is localized and ipsilateral to it
D. Not better accounted for by another ICHD-3 diagnosis.

• Head trauma-related headache

Diagnostic criteria: Head trauma-related headache

A. Any headache fulfilling criteria C and D
B. Traumatic injury to the headi has occurred
C. Headache is reported to have developed within seven days after one of the following:
   1. The injuy to the head
   2. Regaining of consciousness following the injury to the head
   3. Discontinuation of medication (s) impairing ability to sense or report headache following the injury to the head
D. Either of the following:
   1. Headache has resolved within three months after its onset
   2. Headache has not yet resolved but three months have not yet passed since its onset
E. Not better accounted for by another ICHD-3 diagnosis.

• Intracranial mass related headache

Diagnostic criteria: Intracranial mass related headache

A. Any headache fulfilling criterion C
B. A space-occupying intracranial neoplasm has been demonstrated
C. Evidence of causation demonstrated by at least two of the following:
   1. Headache has developed in temporal relation to development of the neoplasm, or led to its discovery
   2. Either or both of the following:
      a) Headache has significantly worsened in parallel with worsening of the neoplasm
      b) Headache has significantly improved in temporal relation to successful

treatment of the neoplasm

3. Headache has at least one of the following four characteristics:
   a) Progressive
   b) Worse in the moming and/or when lying down
   c) Aggravated by Valsalva - like manoeuvres
   d) Accompanied by nausea and / or vomiting

D. Not better accounted for by another ICHD-3 diagnosis.

- **Benign intracranial hypertension**

Diagnostic criteria: Benign intracranial hypertension

A. New headache, or a significant worseningl of a pre-existing headache, fulfilling criterion C
B. Both of the following:
   1. Idiopathic intracranial hypertension (IIH) has been diagnosed
   2. Cerebrospinal fluid (CSF) pressure exceeds 250 mm CSF (or 280 mm CSF in obese children)
C. Either or both of the following:
   1. Headache has developed or significantly worsened in temporal relation to the IIH, or led to its discovery
   2. Headache is accompanied by either or both of the following:
      a) Pulsatile tinnitus
      b) Papilloedema
D. Not better accounted for by another ICHD-3 diagnosis.

- **Meningeal irritation**

Diagnostic criteria: Meningeal irritation

A. Headache of any duration fulfilling criterion C
B. Bacterial meningitis or meningoencephalitis has been diagnosed
C. Evidence of causation demonstrated by at least two of the following:
   1. Headache has developed in temporal relation to the onset of the bacterial meningitis or meningoencephalitis
   2. Headache has significantly worsened in parallel with worsening of the bacterial meningitis or meningoencephalitis
   3. Headache has significantly improved in parallel with improvement in the bacterial meningitis or meningoencephalitis
   4. Headache is either or both of the following:
      a) Holocranial
      b) Located in the nuchal area and associated with neck stiffness
D. Not better accounted for by another ICHD-3 diagnosis.

- **Medication overuse headache**

Diagnostic criteria: Medication overuse headache

A. Headache occurring on 15 days/month in a patient with a pre-existing headache disorder
B. Regular overuse for >3 months of one or more drugs that can be taken for acute and/or symptomatic treatment of headachel-3
C. Not better accounted for by another ICHD-3 diagnosis

Out of these headache types, analgesic headache/medication overuse headache is said to be the result of an interaction between an exposure (such as overuse of analgesics) and a vulnerable individual such as a migraineur). Thus, the importance of seeking proper medical care for children with headache without overuse of analgesics must be emphasized.

Approach to evaluation of a child with headache

Headache-Evaluation algorithm

History should focus on elaborating the symptoms of different types of headache as well as excluding the possibility of secondary causes of headache. The following red flag signs must be specifically sought for in every patient so as not to miss the possibility of a more sinister diagnosis.

Physical examination should include assessment of important parameters such as vital signs, skin rashes or lesions, signs of neurologic abnormalities, haematomas or other signs of trauma, papilloedema or sub-hyaloidhaemorrhage on fundoscopy and meningeal irritation.

Headache history and Physical Examination[12]

History

- Important to talk with parent and child about the problem; use open-ended questions
- Type of pain
- Location of pain
- Daily timing of the pain
- Duration of episodes
- Chronicity of the problem
- Sleep disturbances
- Headache triggers: foods, environmental factors, situations
- Psychosocial factors:
  - patient-parent relationship,
  - alcohol/drug/tobacco use,
  - stressors,
  - bullying
  - learning disability,
  - happiness with school situation,
  - parental discord,
  - chronic family illnesses,

Physical Examination

- Blood pressure
- Review growth chart
- Pubertal assessment
- Cutaneous abnormalities
- Head and neck
- Nose and throat inspection
- Temporomandibular joints
- Funduscopic
- Extraocular movements
- Deep tendon reflexes/strength
- Tandem (heel-to-toe) gait

Pronator drift on Romberg (stand with eyes closed, put hands out with palms up and observe for unsteadiness, hand drift to prone position)

Awakening from sleep due to headache, change in headache quality or intensity, associated neurological symptom or exam findings should indicate the need for specific neuroimaging investigations. Computed tomography (CT) is usually performed when acute increased intracranial pressure is suspected (e.g.: haemorrhage, mass lesions, hydrocephalus), in the presence of focal neurological signs and in unstable patient, while magnetic resonance imaging (MRI) is done in cases of suspected posterior fossa masses.

Red Flags: History

- Worst headache of their life
- First thing in the morning, positional headaches, especially with
- Vomiting
- During sleep, especially with vomiting
- Occipital location
- Atypical or change in pattern (without obvious stressors)
- Accelerating course (increasing frequency or increasing severity)
- Recurrent severe headache(s) unresponsive to treatment
- Worse with exertion, particularly in post-pubertal children
- Headaches associated with neurological deficits (e.g., hemiparesis, ophthalmoparesis, seizures)

Red Flags: Physical Examination

- Signs of increased intracranial pressure
  - Large or accelerating head circumference
  - Papilledema
  - Cranial nerve VI palsy
- Meningeal signs, fever, rigors
- Evidence of recent head trauma
- Focal neurological signs (e.g., brainstem or cerebellar signs like
- ocular paralysis or nystagmus and other cranial nerve abnormalities,
- ataxia, or hemiplegia)
- Altered mental status

- Confusion, impaired consciousness
- Sudden, complete loss of vision
- Diplopia
- Focal weakness
- New onset of seizures
- Personality changes
- Abrupt decline in school performance
- Paraesthesia, tingling

❖ **Headache Red Flags - History and Physical Examination[12]**

Appropriate vessel imaging should be done if there is any suspicion of haemorrhage, infarction or thrombosis. Blood investigations include a complete blood count, erythrocyte sedimentation rate (ESR), toxicology screening when indicated, thyroid function testing etc.

"Headache diary" is an important component in the follow-up and assessment of treatment response. It includes a graphical pain scale, a calendar to mark the frequency of headache events and other relevant questions. Other evaluations such as lumbar puncture, electroencephalogram (EEG) should be performed when deemed necessary.

Management

In the treatment of a primary headache, preventive treatment and symptomatic therapy has to be always considered. Treatment of a secondary headache is focused on identifying a specific cause, in addition to symptomatic therapy when the cause has not yet been eradicated.

Treated headache is more cost effective than untreated headache. In most cases, only reassurance is needed. Treatment of paediatric headache includes three approaches:

1. Symptomatic therapy
2. Abortive therapy
3. Preventive therapy

Symptomatic therapy

Drugs should be chosen carefully according to headache type and frequency as self-treatment can lead to medication-overuse headache. Therapy must be monitored by parents.

Abortive therapy

Abortive therapy is to interrupt a headache after its onset. All abortive medicines carry the risk of overuse in patients with frequent headaches Medicines such as triptans - sumatriptan, a 5-HT1 receptor agonist, isometheptene and ergotamines and analgesics such as paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) can be used in abortive therapy.

Preventive therapy

Preventive therapy is considered when headaches are frequent enough to interfere with the patient's lifestyle. The effect is not immediate, often taking as long as 6-8 weeks before improvement occurs. Migraines are known to remit spontaneously in some patients during childhood. Reassessment should be done every 6-12 months to decide on the need for continued prophylaxis. Medicines used in preventive therapy include beta-blockers (propranolol and nadolol), tricyclic agents (amitriptyline, nortriptyline) and cyproheptadine, anticonvulsants (valproic acid, zonisamide, and topiramate), calcium channel blockers (verapamil, flunarazine), selective serotonin reuptake inhibitors (SSRI).

Nonpharmacological Therapies

In addition to these pharmacological aspects of management, several lifestyle modifications can help in treating and

preventing childhood headaches. Ensuring a healthy lifestyle by good hydration, adequate rest, sleep and relaxation, timely meals with nutritious foods, regular exercise or physical activity, and minimizing screen time of the child are essential.

Alternative Treatment

Complementary and integrative treatments, may be beneficial although there is currently not enough evidence to recommend them as a patient's primary form of treatment. These include:

electromyographic (EMG) biofeedback,
botox,
stress management,
acupuncture,
massage,
herbal preparations,
aromatherapy and
dietary changes.

Challenges in management of childhood headache

Presentation of childhood headache is vague, evolve over time and unlike in adults, children are unable to express their symptoms adequately. Therefore, the histories are frequently obtained from a third party, mostly parents, who with their busy lifestyles are often unable to recognise the severity of the headaches.

Having a separate clinic for headache enables us to spend more time with the patients and involves both the child and their parents in history taking. This allows us to obtain a holistic view of the child's symptoms. Often parents are unaware of associated symptoms and these are identified gradually during the subsequent clinic visits.

Having a dedicated clinic for headache is also cost effective as only a funduscope is required for further evaluation of most patient. The majority require mostly reassurance and lifestyle modifications after excluding sinister causes as most parents who seek help for a child with headache are looking for reassurance that the headache is not due to a serious cause[8].

Furthermore, research on patterns of childhood headache with the help of our clinic patients can help us create a national guideline for childhood headache in the near future.

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Prebiotics, Probiotics and personalized nutrition in modification of gut microbiota

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Keywords: Gut microbiota, Prebiotics, Probiotics and Personalized nutrition.

Abstract

The human gastrointestinal tract is colonized by trillions of microorganisms including bacteria, fungi, viruses and protozoa. The complexity and diversity of the gut microbiota have been recognized and even considered as a 'new organ'. The diversity of the gut microbes is strongly influenced by diet and dietary patterns. Recent studies highlight the impact of gut microbiota on the host's metabolism. Since, the gut microbial profile is unique to each individual, the interplay among the diet, gut microbiota and the host may play a role in health and disease. Dysbiosis of the gut microbiota is associated with disease. Many studies have shown the effects of prebiotics and probiotics on health. Probiotics have been considered as preventive and therapeutic measures and assist in restoring the healthy composition and function of the gut microbiota. Personalized nutrition approaches have been developed to provide healthy eating advice tailored to the nutritional needs of the individual. This review discusses the role of prebiotics, probiotics and personalized nutrition on human health.

Background

The gut microbiota consists of the trillions of microorganisms that inhabit our gastrointestinal tracts. These microbes are not simply commensal organisms, but instead serve as an important 'organ' that regulates the metabolic processes which include the digestion and absorption of nutrients, synthesis of vitamins and modulation of mucosal immunity. In addition to these processes, microbes produce toxins and carcinogens [1, 2]. The gut microbial profile is unique to each individual, evolving over the lifetime. It can be altered by internal and external factors, especially the food and dietary patterns. Prebiotics are substrates that are selectively used by host microorganisms conferring a health benefit. Probiotics are live microorganisms (bacteria and yeasts) that are administered in a viable form in adequate amounts. Probiotics are beneficial to human health. Synbiotics contain a mixture of prebiotics and probiotics [3,4].

It is essential to recognize the interplay among the diet, gut microbiota and the host. Developing dietary interventions based on one's profile to optimize gut microbial composition is an important practice for personalized nutrition. So, that personalized nutrition is an approach that "assists individuals in achieving a lasting dietary behavior change that is beneficial for health" [5].

Specifically, understanding which nutrients can increase the beneficial bacteria and which can suppress the harmful bacteria, is mandatory in order to formulate dietary regimens and food products. These products can be used to normalize gut microbial composition. Host - gut microbiota interconnection

through personalized nutrition is a new therapeutic area for both disease control and prevention. In this review, the role of prebiotics, probiotics on human health and strengths and weaknesses of personal nutrition will be discussed.

The gut microbiota in health

The gut microbiota is a complex and diverse collection of microorganisms which when compared to the other body sites, has a very high density of microorganisms. More than 90% of the microbes belong to the phyla Firmicutes, Bacteroidetes, while other groups Actinobacteria, Fusobacteria, Proteobacteria, Verrucomicrobia and Cyanobacteria are also reported [6]. The microbial diversity varies depending on the metabolic function and microenvironment of the various parts of the GIT tract. Seven main bacterial phyla are considered as the main residents of the gut and contribute to a diversity of functions. Rajilic-Stojanovic M and de Vos WM 2014 suggested the presence of more than 160 species of bacteria in the large intestine alone [7]. The microbiota plays a major role in food digestion, for example in the colon the microbiota helps the host to conserve energy by assisting the carbohydrate digestion. Production of short chain fatty acids (SCFA) by the microbiota specially in the colon as a result in carbohydrate digestion, has many benefits for the host as well as providing the required carbon and energy source for some resident microbial species. The microbial action contributes to digestion of food components that would otherwise not be digestible by the human digestive system. The contribution of gut microbes to maintain health is also important because of their role in prevention of colonization by pathogens and modulating and stimulating the immune system. When moving deeper towards the large and small intestine, the focus of digestion will be on proteins and fermentation of amino acids which also can release SCFAs but also other compounds that may lead to illnesses such as gut inflammation, IBD and cancer [8]. The ratio of Firmicutes and Bacteroidetes are important in maintaining health.

Recent studies have suggested a wider role in the gut microbiota in human health. For example, the gut brain axes can be regulated by neurotransmitters produced by gut microbes. Thus, gut microbiota can produce serotonin and dopamine which is responsible for controlling the mood of the host [9].

Prebiotics and dietary fibers

A prebiotic is defined as "a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon" by Gibson and Roberfroid in 1995 [3]. Later in 2016, the definition of prebiotic was modified as "a substrate that is selectively utilized by host microorganisms conferring health benefit" [10]. Prebiotics include human milk oligosaccharides, inulin, fructo-oligosaccharides, and galacto-oligosaccharides and also noncarbohydrates may act as prebiotics [11]. Venkataraman et al in 2016, had shown that consuming resistant starches has been linked to enrich specific bacterial groups (Bifidobacterium adolescentis, Ruminococcus bromii, and Eubacterium rectale) in some people [12]. It has been found that low fiber intake reduces production of small chain fatty acids and shifts the gastrointestinal microbiota metabolism to use less favorable nutrients. It has been observed that this has led to the production of potentially detrimental metabolites [13].

According to two studies conducted in 2015 and 2017, low fiber western diet

degrades the colonic mucus barrier, causing microbiota encroachment, which results in pathogen susceptibility and inflammation [14,15]. This finding suggests a potential mechanism for the links of western diet with chronic diseases. In a recent study it has been shown that the detrimental effects of high fat diets on penetrability of the mucus layer and metabolic functions could be prevented through dietary administration of inulin [16]. Available findings alone with the role of butyrate prevent oxygen induced gut microbiota dysbiosis. Therefore, this provides a strong rationale to enrich dietary fiber consumption to maintain intact mucosal barrier function in the gut [17]. Clinical trials using prebiotics like arabinoxylan and inulin-type fructans have shown positive results in diabetic, overweight and obese populations [18].

Probiotics

Probiotic is "a preparation of, or a product containing viable, defined microorganisms in sufficient numbers, which alter the microflora (by implantation or colonization) in a compartment of the host and by that exert beneficial health effects on the host" [4]. Mostly Bifidobacterium and

Lactobacillus species are included in a variety of products, including foods, dietary supplements or drugs. Probiotics can affect health independently of the gut microbiota through direct effects on the host. It is led through immune modulation or the production of bioactive compounds. The effects of probiotic supplementation have been studied in a broad range of diseases. Substantial evidence is available for beneficial effects of probiotic supplementation in different disease conditions such as diarrhoea, necrotising enterocolitis, acute upper respiratory tract infections, pulmonary exacerbations in children with cystic fibrosis and eczema in children [19,20, 21 & 22]. Further, Probiotics can improve cardiometabolic parameters and reduce serum concentration of C reactive protein in patients with type 2 diabetes [23].

Through a cascade of immunological reactions, probiotics mimics the tolerance induced by commensal organisms and contrasts with the inflammatory response to pathogens. Use of newer microbes and combinations, combining probiotics and prebiotics (synbiotic refers to the combination of a prebiotic with a probiotic) have been identified as emerging areas of probiotic treatment.

Personalized nutrition

Gut microbiota between people shows vast diversity. Personalized nutrition approaches aim to identify key microbiome features that predict the response to particular food components, which can then inform the design of a diet leading to favourable outcomes. Many studies have been shown that variations in dietary macronutrients, including fat, protein and carbohydrates, lead to significant alterations in the human gut microbiota [24 & 25]. Extreme changes during the short time period of a diet are necessary to alter the gut microbiome. Animal based food or plant products consumed, or the fat content or fiber content of the diet may be entirely changed within a few days [25]. However, in addition diet, personalized gut microbiota composition is affected by many other factors, such as gastric diseases, age, sex, medications and ethnicity. Composition of the gut microbiota is strongly influenced by dietary fat intake, and also has an impact on the host's metabolism as well. A study done on mice models found that high saturated fat and low fiber diet results in reduction in Bacteroidetes and an increase in Firmicutes

and Proteobacteria [26]. In humans, a high consumption of dietary fat including saturated fatty acids is associated with reduced gut microbial diversity. Similarly, protein content of the diet affects the gut microbial diversity, species composition and abundance, in a significant way. In humans, Bacteroides enterotype found to be associated with a long-term animal protein-rich diet [27].

In 2014 Korpela K et al showed that some obese individuals gain health benefits from a very simple and easily managed dietary change, while others show no or even adverse responses [28]. However, No personalized nutrition study has been carried out at a large scale, in an appropriate population group and over a sufficiently long time to show result in better health and wellbeing. Whether the personalized nutrition is feasible, sustainable and has a positive effect on clinical outcomes than conventional approaches is to be investigated.

Conclusion

Probiotics, prebiotics and combinations have been found to be clinically effective for disorders like IBD, digestion, travelers' diarrhea, and for improving/helping to maintain general health. Personalized nutrition is a new therapeutic approach for both disease control and prevention.

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No Reversals from Nature for us to stop Climate Change Results

Dr Sarath de Silva

The only animal group which is almost totally out of step with Nature is the species *Homo sapiens*. An example of this is the way they look at the climate change process which is currently happening.

In the long journey through prehistoric times even after acquiring the skills of working with deliberately shaped stones and later, after learning to use fire safely, the humans went on to live in natural surroundings, quite will adapted as any other animal group.

The acceptance of the processes of Nature such as lightning, torrential rains, storms and the powers of the seas and also the sights of the moon, the sun and the stars, gave them a realization that those forces and visual objects were completely superhuman, and that they were beyond their world. As a logical result, various methods of respecting and worshiping such processes and objects became a part of their behavior. At times, in different settings, traditional sacrifices were made and the deep forces beyond this world were acknowledged.

The Central Nervous System which the humans possessed produced thoughts and feelings inside them while the other living beings did not have the ability to do that at the same level, and yet, the humans appear to have shared the natural world with them as a part of adaptation. In addition, there is enough evidence from the past to indicate that our long ago ancestors learned some of the ways of surviving by studying the behaviour of those animals while exploring the world with them.

In other words, even up to about 10,000 years ago the humans did not go against the natural phenomena the way they are doing now. They did what was necessary for their own survival with a total respect towards, and an instinctive understanding of, Nature. They did not look down on natural ways of living.

Over the last 2000 years or so the humans clearly have become very different in the way they use their intelligence. A significant change has started to happen over that period of time and it has accelerated very much and become more extensive and deep over the last five hundred years. The humans have gone quite beyond nature and have started to feel as if this world has been made specially for them.

They have developed a view that they are in full control of this world now and the respect they had for Nature has been thrown to the winds. Instead, Nature is looked at as a hindrance.

The clear statement emanating from the human beings nowadays is, "We are the real ones and the rest of the living beings and their natural environments can be disregarded".

It is true that the humans have gone to the moon, true that they have analysed the

stars of the other galaxies, have found the forces which govern the atomic structures, have found new species of animals perhaps five miles under the sea and also have even created, using genetic engineering, new organisms which are not found within natural settings.

And yet the *Homo sapiens* are still the same animals that got established about half a million years ago. Nothing significant has changed inside them in evolutionary terms. Their biological processes and the bodily systems are essentially the same as they were then.

While that is the situation, the human Central Nervous System, in contrast to the other bodily systems, has created new feelings, new desires and new ways of living which are quite beyond what is natural. Unfortunately, in recent times, the humans have gradually forgotten the fact that the physical world they live in is actually the very same world that Nature produced for all the living creatures and the vegetation on this planet.

So, the world which is currently structured by *Homo sapiens* for them to live in, and the world of Nature, have clashed with each other. It does not need much reasoning to know which world will win at the end.

In this type of setting, when it comes to climate change, the self-centered and severely overconfident humans with their super ego have started to think of, and actually talk about, inducing Nature to reverse her hugely complex dynamic forces across the whole planet; the forces which have been going on for nearly four thousand five hundred million years.

If a group of other living beings in another world in a nearby galaxy can see and hear all this uproar about stopping climate change while being not able to reverse natural changes in the physical world, they will send us an award for the Best Comedy Act in the Universe.

The humans with their egoistic visions have become blind to the fact that Nature will not do reversals. It does do cycles of course, as one can see such as in the ice ages with gaps ranging from thousands to hundreds of thousands of years; but not reversal.

One must keep in mind that even in a relatively simple process such as making a cake, once the semi liquid mixture is put in the oven and the heat has started to act on it for just a few minutes, there is no getting it back to the original semi liquid mixture as the physical and chemical changes which have started to happen inside the cake mixture cannot be reversed. This is because, even though the humans have produced the oven, the processes acting on the cake mixture inside it are actions and forces of Nature.

The practicalities of the climate change are clearer now.

Over the last 140 years or so the excessive dynamics of one type of energy, heat, have stared to act on other type of energy, on physical matter, and on chemical processes precipitating serious changes in the atmosphere, severe changes in the oceans and changes in billions of tons of ice on sea and land. These changes are at microscopic and macroscopic levels, with time as an active factor in the processes, and hence they are long term physical and chemical reactions which cannot be reversed.

Biologically, as in a living cell, changes induced by such dynamics, if within extremely narrow limits, may be reversed

as that cell is alive and reversal of changes is part of its life.

But, the climate change dynamics are different.

They do not work on living beings directly. They always work on the environment and that gets changed gradually. Then the living beings, including the supposed to be extremely powerful humans, become the helpless victims of that changed environment. Subsequently, getting Nature to reverse the chain reactions and get the original environment back is impossible.

Do the humans forget that they cannot even reverse the changes in that tiny cake in the oven? Honestly, there is no animal on earth which can beat the humans when it comes to living in fantasy worlds.

Further serious processes are getting active. These are the results of the removal of whole oceans of crude oil and millions of tons of solid substances to derive energy from them. The humans do think that Nature will fill those emptied underground areas quite correctly, on their behalf, to balance the drastically changed huge internal pressures. Well, wishful thinking is another specialized area of the human mind.

The reality is that the number of earthquakes in the last 140 years or so is significantly more than what it was in a similar period of time before that year 1870.

Something which happened millions of years ago when the anaerobic organisms started to expel oxygen as a waste product into the atmosphere is important. To put it simply, those organisms had to go underground because the resulting new atmosphere did not get reversed.

So, the climate change cannot be stopped as its causative worldwide factors are irreversible. Additionally, as a result of the vast scale removal of underground fossil substances, there is also the possibility of subterranean changes in the planet, which can cause immense destruction.

We are now into a non-reversible process of dynamic change in the natural environment available to living beings on this planes, not due to a huge extraterrestrial objet crashing on to it, but as a result of the activities of the latest animals to evolve, the humans.

An unstoppable, and collective, chain reaction of horrendous extent, killing billions of humans and millions of other animals, will descend and continue till it ends after new equilibriums are established by Nature itself. It might go on for about eight hundred years into the future.

The irreversible, merciless and acutely traumatic end of the man-made world will start first in all the big cities of this planet.

In the early centuries of that period there will be the added and inevitable disaster of humans killing each other in millions which is a typical human activity, as hugely complex conflicts arise.

By that time, the mankind across the world would have completely failed to develop and use fusion power, after extensive efforts to succeed.

Fortunately, there is no risk of extinction of the *Homo sapiens*, as their current numbers can withstand the premature loss of many billions of them over the next six centuries or so. Another reason for that is the fact that they are well distributed across the planets Earth.

Ultimately, their total population will come down to about 15% of what it is now and there will never be a surge of their numbers after that.

The *Homo sapiens* will certainly fall into step with Nature again and their ways of living will change irreversibly and absolutely to an unimaginable extent.

Dr Sarath de Silva MBBS, MRCPsych

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