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"Pushpagiri Medical Journal" is the Official Journal of Pushpagiri Institute of Medical Sciences & Research Centre, Tiruvalla. It is an essential indexed peer reviewed multidisciplinary journal providing professionals with a forum to discuss today's challenges, sharing innovative evaluation and treatment techniques, learning about and assimilating new methodologies developing in related professions, and communicating information about new developments and research programmes. The journal serves as a valuable tool for helping therapists deal effectively with the emerging problems, stumbling blocks and challenges of the field. It emphasizes articles and reports that are directly relevant to practice. The journal would shortly be indexed with many international database. The journal, intended initially for private circulation only, will be published half-yearly, in March (January-June) and September (July-December) .

PUSHPAGIRI MEDICAL JOURNAL

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EDITORIAL

Scientific Communication

K Abraham Jose

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The objective of the Pushpagiri Medical Journal is to provide high quality peer reviewed articles in the form of original research publications. Scientific writing is a demanding creative process and not merely an act of reproducing available data. The process of writing modulates thoughts, and thoughts change writing. The quality of a report depends on the clarity of thought in the design, and the rigor of the conduct of research. The brevity and focus on core issues are critical to the effectiveness of the report.

In Medicine scientific communication is an important tool for the growth and improvement of the quality of day-to-day clinical practice. Scientific writing is a tool by which the knowledge that a person has gained by evaluation of patients becomes helpful to others. Sir Graham Apley once said,

"Writing is like having a baby;

the gestational period is long, and the labour painful,

but in the end you have something to show for it".

The Editors' responsibility to the authors is to help them present their materials clearly, concisely and accurately. The editor has to ensure that only valid, accurate articles that benefit the readers and are worth spending their valuable time on, are published. The write up should be crisp, clear and informative.

The authors and editors have to work in perfect co-ordination without losing the focus on achieving the upgradation and continuum of scientific growth, in the best interest of the patients in particular, and the society at large. The editing of a manuscript involves correction of the article without altering the meaning of the manuscript and without expressing disapproval to the author. It involves exchange of ideas and clarifications between the authors and the editor. Together they should try to find out what the readers would like to gain, and how to provide this specific information. The editor asks question that he/she thinks will be asked by the readers, and the answers will result in a very comprehensive article.

K Abraham Jose MS,
Prof. of Orthopaedic surgery &
Dean, PIMS & RC

There is permanence to the material published in the journal, and hence the editor attempts to save them from inaccurate publication. An improvement in communication skills will make the author communicate better with the patient, peers and society. The practice of Medicine depends on accuracy in the scientific literature. Thus the ultimate goal of the editorial process is the presentation of precise and valid information to all readers.

The **'Pushpagiri Medical Journal'** would strive to publish articles with high levels of evidence. As *Geoff Watts* has written, "Knowledge does not suddenly appear in neat and tidy quanta. Like patches of lichen spreading over a rock face, it accretes over decades".

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✪ ORIGINAL ARTICLE

Growth pattern of school children of age group six to ten years in Kerala, South India

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Abstract

Objectives: To assess the growth pattern and the prevalence of under nutrition and obesity in children of age group 6 to 10 years from low and low middle income groups. **Methods:** 2065 healthy school children (995 boys and 1070 girls) were cross sectionally studied in one month for weight and height by standard techniques. Family details, dietary habits, socioeconomic and environmental conditions etc., were collected from a pre-tested proforma. The data were compared with 2000 CDC growth tables for weight, height and body mass index. Undernutrition was diagnosed as weight below 3rd percentile and over nutrition as body mass index more than 85th percentile of CDC 2000 data. Socioeconomic grading was assessed by modified Kuppuswami scale. The factors influenzing under nutrition and over-nutrition of the children were statistically analyzed using chi-square test. **Results:** 67.1% were from lower middle class families and 32.9% were from low-income families. Yearly increments in weight were 2 to 3 kg in boys and girls up to 9 yrs. Between 9-10 yrs it was 4 to 4.5 kg. Yearly increments in height were 5 to 6 cm in boys and 5 to 7 cm in girls. The mean values of weight in the study group were coinciding between 10th and 25th percentiles and of height between 25th and 50th percentiles of CDC 2000 values for both sexes. 28.8% of the study group (31.6% boys and 26.1% girls) were below 3rd percentile of CDC 2000 values for weight i.e., undernourished or wasted. 6.8% of study children (6.6% boys and 7.1% girls) were below 3rd percentile of CDC 2000 for height i.e., stunted. 3.7% were over weight (4% boys and 3.4% girls) and 1.3% were obese (1.5% boys and 1.1% girls) according to body mass index. Statistical significance was observed independently between low income and maternal education below VIth standard in children with wasting. **Conclusions:** The mean weight and height of children of 6-10 years from a developing country were coinciding between 10th and 25th percentiles, and 25th and 50th percentiles of CDC 2000 data respectively. The overall prevalence of under nutrition, overweight and obesity were 28.8%, 3.7% and 1.3% respectively. Low family income and maternal education below VIth standard had significant relation with wasting.

Keywords: Growth pattern, Body mass index, Obesity, Under nutrition.

Introduction

Growth pattern of children of a country is considered as the single best indicator of a nation's public health, economic and psychological well-being. Children between 6 to 10 years of age contribute to 15 percent of India's population. Due to the large proportion and vulnerability to become malnourished, they exercise a dominating influence on the overall health status of the country. Defining the optimum growth of Indian children is a complicated problem due to the multivariate relationship of growth with factors like region and religion. Presently the CDC 2000 growth charts approved by WHO is used as the reference standard all over the world. Physical growth and ultimate size of an individual is under the influence of genetic as well as environmental factors like nutrition, education and economic status. Hence the observed values are to be compared with a standard, which is considered the best to represent the “normal growth” .

Objectives

The objectives of this study were to assess the growth pattern of children of age group 6 to 10 years and the prevalence of under nutrition and obesity among them.

Subjects and methods

2065 apparently healthy school children of age group 6 to 10 years from Government primary schools around Pushpagiri Medical College were selected for the study. Children with a history or evidence of chronic illnesses and on long term drug therapy were excluded. The design was cross sectional, completed during the period from 1st to 30th of June 2005 and was conducted by a team of two doctors and one health worker.

Prior to school reopening after the long summer vacation, permission was sought from the school authorities for the study. The objectives and methods were explained to the school teachers during the vacation conducting an orientation class regarding the growth pattern and health problems of school children. A carefully planned proforma to be completed by the parents was distributed through teachers at the time of result announcement. The proforma included personal data, health status, food habits and physical activities of the child and details of family members so that Kuppuswami grading could be done. Only those children who had completed the proforma were included in the study. Dates for medical checkup were informed sufficiently early so that the school authorities could make arrangements without disturbing the teaching programs. History and physical examination were done in the forenoon to exclude sick children. Height and weight were recorded by a single doctor between 1.30 pm to 3.30 pm. Weight was recorded by a portable weighing machine taking care to correct zero error before weighing each child. Height was measured by a stadiometer, the child standing without shoes in the correct posture, with the Frankfurt line parallel to the ground. Due to problems of privacy and consent, sex maturity rating could not be attempted.

The data were analyzed for weight and height increments and compared with 2000 CDC growth tables for weight, height and body mass index (BMI). Under nutrition was diagnosed as weight below 3rd percentile and over nutrition as BMI above 85th percentile of CDC 2000 growth tables. Statistical analyses were done by applying 't' test and Chi-square.

Results

After excluding children with incomplete proforma and chronic illness (n-46) data of 2065 (995 boys and 1070 girls) were analyzed.

Age and sex distribution:

Table 1 shows the age and sex distribution, and the pattern of weight and height gain in the study group. Progressive increment in mean weight of 2 to 3kg/ yr was observed in both boys and girls up to 9 years reaching up to 4 to 4.5 kg in the age group 9 to 10 years. Increments in mean height in both age groups in 6 to 9 years age was 4.5 to 6 cm and was reaching up to 7 cm between 9 and 10 years.

a. Weight - Comparison with 2000 CDC table

Boys

Table 2 depicts the weight of study group boys compared to 2000 CDC data. At all age groups, the present study children were lighter, the difference being 2.8 kg at 6 years to 4.8 kg at 10 years. The 50th percentile values of study group were coinciding between 10th and 25th percentile of CDC 2000 data at all age groups.

Girls

Table 3 shows the weight of study group girls compared to CDC 2000 data. Girls were thinner at all age groups, the difference ranging from 2.9 kg to 5.7 kg, more obvious with increasing age.

Fig.1 is a diagrammatic representation of percentage of study group children as compared to CDC 2000 percentiles for weight. Of the 2065 children, extreme wasting, i.e. less than 3rd percentile, was observed in 593 (28.8%) among which boys contributed 31.6% (314/ 2065) and girls 26.1% (270/ 2065)

b. Height - Comparison with 2000 CDC table

Boys

Table 4 studies the height of boys in the present group compared to CDC 2000 data. At all age groups, the study group boys were shorter, the difference ranging from 1.4 cm to 2.1 cm in the mean values. There was no increasing difference with advancing age as seen in weight pattern. 50th percentile height of study group were coinciding between 25th and 50th percentile of CDC 2000 data.

Girls

Table 5 compares the height of study group girls with the 2000 CDC data. The present group girls were shorter at all ages, the difference being 0.8 cm to 2.8 cm in the mean values. The 50th percentile values of the study group were coinciding between the 25th to 50th percentile values in CDC 2000 data.

Fig. 2 is the diagrammatic representation of the percentage of study children as compared to CDC 2000 percentiles for height. Almost 6.8% (142/ 2065) children were below 3rd percentile in height. Of these 7.1% were girls (76/ 1070) as compared to 6.6% boys (66/ 995).

c. Body mass index

On applying BMI, 77/ 2065 (3.7%) were over weight (1.9% boys, 1.8% girls) and 27/ 2065 (1.3%) were obese (0.7% boys, 0.6% girls).

Table 6 reveals the number of children with over weight and obesity.

Table 1 : Weight and height of study group according to age and sex

Age	Boys (No)	Girls (No)	Weight in kg		Height in cm	
			Boys (Mean)	Girls (Mean)	Boys (Mean)	Girls (Mean)
6 yrs	133	174	17.9	17.9	113.9	113.3
7 yrs	202	224	19.9	20.1	119.9	119.8
8 yrs	196	232	22.6	22.1	126.3	125.1
9yrs	183	236	24.7	23.9	130.9	130.4
10 yrs	281	204	28.7	28.5	137.6	137.6

Table 2 : Present study weight (kg) percentiles of boys compared to CDC 2000

Age	Percentiles									
	3rd		5th		10th		50th		97th	
	CDC	PS	CDC	PS	CDC	PS	CDC	PS	CDC	PS
6 yrs	16.5	12	16.9	14	17.7	15	20.8	18	28.3	25.1
							(10 - 25th)		(90th)	
7 yrs	18.3	15	18.7	15	19.6	15.6	23.2	20	32.5	27
							(10 - 25th)		(70 - 90th)	
8 yrs	20.1	17	20.7	17	21.6	18.5	25.8	21.3	37.4	33.2
							(10 - 25th)			
9yrs	21.7	17	22.4	18	23.4	20	28.2	24	42.1	38.6
							(10 - 25th)		(90 - 95th)	
10 yrs	24	20	24.7	20	26	21	31.8	27	48.9	45.6
							(10 - 25th)		(90 - 95th)	

PS: Present Study
Figures in parenthesis depict present study centiles as compared to CDC centiles.

Table 3 : Present study weight (kg) percentiles of girls compared to CDC

Age	Percentiles									
	3rd		5th		10th		50th		97th	
	CDC	PS	CDC	PS	CDC	PS	CDC	PS	CDC	PS
6 yrs	16	14	16.4	14.3	17.1	15	20.3	17	28.9	24
							(10 - 25th)		(75 - 90th)	
7 yrs	17.7	15	18.2	15	19.1	15	22.9	20	33.4	30.7
							(10 - 25th)		(90 - 95th)	
8 yrs	19.5	16	20.1	16	21.2	17	25.8	21	38.5	32.1
							(10 - 25th)		(75 - 90th)	
9yrs	21.2	17.1	21.9	18.6	23.1	20	28.5	23.8	43.5	32.9
							(10 - 25th)		(75- 90th)	
10 yrs	23.8	20	24.6	20	26.1	20	32.7	27	50.8	44
							(10 - 25th)		(90 - 95th)	

Table 4 : Present study height (cm) percentiles of boys compared to CDC 2000.

Age	Percentiles									
	3rd		5th		10th		50th		97th	
	CDC	PS	CDC	PS	CDC	PS	CDC	PS	CDC	PS
6 yrs	106.1	104	107.3	105.6	109.2	106.2	115.7	114	125.1	124
							(25 -50th)		(95 - 97th)	
7 yrs	111.9	109	113.2	110	115.1	113	122	120	132.3	129
							(25 -50th)		(90th)	
8 yrs	117.5	115.9	118.8	118	120.8	119	128.1	126	139.3	136.2
							(25 -50th)		(90 - 95th)	
9yrs	121.6	119.5	123	120	125.1	122	132.8	131	144.6	143.5
							(25 -50th)		(95 - 97th)	
10 yrs	126.3	124	127.8	125	130.1	129	138.4	137	151.1	154
							(25 -50th)		(95 - 97th)	

d. Socioeconomic and educational status

Of the total 2065 1386, (67.1%) were from low middle and 679 (32.9%) from low-income group. Wasting below the 3rd percentile was observed in 64.3% (437/ 679) children from low income group compared to 11.25% (156/ 1386) children from low middle income group; this reveals a high statistical significance (P value < 0.000003) between low income and wasting.

Amoung the mothers 524/ 2065 (25.3%) had education below VIth standard. Of the group 416/ 524 (79.4%) children were wasted compared to 177/ 524 (11.4%) of wasted children from low middle income group. The values were statistically significant (P value < 0.000003) showing the relation between low maternal education standards and significant wasting in children. When obesity and over nutrition were considered together 104/2065 (5.03%) children were found affected. Of these 4.8% (66/ 1386) were from low middle income group and 5.4% (38/ 679) were from low income group. The results were not statistically significant.

Discussion

No recent studies are available from India for comparing the growth pattern of children in the age group 6 to 10 years. The available data are from studies conducted about 10 to 15 years back.

Weight

The mean increment of 2 to 3 kg / year observed in this study was similar to that reported by K. N. Agarwal et al, while Sathyavathi et al had reported 3 to 4kg/ year weight gain for girls and Quima et al had reported 4 to 5 kg/ year for boys and girls in their study[1,2,3]. British children had the annual weight gain of 8 to 9 kg/ year. [3]

Children of present study were lighter than those reported by D. K. Agarwal et al and those from Varanasi and Haryana. They were heavier than Garhwali girls, and average urban and rural Indian girls, but far below the well nourished Indian girls[4, 5, 6, 7, 8, 9].

American girls were heavier at all age groups compared to most Indian studies and present study[10]. Comparing with ICMR study, children in the present study were heavier at all age groups except in the group of 6 to 7 years where the values were similar.[11]

On comparison with CDC 2000 values it is seen that 50thpercentile weight of boys as well as girls in the present study were tallying only with 10th to 25th percentile. Similar findings were observed by Seth et al, ICMR, Rath et al and D.K. Agarwal et al[12, 13,14]. About 28.8% were under nourished i.e., less than 3rd percentile of CDC 2000 data in this study. This is lower as compared to the values reported by Srivastava et al (62%)[14].

Height

The mean increment of height of 5 to 6 cm/ year in this study was similar to those reported by D. K. Agarwal et al and Quima et al where as it was 4cm/ yr as observed by K.N. Agarwal[3, 4, 1]. The mean height of children were similar to those from Delhi, Gwalior and Varanasi but more than children from Hyderabad, Garhwali girls and urban and rural Indian girls[15, 16, 17] . But well nourished Indian girls were taller than them[18]. The study group were taller than children from Tanzania and Tunisia [19, 20].

Comparing with ICMR study the present group were taller at all ages and both sexes except male children of 6 to 7 years where the values were similar with ICMR study[11]. 50th percentile height of study group boys and girls were coinciding between 25th and 50th percentiles of CDC 2000 values. The difference in mean values were 1.4 cm to 2.1 cm for boys and 0.8 cm to 2.8 cm for girls, revealing that height was less affected than weight. Since midparental heights were not evaluated in this study, the role of genetic factors influencing height could not be postulated in these children.

Limited data is available from India about obesity. Vedavathi et al observed 9.6% prevalence of over weight and 6% of obesity[21]. Data from Umesh Kapil reveals 7.4% obesity in boys and 6% in girls[22]. According to Gupta the prevalence of obesity was 7.5%[23]. During the past 20 years prevalence of obesity in children has doubled in America[24]. The NCHS suggest that nearly 15% adolescents are overweight or obese [24, 25]. Since the above quoted studies were from children above 10 years a definite comparison on prevalence of obesity was not possible in this study.

The single study available for comparison of nutritional status of children of 6 to 10 years is that by Haseena et al in children of low income group from coastal areas of Kerala in which 15.2% stunting, 53% wasting and 1.3% overweight were observed[26]. The present study children revealed wasting (28.8%), stunting (6.8%), over weight (3.7%) and obesity (1.3%). Thus the over all nutritional status of present study group was better and the major problem was wasting.

Statistically significant relation was observed between low socioeconomic status of family and maternal education (below VIth standard) with wasting in this study. Also overweight was found to be equally prevalent among low middle income and low income groups indicating that even in low socioeconomic groups there is a tendency for obesity in children even though wasting is more prevalent.

Key messages

The mean weight and the mean height of children of 6 to 10 years from a developing country were coinciding between 10th and 25th percentiles and 25th and 50th percentiles of CDC 2000 data respectively.

The over all prevalence of under nutrition, over weight and obesity in 6 to 10 years age group were 28.8%, 3.7% and 1.3% respectively.

Low family income and poor maternal education (below VIth standard) have significant relation to wasting in children of 6 to 10 years age.

Table 5: Present study height (cm) percentiles of girls compared to CDC 2000

Age	Percentiles									
	3rd		5th		10th		50th		97th	
	CDC	PS	CDC	PS	CDC	PS	CDC	PS	CDC	PS
6 yrs	105.8	104.2	106.9	105.7	108.6	107	115	113	125.3	123.8
							(25 - 50th)		(95th)	
7 yrs	111.9	109	113.1	110	114.9	111	121.8	119	123.3	133
							(25 - 50th)		(97th)	
8 yrs	117.3	115	118.5	117	120.5	119	127.8	125	139.4	136
							(25 - 50th)		(90 - 95th)	
9yrs	121.1	120	122.5	121	124.6	122	132.3	130	144.4	142
							(25 - 50th)		(90 - 95th)	
10 yrs	125.6	124	127.1	125	129.4	128	137.8	137	150.8	154
							(25 - 50th)		(90 - 95th)	

PS: Present Study
Figures in parentheses depict present study centiles as compared to the CDC centiles.

Table 6 - Body mass index compared to 2000 CDC

Age	Sex	BMI			
		< 85	85 - 95 Over weight	> 95 Obesity	Total
6 yrs	M	127	4	2	133
	F	172	1	1	174
7 yrs	M	195	4	3	202
	F	206	13	5	224
8 yrs	M	188	7	1	196
	F	220	9	3	232
9yrs	M	168	13	2	183
	F	231	3	2	236
10 yrs	M	262	12	7	281
	F	192	11	1	204
Total		1961 (95%)	77 (3.7%)	27 (1.3%)	2065

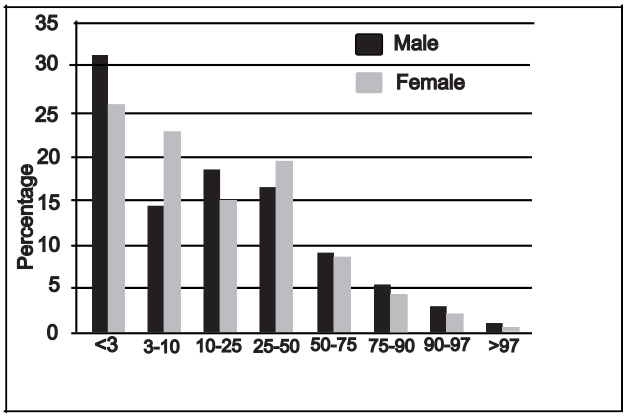

Fig. 1: Percentage of children as compared to CDC 2000 - weight

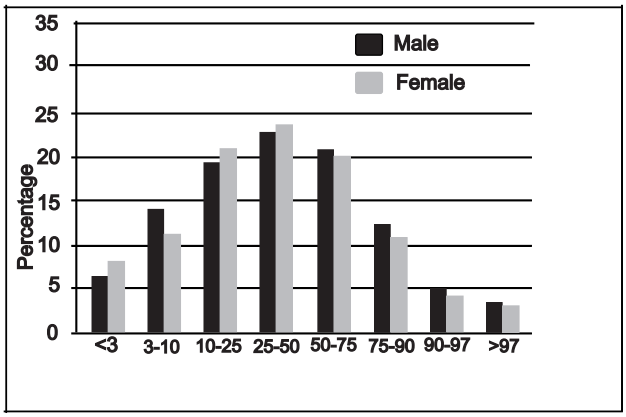

Fig. 2: Percentage of children as compared to CDC 2000 - height

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PUSHPAGIRI MEDICAL JOURNAL

✪ ORGINAL ARTICLE

A comparison of Hospital and Community acquired Methicillin resistant *Staphylococcus aureus* infections in a tertiary care hospital

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Abstract

Objectives: Traditionally, MRSA infections occurred exclusively in hospitals namely Hospital-acquired Methicillin-resistant *Staphylococcus aureus* (HA-MRSA). Recently however, community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) has emerged in young individuals without risk factors for MRSA acquisition. Prevalence of CA-MRSA and its susceptibility to antibiotics have shown geographic variability. **Methods:** This study aims to provide regionally specific information on the proportion of CA-MRSA cases. Thirty non-duplicate MRSA isolated from different specimens for a period of three months were included in the study. Antibiotic susceptibilities and the important risk factors for infection were studied. The Fisher's exact test was done to determine the statistical significance. **Results:** 16.67% of our isolates were community-acquired and 83.33% were hospital-acquired. CA-MRSA isolates were distinct from HA-MRSA by their susceptibility patterns and risk factors. **Conclusions:** Beta-lactam antibiotics are usually the first line antibiotics used to treat a staphylococcal infection. Awareness about the existence of MRSA in the community is a must as the commonly used beta lactams have no role in treatment of these staphylococcal infections.

Keywords: MRSA, CA-MRSA, HA-MRSA, Methicillin resistant *Staphylococcus aureus*

Introduction

Abuse of antibiotics can lead to an increased risk of infection with a multi-drug resistant pathogen. *Staphylococcus aureus* has proven itself to be adept at developing resistance. The inappropriate and widespread use of quinolone has been implicated to the rise of MRSA (Methicillin Resistant *Staphylococcus aureus*)[1]. Indeed, there is a clear association between exposure to antibiotics and rising incidence of MRSA[2]. Traditionally, MRSA infections occurred exclusively in hospitals, namely the Hospital-acquired MRSA (HA-MRSA). Recently however, Community-acquired MRSA (CA-MRSA) has emerged in young individuals without risk factors for MRSA acquisition.

CA-MRSA strains can cause a spectrum of diseases ranging from uncomplicated skin infections[3] to necrotizing soft-tissue infections, such as pneumonia[4] or osteomyelitis[5], while hospital acquired isolates are more likely to cause bloodstream infections. CA-MRSA isolates are found to be more susceptible to Ciprofloxacin, Clindamycin, Gentamicin and Trimethoprim-Sulfamethoxazole than their hospital acquired counterparts[6]. The advent of CA-MRSA has significantly changed our medical practice. Beta-lactam antibiotics are usually the first line antibiotics used to treat any staphylococcal infection. Awareness about the existence of MRSA in the community is a must, as these commonly used beta lactams have no role in treatment of these CA-MRSA infections. Moreover, the incidence of CA-MRSA and its susceptibility to certain antibiotics have shown geographic variability[7]. Hence, regionally specific information on CA-MRSA incidence and susceptibilities are made available, for appropriate empirical antimicrobial therapy[8].

Thus this study is aimed to provide details of incidence of HA-MRSA and CA-MRSA in a tertiary care hospital in Kerala. Information pertinent to risk factors, prevention, diagnosis and treatment was explored.

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Materials and methods

Patients eligible for this study were those with cultures positive for *Staph. aureus*. The isolates were identified as *Staphylococcus aureus* by routine microbiological procedures.

Detection of Methicillin resistance was carried out by using Oxacillin (1µg) and Cefoxitin (30µg) discs as per Clinical Standards Laboratory Institute (CLSI) 2008 guidelines[9]. Oxacillin (Methicillin) resistance was confirmed using an oxacillin agar screen test. All *Staphylococcus aureus* isolates that were found to be resistant to Cefoxitin and Oxacillin were included in the study. Antimicrobial susceptibility testing was done according to the CLSI standards by disk diffusion method. D zone test was done do determine inducible resistance to Clindamycin.

A Methicillin resistant *S. aureus* isolate was classified as CA-MRSA if the patient met three[10] criteria:

(i) culture sample was obtained during an outpatient visit or within 48 hours of hospitalization

(ii) the subject had not been admitted to a hospital, nursing home, or any other long-term care facility within the last 1 year

(iii) the subject had no history within the past year of known risk factors for MRSA such as dialysis, an indwelling catheter or a percutaneous medical device.

Patients were reviewed for data regarding risk factors in order to find associations between the clinical history and the type of MRSA infection. Details regarding the following were collected and documented: (1) time between admission and positive culture for MRSA, (2) reason for hospitalization, (3) history of previous hospitalizations, (4) anti-microbial exposure before MRSA infection and (5) site of MRSA infection .

Statistical Methods

Proportions of CA-MRSA and HA-MRSA from the samples identified were calculated. All clinical variables were tabulated using frequency tables, along with pattern of susceptibility to commonly used antibiotics. Fisher's Exact test was done to determine the statistical significance. A *p value* < 0.05 was considered statistically significant.

Results and Observations

Data was collected from 30 patients and were analyzed using Microsoft Excel and EPI INFO Version 3.3.2. Among the 30 cases, 5 (16.67%) were Community-Acquired and 25 (83.33%) were Hospital-Acquired (Fig.1).

Out of the 30 patients, 20 were males while 10 were females (Table 1). The mean age among HA-MRSA cases was 56 years (SD 22.16) while the mean age among CA-MRSA cases was 39 years (SD 22.62)

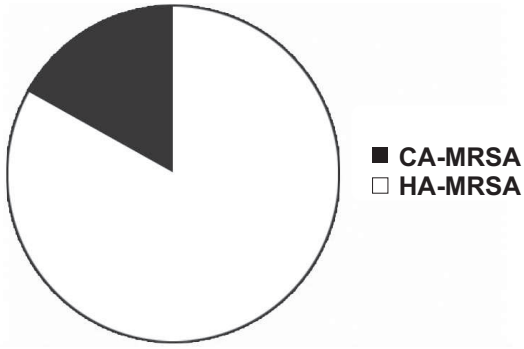

Fig.1 - Pie chart showing proportion of CA-MRSA and HA-MRSA among cases

Table 1: Distribution of CA-MRSA and HA-MRSA cases by sex

Sex	Isolate		TOTAL
	CA-MRSA	HA-MRSA	
Male	3	17	20
Female	2	8	10

Table 2: Distribution of CA-MRSA and HA-MRSA cases by age

Age	CA-MRSA	HA-MRSA	TOTAL
< 40	2	7	9
41- 60	2	6	8
> 60	1	12	13
TOTAL	5	25	30

Table 3: CA-MRSA and HA-MRSA by infection type

Infection type	HA-MRSA (N=55)	CA-MRSA (N=5)	p value
SSTI	4 (80%)	7 (28%)	0.047
Otitis Media	1 (20%)	0 (0%)	NA
Respiratory tract*	0 (0%)	7 (28%)	NA
Bone	0 (0%)	4 (16%)	NA
Others+	0	7 (28%)	NA

When compared with HA-MRSA cases, CA-MRSA infections were also more likely to involve the skin and soft tissue, the differences being statistically significant ($p < 0.05$) (Table 3).

* Among the HA-MRSA cases, 5 respiratory tract isolates were obtained from endotracheal tubes, while the rest were pneumonia
* Others included isolates from postoperative wounds, Foley's catheters and surgical specimens.

The most common underlying condition in both HA-MRSA and CA-MRSA cases was diabetes mellitus (Table 4).

Table 4: Underlying conditions present in CA - MRSA and HA - MRSA cases

Conditions	CA-MRSA (n=5)	HA-MRSA (n=25)
Alcohol abuse	0 (0%)	5 (20%)
Diabetes mellitus	5 (100%)	16 (64%)
Hypertension	1 (20%)	2 (8%)

Table 5: Risk factors for CA-MRSA and HA-MRSA infection

Risk Factor	CA-MRSA (n=5)	HA-MRSA (n=25)
Steroids	1 (20%)	6 (24%)
Prosthetics	0 (0%)	3 (12%)
Closed community*	1 (20%)	0 (0%)
Family history	3 (60%)	0 (0%)

**Closed communities are places where people live in close proximity to one another such as in military barracks, hostels and prisons.*

Antibiotic susceptibility of isolates

Table 6: Antimicrobial susceptibility profiles of CA-MRSA and HA-MRSA isolates

Type of Antibiotic	No. of isolates susceptible		p value
	CA-MRSA (n=5)	HA-MRSA (n=25)	
Erthromycin	4 (80%)	8 (32%)	0.068
Co-trimoxazole	4 (80%)	3 (12%)	0.006
Clindamycin	4 (80%)	9 (36%)	0.094
Vancomycin	5 (100%)	25 (100%)	NA

The most common risk factor for CA-MRSA acquisition was a history of similar lesion in the family, which was present in 60% of the cases (Table 5).

On evaluating the antibiotic sensitivity profiles it was found that CA-MRSA isolates were more likely to be susceptible to co-trimoxazole than HA-MRSA isolates,

Discussion

Over the past 10 years, MRSA has emerged in the community with clinical, epidemiologic and bacteriologic characteristics distinct from hospital-acquired MRSA (HA-MRSA). Community-acquired MRSA (CA-MRSA) has its onset in the community in an individual lacking the established MRSA risk factors, such as a recent hospitalization, surgery, residence in a long-term care facility, receiving dialysis, or the presence of an invasive medical device.

About 16.67% of our isolates were community acquired, corresponding with other reported rates in India which vary from 10.9% to 18.1%[11,12]. This is lower than rates reported in western countries, where, in a review of 104 studies of CA-MRSA infections, pooled CA-MRSA prevalence was 30.2%[10].

Emergence of CA-MRSA colonization represents a new, unrecognized reservoir of MRSA within the community and hospitals, potentially increasing risk for horizontal transmission[13].

Common Sites of Infection

In the present study, 80% of CA-MRSA infections were found to involve the skin and soft tissue. When compared with HA-MRSA cases, CA-MRSA infections were also more likely to involve the skin and soft tissue, the differences being statistically significant ($p < 0.05$). This is in agreement with various other studies which reported that CA-MRSA commonly caused skin and soft tissue infections[6,14,15].

An important source of infection for these cases is thought to be the colonization of MRSA in various body sites. Suggested sites are the nares, the axilla, the inguinal area and the rectum, the most common site being the nares. This colonization has been implicated as a risk factor for MRSA infection[16].

However, another study has shown that non-nasal colonization was more common (25%) among CA-MRSA patients, as compared to HA-MRSA patients (6%), suggesting that the CA-MRSA colonization patterns are distinct[17].

The relatively high prevalence of non-nasal colonization may play a key role in CA-MRSA transmission and acquisition of infection. This suggests that the spread could be due to close contact in overcrowded or unhygienic living conditions common among low-income groups[18].

Risk Factors

The most common underlying condition present for CA-MRSA and HA-MRSA cases was diabetes mellitus, which is known to be a risk factor for infections in general.

The most common risk factor for CA-MRSA acquisition was found to be a history of similar lesions in the family, which was present in 60% of the cases. It has been shown that patients who had household contacts colonized or infected with MRSA were 14 times more likely to be colonized themselves, further increasing risk of infection[13,19].

Unhygienic conditions, poor living environment and low socioeconomic status have all been shown to play a key role in the incidence of CA-MRSA[18].

Antimicrobial susceptibility patterns

In our study, 80% of CA-MRSA isolates were sensitive to Clindamycin and Co-trimoxazole. This correlated well with studies which reported sensitivity rates of 87 - 95% for Clindamycin and 92% - 96% for Trimethoprim-Sulfamethoxazole[20,6].

However, in the above studies, percentage of isolates susceptible to erythromycin varied from 6-44%, which did not agree with the 80% reported in our study.

All of our MRSA isolates were susceptible to Vancomycin. CA-MRSA isolates were more likely to be susceptible to Co-trimoxazole than HA-MRSA isolates, the difference being statistically significant. Hence this antibiotic appears to be a good option for empiric out-patient treatment of Staphylococcal infections.

Clindamycin, Trimethoprim and Vancomycin among others are the older antimicrobials that may be used in the treatment after susceptibility testing results are available, while Linezolid, Daptomycin and Tigecycline are the newer treatment options[21].

The emergence of CA-MRSA has forced public health practitioners to face challenging issues in surveillance, education, and community prevention.

Steps to ensure the prevention of spread include screening of body sites for colonization, decolonization by antibiotics and contact isolation. Improved physician recognition of CA-MRSA as the major cause of staphylococcal skin and soft tissue infections is the key to ensuring initiation of appropriate therapy. Awareness and knowledge of the local epidemiology of MRSA can help guide appropriate treatment.

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PUSHPAGIRI MEDICAL JOURNAL

✪ ORIGINAL ARTICLE

Ultrasound guided hydrostatic enema reduction of Intussusception: Guidelines in therapy and Review of Institutional experience

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Abstract

Acute Intussusception is one of the commonest paediatric surgical emergencies. The advent of sonologically guided hydrostatic reduction as an option of non-operative treatment in selected patients has simplified therapy and reduced surgical morbidity. The procedure employed, and the broad guidelines in the use of this therapy are discussed here. Also reviewed is the institutional experience in the treatment of intussusception.

Keywords: Acute Intussusception, Ultrasound guided hydrostatic reduction

Introduction

The common options available for non operative treatment of intussusception include:

1. Ultrasound guided hydrostatic saline enema reduction
2. Fluoroscopy guided air insufflation (Pneumatic reduction)
3. Fluoroscopy guided hydrostatic barium enema reduction

Sonological diagnosis of Intussusception:

The classical USS feature of intussusception is the *'Target' sign*, also called the *'Donut' sign* or '*Pseudo-kidney' sign*. (Fig.1) The extent of progression and presence of bowel wall oedema can also be assessed. The mass becomes more prominent on infusing saline for hydrostatic reduction, and this can be used to clarify the diagnosis in a doubtful situation.

Pre-treatment scoring for feasibility of non-operative treatment:

❖ **Favourable factors :**

1. Short history of less than 24 hours
2. Age group less than 2 years
3. No clinical features of advanced intestinal obstruction (bilious vomiting/ severe bleeding)
4. Absence of abdominal signs (distension/ tenderness/ guarding)
5. Absence of radiological signs (obstructive pattern on X ray)[2]
6. Absence of systemic complications

❖ **Contraindications:**

1. History more than 48 hours
2. Clinical evidence of advanced intestinal obstruction [severe bleeding per rectum, abdominal distension, abdominal tenderness and guarding, poor general condition like acute circulatory failure/ dyselectrolytemias]
3. Any Radiological evidence of advanced intestinal obstruction[3]. [X-ray abdomen showing multiple small bowel air fluid levels with sparse gas in colon - a feature of advanced intussusception/ small bowel intussusception]
4. Age of child more than 5 years (high probability of lead point)
5. Diagnosis of small bowel Intussusception (post operative/ other): Ultrasound scan demonstration of a thick irregular rim of the 'target sign' measuring more than 10 mm, absence of Doppler signal on a colour Doppler indicating non-viable bowel and sonological evidence of a lead point are relative contra- indications.

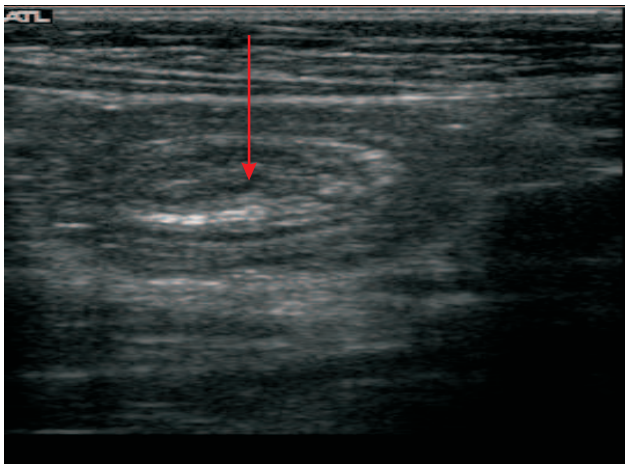

Fig. 1: USS demonstrating the 'Target sign'

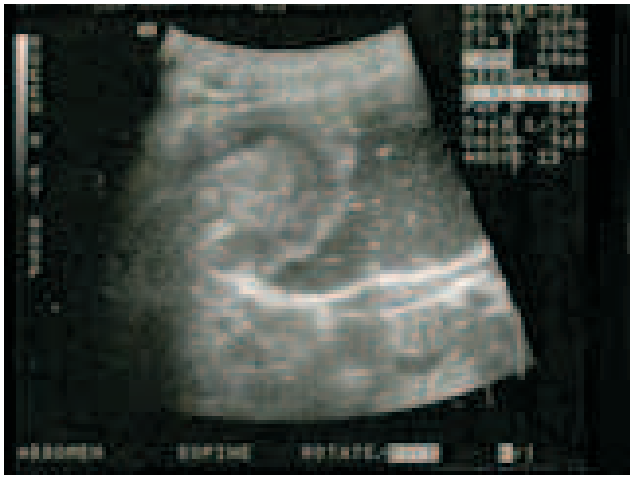

Fig. 2 : USS showing hydrostatic reduction

Ultrasound guided hydrostatic saline enema reduction

- *Preparation of the patient:*
  The diagnosis, planned therapy, success rate and possibility of need for surgery should be discussed and informed consent obtained. The child should be kept nil per orally and nasogastric tube inserted if there is vomiting. Parenteral fluid, preferably normal saline, is started. Haemogram and serum electrolytes should be assessed. The child is sedated with Inj. Pethidine (0.5 mg/kg IM) and Inj. Phenergan (0.5 mg/kg IM)/ Inj. Midazolam (0.1 mg/kg slow IV).
- *Necessary equipments:*
  Foley's catheter - 16 Fr, Normal saline – 1 litre, warmed to body temperature, Macro infusion set, Inj. Buscopan, Inj. Midazolam
- *Procedure:*
  Confirm the presence and the site of the mass on USS. Insert the Foley's catheter into the rectum and inflate the bulb gently to 30 ml; infuse the NS at feet height there from the patient. Watch for the gradual reduction by the filling up of colonic loops proximally with saline and the retrograde movement of the mass along the colon. (Fig. 2) Make sure that the saline is flowing freely and no leakage of saline is present through anus. The terminal part of reduction at the caecum is the most difficult and takes time. The child will usually strain severely and flow of NS will be slow at this point. Inj. Buscopan can facilitate reduction of the terminal part of intussusception.
- *Features of reduction of intussusception:*
  1. The child suddenly becomes comfortable and asymptomatic
  2. Normal saline flows freely
  3. Disappearance of the 'target' sign
  4. Appearance of filled small bowel loops ('honey comb' sign)
  5. Disappearance of previously filled colonic loops

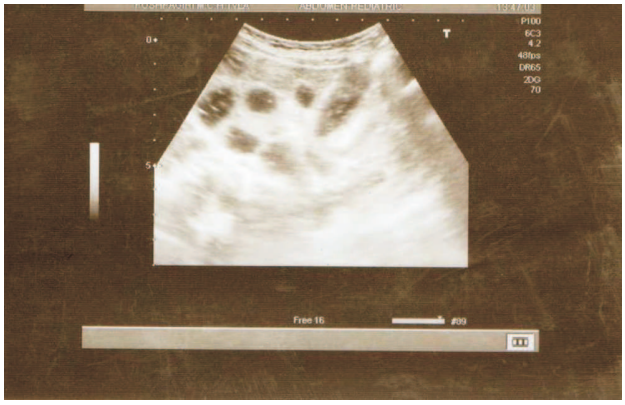

Fig.3 : USS demonstrating 'honeycomb sign'

- *Concluding the procedure:*
  Wait for the small bowel loops to fill well before stopping the infusion. Empty the fluid in the colon by gravity drainage of the infusion set. Deflate the Foley's catheter bulb and remove after five to ten minutes. The child is kept NPO for six hours and closely monitored.
- *Repeated attempts at reduction:*
  If some movement of the mass was present initially /mass reduced till the cecum initially, and the child has no abdominal signs, a repeated attempt at reduction can be made after about two hours. Antibiotics may be started. Not more than three attempts of hydrostatic reduction should be tried, and proceeding with hydrostatic reduction for more than six hours is not advisable. In a child older than two years, not more than two attempts is advisable.

Factors predicting failure of hydrostatic reduction:

1. Persistence of the mass at the initial point
2. The mass does not move proximally
3. Proximal colonic loops do not fill up

4. The mass does not reduce beyond the caecum
5. Severe bowel wall oedema
6. Absence of free flow of NS
7. Child strains continuously

Causes of non reduction of intussusception:

1. Ischaemic intestine
2. Oedematous intestine
3. Presence of a lead point
   (Meckel's diverticulum/ small bowel lesion etc.)
4. Ileo ileo colic intussusception

Indications to proceed to surgery:

1. Any contraindication to non operative treatment
2. When there is no movement of mass from initial position, with saline infusion
3. When the mass does not move beyond the caecum
4. Failure of three attempts at reduction

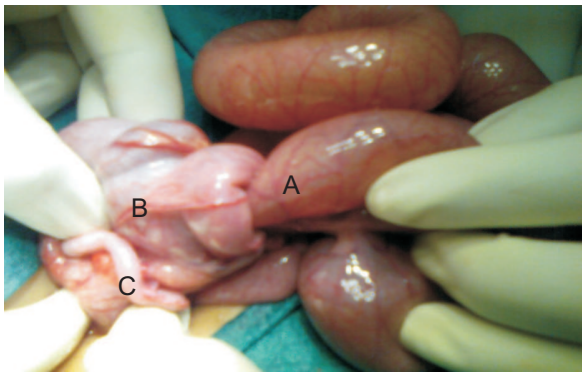

Fig.4 :Operative reduction of ileo-colic intussusception
(A - ileum B - colon C - Vermiform appendix)

Specific situations with regard to intussusception:

Small bowel intussusception and Compound intussusception (ileo-ileo-colic)

It is clinically suspected in children with early onset of abdominal distension, bilious vomiting and systemic complications. Plain X-ray will show features of distal small bowel obstruction with multiple central air fluid levels and sparse gas in colon. When the mass is surrounded by fluid in the caecum, the ileocolic type of intussusception could be differentiated from the ileo-ileo-colic type[1]. A typical complex fronded appearance is seen in the ileo-ileo-icolic intussusception compared with the appearance of a simple mass in the ileo-colic type[1]. An ileo-ileal intussusception can not be seen or reduced by USS guidance and ileo-ileo-colic intussusception should be considered in all cases of difficult reduction. Treatment is essentially surgical.

Post operative intussusception

This usually occur mainly after retroperitoneal surgeries like nephroureterectomy for Wilm's tumour and pyeloplasty. Classical presentation is with features of early onset of intestinal obstruction. The intussusception is usually jejuno-jejunal or ileo-ileal. An X-ray will show features of small bowel obstruction. The treatment is surgical.

Recurrent intussusception

Recurrence can occur following non-operative treatment or operative treatment. A high index of suspicion is required to make the diagnosis. Two more trials of non-operative treatment can be given in the absence of abdominal signs or complications.

Advantages of Ultrasound guided hydrostatic saline enema reduction

1. Easy and reproducible technique
2. No radiation exposure to the patient or doctor
3. Lesser risk of bowel perforation
4. High success rate comparable to other techniques of non operative treatment[4,]
5. Repeated attempts are easier

The most difficult part of the procedure which can be learned only from experience is the declaration of the end point of trials of hydrostatic reduction and the decision to proceed to surgery.

Institutional experience: A review

The study was done during the period of Nov '08 to Oct '09. A combined prospective and retrospective analysis was done. Twenty four cases of intussusception were included in the study. The age group included is 4 months to 3 years. The mean age was 8 months. The sex incidence was 15 cases in males and 9 in females.

The various aspects of the study and the observations are summarized in Tables 1 to 8 depicted below:

Table1: Clinical presentation of Intussusception

Clinical presentation	No. of cases (total 24)
Abdominal pain, vomiting	24
Red currant jelly stools	15
Palpable abdominal lump	20
Mass palpable per rectum	1
X-ray evidence of advanced obstruction	1
Systemic complications	2

Table 2: Treatment options used

Treatment of intussusception	No. of cases (total 24)
US guided Hydraulic saline enema reduction	17 (70.83%)
Laparotomy hydraulic saline enema	7 (29.17%)

Table 3: Attempts made at hydrostatic reduction

Attempts at hydrostatic reduction	No. of cases (total 17)
Single attempt	15
Two attempts	2

Table 4: Incidence of recurrence

Recurrence of intussusception	No. of cases (total 24)
After hydrostatic reduction	1
After laparotomy	0

Table 5: Surgical treatment

Surgery for intussusception	No. of cases (total 7)
Primary laparotomy (for intestinal obstruction)	1
Laparotomy after failed trial of hydrostatic reduction	6

Table 6: Intra operative findings

Intra-operative findings	No. of cases (total 7)
Ileo-colic intussusception	4
Additional Ileo-ileal component	2
Ileo-ileo-colic intussusception	3
Mesenteric adenitis	4
Lead point (Meckel's diverticulum)	1

Table 7: Recovery after hydrostatic reduction

Post procedure recovery	No. of cases (total 17)
Initiation of oral feeds	After 8 hours
Duration of hospital stay	48 hours
Recurrence	1
Post procedure loose stools	10

Table 8: Recovery after surgery

Post operative recovery	No. of cases (total 7)
Initiation of oral feeds	After 24 hours
Duration of hospital stay	5 days (3-8 days)
Passage of blood in stool	2
Prolonged ileus (> 24 hours)	2
Wood infection	0
Recurrence	0

Conclusion

In a population where the patients tend to present early, sonologically guided hydrostatic reduction of intussusception is possible in the vast majority of cases. Although broad guidelines in treatment are helpful, therapy of each patient should be individualized.

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PUSHPAGIRI MEDICAL JOURNAL

✪ CASE REPORT

Unusual presentations of Non Hodgkin lymphoma

Part I: A rare case of Primary malignant lymphoma of spleen presenting as splenic abscess

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Abstract

Non Hodgkin lymphoma (NHL) is well known for its unusual clinical presentations, varying sites of origin and spread in an unpredictable fashion. Each case of extra nodal lymphoma will have some unique feature. We worked up a series of very unusual cases of NHL, with rare clinical presentations, histopathological features, management modalities and prognosis.

Here we are reporting a case which presented as a retroperitoneal abscess and massive splenomegaly, along with auto-immune haemolytic anemia. Splenectomy was done and the final histopathological diagnosis was Non-Hodgkin's lymphoma, large cell type, with dominant splenic involvement. The condition is also termed primary malignant lymphoma of spleen (PMLS). The patient's haemotological status improved immediately after splenectomy.

Key Words: Non-Hodgkin's lymphoma, Splenectomy, Autoimmune haemolytic anaemia, primary malignant lymphoma of spleen

Introduction

Non-Hodgkin's lymphoma is the most common malignant neoplasm of the spleen. A dominant splenic involvement in Non-Hodgkin's lymphoma is very rare, seen in only 1% of patients. Thrombocytopenia, anaemia, and neutropenia are seen associated with the disease.

Case report

A fifty year old female was referred to our Institute as a case of retroperitoneal abscess with splenomegaly and multiple splenic abscesses. The patient presented to us with a two weeks history of severe back pain, pain along the left lower limb and difficulty in walking. She also had abdominal pain, low grade fever and difficulty in micturition for the past seven days. The abdominal pain was continuous and of throbbing type in the left iliac fossa and radiating down to the left lower limb, and was not relieved by analgesics. She was apparently comfortable before the past one month, during which she had loss of appetite, loss of weight and generalized weakness. There was no history of trauma, vomiting, diarrhoea or constipation.

The patient was not a known diabetic or hypertensive; there was no significant family history. She was diagnosed to be diabetic after admission. She give a had past history of several episodes of generalized weakness and was found anaemic; she was treated with repeated blood transfusions during the period 1991-2001. They had consulted a Physician at CMC Vellore as per the advice from Government Medical College,TVM. There the condition was diagnosed as ***autoimmune haemolytic anemia*** after peripheral smear, DCT, ICT and bone marrow aspiration studies. She was advised to take folic acid continuously and steroids whenever the Hb levels fell below 6.5 gm%. Since then they gave up the follow up in Vellore and was able to maintain reasonable general health with this treatment (without blood transfusions).

On examination, she was very sick looking with gross pallor; the gait seemed abnormal. Blood pressure was 110/60 mm of Hg, pulse rate 90/min, and body temperature 99^{0}F. General examination did not reveal any other

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abnormality. Her abdomen per se was mildly distended; an obvious swelling was seen in the left lumbar region, which extended downwards and backwards up to the spine. There was no erythema over the swelling, or visible pulsations. On palpation it was soft, tender, extending to the left lumbar region and left iliac fossa downwards, and up to the paraspinal region posteriorly. Bowel sounds were present.

Investigations

Hb level at the time of admission was 6.2 gm%; it came up after three blood transfusions to 10.2 gm%.
Reticulocyte count: 3%
LDH : 609U/ L
AND: 5.05 U/ L (negative: 0-10, low positive: 10-12, positive: more than 12)
Peripheral smear: hypochromic anaemia with polychromasia and neutrophilia Direct and indirect Coomb's tests were negative.
All other blood investigations were within normal limits.

USG abdomen :
Splenomegaly with multiple mass lesions, possibly due to secondaries.
Left iliac fossa mass present, with mild hydronephrosis on the left side, possibly due to pressure effects.

CT scan findings:
Massive splenomegaly with multiple hypodense lesions (Fig. 1), most probably abscesses, the largest one had a size 10 cm x 5.5 cm. A retroperitoneal abscess (Fig. 2) was seen, involving left psoas major muscle and left paravertebral and posterior pararenal regions, and extending lateral to the lower pole of spleen and descending colon. The left kidney showed mild hydronephrosis.

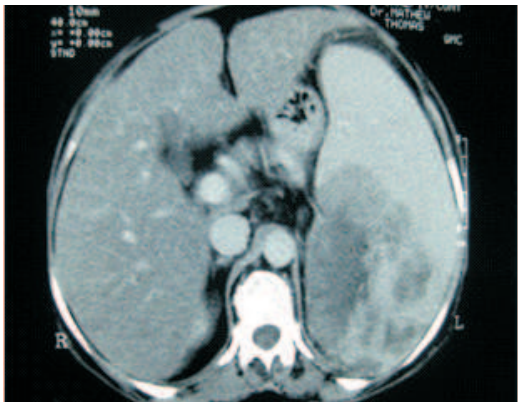

Fig. 1: CT scan showing massive splenomegaly

After stabilizing the patient with blood transfusions, the abscess was drained through a left loin incision. Almost 2.5-3.0 litres of thick pus was removed; the incision was kept open by keeping a drain in situ.

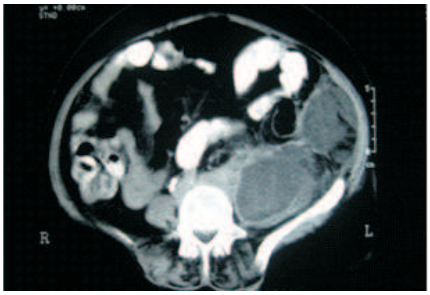

Fig. 2: Huge retroperitoneal mass with psoas abscess

Follow up USG was done on 6th and 10th post operative days, but there was no regression in the size of spleen and the parasplenic collection. USG on the 10th post-operative day revealed a persistent hepatosplenomegaly with multiple splenic lesions, raising strong suspicion of multiple splenic abscesses. Since the abscesses and massive splenomegaly were not resolved, we considered splenectomy as the only option left for the patient.

Laparotomy was done; peroperatively spleen was huge, with enlarged hilar lymph nodes. Moderate hepatomegaly was also noted. No lymph nodes were seen enlarged. Macroscopically there was no evidence of secondaries in any of the intrabdominal organs or peritoneum. There was no residual pus. Splenectomy was done and the specimen was sent for histopathology.

Post operative period was uneventful. Her haematological status improved significantly. The initial drainage site was also closed secondarily.

Histopathological examination

Macroscopically the spleen was solid, with no evidence of any abscess (as suggested by CT or USG). Isolated as well as fused, multiple, large, fleshy nodules (Fig. 3) were noted, with interspersed nodal tissue. Enlarged hilar lymph nodes (Fig. 4) were seen.

Fig. 3: Splenic tissue replaced by lymphoma

Fig. 4: Hilar lymph nodes

Macroscopic final diagnosis: Large cell lymphoma of B cell origin, a type of Non-Hodgkin's lymphoma

Post operatively the general condition of the patient had improved. Her anaemia also had been steadily improving, with the Hb level above 10 gm% without steroids or blood transfusions.
She was then referred to Regional Cancer Centre, Trivandrum for further management.

Discussion

Primary malignant lymphoma of spleen (PMLS) is an uncommon presentation, seen only in 1% of patients with non-Hodgkin's lymphoma. Patients may have isolated splenic lymphoma (Group I), may have associated splenic hilar adenopathy (Group II), or abdominal lymph node or liver involvement (Group III). Thrombocytopenia, anemia, and neutropenia are associated with the disease.

Lymphomas and leukemias with dominant splenic involvement include Large cell lymphoma, Marginal zone B-cell lymphoma, Hepato splenic hilar cell lymphoma, Follicular lymphoma, Lymphoplasmacytic lymphoma and Hairy cell leukemia. The disease that clinically appears confined to the spleen has been called ***malignant lymphoma with prominent splenic involvement***. Most affected patients have low-grade NHL. CT scan typically reveals splenomegaly with a solitary large mass, but multiple masses may be seen rarely.

In a series of 59 PMLS patients reported by Morel and associates, 40 underwent splenectomy, and 19 did not. Eighty-two percent of the cytopenic patients who underwent splenectomy had correction of their haematologic abnormalities postoperatively. For those patients with low-grade NHL who had spleen-predominant features, survival was significantly improved after splenectomy (median 108 months) as compared with patients receiving similar treatment without splenectomy (average 24 months)

In advanced cases **interferons** can be used in addition to chemotherapy. **Monoclonal antibody** Rituximab is being used frequently now-a-days.High dose chemotheraphy with **autologous stem cell transplantation** is in the final clinical trial stage in the treatment of NH Lymphoma.

S Abraksia, et al reported the case of a 75-year-old woman who presented with similar clinical findings[2]. Splenic abscesses and metastatic tumor were considered; histopathology showed diffuse large-cell lymphoma with uniform sheets of moderately large lymphocytic cells with focally prominent mitotic activity. Some authors consider PMLS to be an entity limited to the involvement of spleen and splenic hilum[3]. Others consider PMLS to be an entity that develops in the spleen with the potential for spreading to adjacent organs or distant metastasis[4]. The clinical features arecharacterized by nonspecific systemic symptoms. Majority are of B-cell origin, with the most common histologic diagnosis being a low-grade or intermediate-grade lymphoma[5]. Splenectomy is still the most effective therapy for all PMLSs[5-7]. Although there are no controlled trials, some authors believe that multiagent chemotherapy and/or radiotherapy is useful[8]. Reversal of cytopenia early after splenectomy is associated with prolonged survival[1].

Two unusual cases of large B-cell lymphoma with predominant splenic and bone marrow (BM) involvement[9] and similar clinical and histopathologic features have been described. Splenectomy revealed diffuse red pulp involvement by large B-cell lymphoma. The perisplenic lymph nodes were also involved diffusely with effacement of normal nodal architecture, excluding a diagnosis of intravascular large B-cell lymphoma. Given the difficulties in clinical and histopathologic recognition of lymphoproliferative disorders with significant splenic involvement, the use of ancillary immunoperoxidase stains should be considered in the evaluation of BM biopsies obtained from patients in which splenic lymphoma is a diagnostic consideration.

Conclusion

Non-Hodgkin's lymphoma is the most common malignant neoplasm of the spleen. About 75% cases exhibit clinical evidence of hypersplenism. Splenectomy is often required to make a definitive diagnosis, and resection is indicated in patients with systemic disease, and splenomegaly with cytopenias.

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PUSHPAGIRI MEDICAL JOURNAL

✪ CASE REPORT

Leech bite - A rare case of mass per vaginum

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Abstract

We report a very rare case of mass per vaginum in a lady, which resulted from a leech bite and required immediate intervention. Health professionals working in rural areas where leech infestation is common should be aware that people are at risk of bites in the genital region. A high index of suspicion is of great help to make an early diagnosis and ensure prompt treatment

Key Words: Leech bite, Mass per vaginum

Introduction

Mass per vaginum as the result of a leech bite is very rarely seen. There are only a few case reports available in the literature[1,2]. Vaginal mass as the result of a leech bite has not been reported before in the indexed literature, although the case of a 9 year old was reported by Malaysian researchers in an online journal in 2003[4].

Case Report

A 48 year old lady presented to our emergency room as case of mass per vaginum. She was feeling the mass for the first timein her life. She noticed it sometime after she took her bath in a pond. She first conveyed this to her daughter who suspected a prolapse of the uterus. There was no complaint of any bleeding per vaginum. She was haemodynamically stable. On examination a dark brown mass was seen protruding from the vagina and extending to the right thigh; it measured about ten cm in length and two to three cm in width. Slight bleeding was present around the root of the mass. On careful examination it was found to be a leech biting to the right labia majora. We put some common salt (NaCl) on the leech and it got detached immediately. Normal saline vaginal wash was given repeatedly to ensure that the vagina was free of leeches.

On per vaginal examination the uterus was atrophic and there was no evidence of prolapse.

The bite site wound was approximately 0.5 cm x 0.5 cm size; it was reddish in appearance. Compression bandage was given as there was slight oozing from the bite site. As the patient refused admission she was sent home from the casualty itself under antibiotic coverage for five days. She was stable at the time of discharge.

Discussion

Leeches are invertebrates belonging to phylum Annelida and class Hirudinea. A leech is usually about 12.5 -15.25 mm long[5].

In tropical regions, leech bites on the skin, especially over the lower limbs are a common event. However, serious consequences of leech bite injury to the internal viscera are uncommon[6] . If they occur, they can cause significant morbidity and could even be fatal[6,7]. Leech bites to various sites (e.g ; the nose, pharynx, larynx, oesophagus, rectum and bladder) have been reported in the literature[6,10]. Vaginal mass due to leech bite is even rarer.

The morbidity associated with a leech bite could mainly be due to two factors:

- mechanical obstruction of vital organ
- severe bleeding.

The prolonged bleeding after a leech bite is due to the action of factors in the leech saliva left in the bite. These include 1. histamine like vasodilators,

2. hirudin (a potent antithrombin), 3. hyluronidase and 4. calin (a platelet aggregation inhibitor)[11,13].

Interaction of exposed collagen and platelet and/ or von Willibrand factor is believed to be one of the initiating events for thrombus formation at the site of damaged endothelium. Interference with this mechanism may provide an antithrombotic potential.

Calin specially inhibits the human platelet aggregation induced by collagen[14]. In addition, it has been shown that calin inhibits platelet adhesion[14].

Bleeding from a leech bite wound can persist for a mean period of ten hours to as long as seven days[3,12]. In Medicine leeches have been used to treat venous congestion, because of their ability to remove excess blood and temporarily increase blood flow within the compromised tissue[13].

A case of vaginal bleeding following leech bite was first published in Bulgarian literature in 1968[1].

One case reported in the Ethiopian Medical Journal in 1995 [2] describes a 50 year old woman who was referred to a hospital with postmenopausal bleeding with haemorrhagic shock, to rule out endometrial carcinoma. Speculum examination revealed a darkish mass attached to the posterior vaginal fornix, and this was found to be a leech.

In another case, reported in the Spanish literature in 1998, a postmenopausal woman presented with continous bleeding per vaginum for seven days, after a swim in the river[3]. Gynecological examination revealed that the cause of bleeding was a leech bite. A case report of the vaginal leech bite in a nine year old girl from Kelantan, Malaysia was published in online Internet journal of Gynaecology and Obstetrics[4].

A leech bite can be diagnosed simply on the basis of patient history and examination. If a leech is found and is still biting, it should be removed with the help of common salt, a saline solution, or lignocaine solution[2,11].

In parous women, a simple speculum examination without anaesthesia and removal of a leech by surgical forceps from vagina is a good option of management[2,3]. Care should be taken during removal of the leech using surgical forceps; the leech should not be removed forcibly because its jaws might remain in the wound, causing continued bleeding and probable infection[14]. If the patient continues to bleed after removal of the leech, pressure should be applied to the wound with a sterile gauze soaked in thrombin solution.

There have been case reports describing the use of electrocoagulation to stop bleeding from the lesion in leech bite[9,10]. Suturing the lesion has not been recommended.

There is no data to support the use of any systemic drug to alter the coagulation of blood. In animal experiments Desmopressin (DDAVP) has been reported to attenuate bleeding caused by continuous hirudin infusion in rabbits. Bleeding from leech bite can be severe, requiring blood transfusion, and it can even produce shock [2,8,10].

Conclusion

Vaginal mass due to a leech bite is rare. A high index of suspicion is of great help in making the correct diagnosis at an early stage and thus reducing morbidity. Care should be taken during removal of the leech with surgical forceps. We emphasize that the if there is a suspicion as to whether the mass per vaginum is due to leech bite or not, the vagina can be washed with normal saline through a small catheter. The parasite should come out as normal saline causes irritation and dislodges it from the vagina.

To date there is no recommendation to administer any systemic haemostatic agent to stop bleeding. Simple compression packing with Betadine solution should be more than sufficient to stop the bleeding.

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PUSHPAGIRI MEDICAL JOURNAL

✪ CASE REPORT

Degenerating muscles: A paradox

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Abstract

Palmaris longus and flexor digitorum brevis are both phylogenetically degenerating muscles. Palmaris longus was well developed in animals with good brachiation and prehensile function. In man, it has lost its functional significance, as brachiation is not used as a means of locomotion. In concordance with its evolutionary degeneration, it is frequently absent and its agenesis ratio in various populations is on the rise. Flexor digitorum brevis is well developed in animals with arboreal locomotive habits. In humans, due to adoption of bipedal posture and gait, several changes have taken place in the foot-ankle mechanism. Flexion of toes is more dependent on the long flexor tendons rather than the short tendons, making flexor digitorum brevis functionally less significant and prone for evolutionary degeneration. The little toe is less active and muscles acting on it are more liable for degenerative changes. Hence the tendon slip going to the fifth toe is frequently absent. In such a scenario where the muscle bellies are expected to be absent, it is interesting to note a double palmaris longus and a supernumerary muscle slip of flexor digitorum brevis going to the little toe. An analysis of development of these anomalous muscles with reference to evolution is made. Palmaris longus is widely used as an autogenous tendon graft making it imperative to know its morphological variations. Similarly, knowledge of variations of flexor digitorum brevis is required for tendon grafting and reconstructive surgeries.

Key words: Phylogenetic degeneration, Double palmaris longus, Flexor digitorum brevis, Supernumerary muscle slip, Muscle anlagen

Introduction

Palmaris longus is a slender fusiform muscle in the superficial muscle layer of flexor compartment of forearm. It has its origin from the medial epicondyle, adjacent intermuscular fascia and deep fascia. Its tendon passes superficial to the flexor retinaculum, into which it partly gets inserted; then it becomes incorporated into the palmar aponeurosis. It is supplied by the median nerve and acts as an anchor for the skin and fascia of palm.

It is well developed in the brachiators which can suspend themselves from the branches of the trees and swing freely on their arms. In such animals, it consists of four long tendons which pass into the hand and get inserted onto the sides of proximal phalanges of the medial four fingers[1]. In the course of evolution, in man the muscle became almost vestigial[2]. It is more tendinous than muscular and is confined to the forearm; the hand component is represented by palmar aponeurosis.

Flexor digitorum brevis is an intrinsic muscle of foot. It lies deep to central part of plantar aponeurosis. It arises by a narrow tendon from the medial process of the calcaneal tuberosity, central part of plantar aponeurosis, and intermuscular septae separating it from adjacent muscles. It divides into four tendons, which pass to the lateral four toes. At the base of the proximal phalanx, each tendon divides around the corresponding tendon of flexor digitorum longus, and then reunites and partially decussates forming a tunnel for the long flexor tendon. It then divides again and attaches to either side of shaft of middle phalanx. Nerve supply is by a branch from the medial plantar nerve. It causes flexion of the

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lateral four toes at the proximal interphalangeal joint. The muscle plays an important role in the maintenance of longitudinal arches by its muscular tone and by acting as a tie beam holding the ends of the arch together.

This muscle is well developed in apes with arboreal locomotion. They have long toes and an opposable hallux, enabling them to walk along horizontal tree branches. In these animals the muscle consists of two heads. The superficial head has its origin from medial calcaneal process; the tendons pass into the 2nd and 3rd toes. Its contraction is independent of the long flexor tendons. The deep head is fused with long flexor tendon and causes flexion of the 4th and 5th toes. It acts along with the long flexor tendons; hence flexion of the respective toes is accompanied by plantar flexion at the ankle[3]. In man, the muscle has only one head of origin, consists of 3-4 muscle bellies all arranged in one layer, and contracts independent of the long flexor tendons.

Materials and Methods

During routine dissection in the Department of Anatomy Pushpagiri Medical College, Tiruvalla double Palmaris longus was noticed on the right upper limb of a male cadaver aged 50 years. In another male cadaver aged 43 years a deep supernumerary muscle slip of flexor digitorum brevis was noticed; its tendon joined the short flexor tendon going to the little toe.

Observations

Palmaris longus muscle and its tendon were duplicated in right forearm of a male cadaver (Fig. 1).

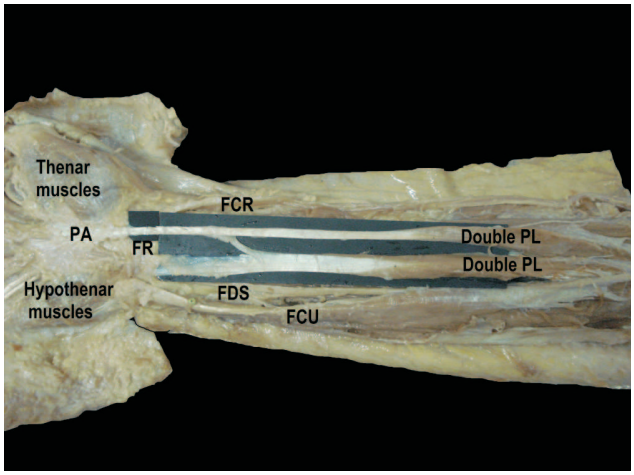

Fig. 1: Double Palmaris longus

FCR – Flexor carpi radialis
Double PL – Double Palmaris longus
FDS – Flexor digitorum superficialis
FCU – Flexor carpi ulnaris
FR – Flexor retinaculum
PA – Palmar aponeurosis

Both bellies took origin from the medial epicondyle along with the other superficial flexors. The medial tendon was flat and broad and was inserted into the flexor retinaculum. The lateral one was narrow and thick and was inserted into the apex of palmar aponeurosis. The two tendons communicated with each other through a tendinous slip passing from the medial to the lateral tendon. A branch from the median nerve divided into two branches to supply the muscle bellies separately.

In another male cadaver, on the left foot, a supernumerary muscle slip was seen deep to the main muscle mass of flexor digitorum brevis (Fig. 2). It had its origin from the medial intermuscular septum; it crossed the muscle deep to it from medial to lateral side and ended as a tendon which joined the short flexor tendon going to the little toe. It was supplied by a branch from the medial plantar nerve.

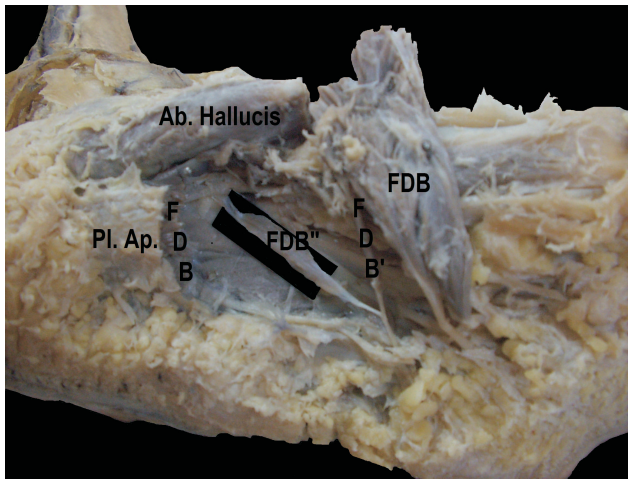

Fig. 2: Supernumerary slip of flexor digitorum brevis going to the little toe

Pl. Ap. – Plantar aponeurosis
FDB – Flexor digitorum brevis
Ab. Hallucis – Abductor hallucis
FDB' – FDB going to the little toe
FDB" – Supernumerary slip going to the little toe

Discussion

Variation is a fundamental evolutionary factor. Evolution is not possible had there been no variations in different organs and their structure. Variations that are not inherited have no role in evolution of the species as they are concerned with the individual but not the race[4].

Palmaris longus is the most variable of all the muscles. It presents a wide spectrum of morphological variations ranging from its absence to its duplication; the commonest being its absence. Its agenesis ratio was reported as 24.4% by Thompson et al (1921)[5], 64% by Ceyhan and Mavt (1997)[6], 16.74% by Gopinathan and Usha Dhall (2000)[2] and 25% by Thompson et al (2002)[7].

During evolution, as brachiation is not used for locomotion, degenerative changes have occurred in the muscle. Therefore, in man, the muscle is often absent unilaterally or bilaterally and the incidence of agenesis is gradually increasing in different races and populations (Ceyhan and Mavt, 1997)[6].

Double Palmaris longus has been reported earlier by various authors[8, 9, 10]. G L Liu et al in 1986[11] detailed the reconstruction of anal external sphincter complex by free autogenous transplantation of double palmaris longus[11].

Variations of flexor digitorum brevis have also been reported in the literature. The different variations affecting any of its tendon slips are agenesis, replacement by a small muscular slip from the longflexor tendon or flexor accessorius, or being joined by a supernumerary slip[12]. Nathan and Gloobe[13] in 1974 noted that the tendon slip going to the little toe was more susceptible to variations compared to the slips going to the other toes.

Flexion of toes is more dependent on the action of flexor digitorum longus, rather than the brevis muscle. Electromyographic studies showed that flexor digitorum brevis is not preferentially recruited over the longus for any posture or locomotion[14]. According to Darwin's disuse theory, the tendon of flexor digitorum brevis may be considered to be undergoing phylogenetic degeneration.

The little toe is functionally more inactive compared to the little finger and opposition is totally absent. This has resulted in gradual reduction in the usage of little toe, and the muscles acting on the little toe are undergoing evolutionary degeneration. Lobo et al conducted a Nepalese cadaveric study in 2009 on sixty soles and the tendon slip of flexor digitorum brevis going to the little toe was found to be missing in all sixty soles i.e. agenesis ratio was 100%[15].

Variations in flexor digitorum brevis were noted in 63% of the limbs; and agenesis of the tendon slip to the little toe was noted in 21% of cases by Macalister A in 1875[16]. The tendon slip going to the little toe was smaller in 36% and absent in 18% in a study conducted by B. Yalcin and H. Ozan[17] in 2005. Supernumerary slip of flexor digitorum brevis to the little toe also has been reported earlier by Nathan and Gloobe (1974)[13] and B. Yalcin and H. Ozan (2005)[17].

Embryological correlation

In a background of phylogenetic degeneration of the above two muscles, where they were expected to be agenetic or reduced, it was interesting to find duplicate and supernumerary muscles. Hence, a detailed review of literature was performed to have a deeper insight into development of muscles in general and origin of anamolous muscles in particular, with special reference and correlation to evolutionary changes.

The development of the tendons and muscles is regulated by the Hox genes and some other transcription factors[18]. The muscles of the limbs develop from myogenic precursor cells derived from the somites. These myoblasts aggregate to form a large muscle mass which splits into dorsal and ventral components[19]. The muscle mass is further subdivided into blocks of muscle anlagen under the influence of extracellular environment adjoining the myoblasts. These blocks of anlagen undergo a series of divisions and subdivisions resulting in the formation of individual muscles[20].

During evolution, new muscles are formed by the process of subdivision, fusion, migration or splitting of the original muscle mass[21]. Similarly, anomalous muscles result from abnormal fusion or splitting of the muscle anlagen. Abnormal fusion results in agenesis whereas abnormal splitting results in formation of duplicate or supernumerary muscles.

Clinical relevance

Absence of Palmaris longus does not cause any significant loss of function. This fact along with its easy accessibility makes it a good choice for various tendon graft, tendon transfer, reconstructive and plastic surgeries. Anomalies of the muscle can cause median nerve[22] and rarely ulnar nerve compression[23] also. A simple hypertrophy can simulate a tumour in the forearm[24] requiring differential diagnosis on MRI. Therefore it is necessary to have a sound knowledge about its normal and variant anatomy.

Similarly, understanding muscle architecture of the foot is essential in the design of surgical procedures such as tendon transfer, biomechanical modeling of the foot, prosthesis design, and analysis of foot function. A knowledge of variations of flexor digitorum brevis is clinically important because FDB musculocutanous flap is used in the reconstruction of the heel pad[15, 17]. The muscle has its application in transfer of its tendon to the dorsum of proximal phalanx for correction of claw or hammer toe deformities[25].

Conclusion

Palmaris longus muscle and flexor digitorum brevis are phylogenetically degenerating muscles with an interesting spectrum of variations. The commonest variation affecting palmaris longus is its agenesis; and its agenesis ratio is on the rise in various populations. The commonest variation affecting flexor digitorum brevis is agenesis of the tendon slip going to the little toe. Sometimes duplicate and supernumerary muscles are observed contrary to agenesis. This is explained by abnormal splitting of muscle anlagen in the embryonic period. Surgical removal of muscles undergoing degeneration does not result in any functional loss. This fact is clinically utilized for tendon transfer and reconstructive surgeries. Therefore it is important to understand both the normal and variant morphology of these muscles.

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PUSHPAGIRI MEDICAL JOURNAL

✪ CASE REPORT

A case of ARDS in Weil's syndrome

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Abstract

We present a case of sepsis with ARDS who had unusual recovery owing to early detection and treatment; he was finally diagnosed to have Leptospirosis with Weil's syndrome. The case is presented to highlight the need of high clinical suspicion for early detection, and the use of appropriate antibiotics which form the cornerstone for the treatment of such dramatic diseases with wide spread complications.

Keywords: Acute respiratory distress syndrome (ARDS), Leptospirosis, Weil's syndrome

Introduction

Acute Respiratory Distress Syndrome (ARDS) is a medical emergency usually associated with poor prognosis and patient outcome. Despite advances in treatment modalities for ARDS, it still remains elusive and is a management challenge even for the best trained specialists. Until the 1990s, most studies reported a mortality rate of 40-70% for ARDS. However, 2 reports in the 1990s, one from a large county hospital in Seattle and one from the United Kingdom, suggested much lower mortality rates, in the range of 30-40%[1,2].

Clinical presentation

A fifty five year old male patient, agriculturist by occupation, with no significant past clinical history was admitted in our hospital with complaints of short febrile episodes with cough and expectoration of five days duration. He also had myalgia and a few episodes of watery diarrhoea. His urine output had been reduced for the past two days.

At admission, his clinical examination was unremarkable except for mild dehydration, without postural hypotension. His blood pressure was 140/ 80 mmHg, pulse rate 100/ minute and respiratory rate 18/ minute. Systemic examination was unremarkable. A provisional diagnosis of infective diarrhoea was made and treatment was initiated in the ward.

Initial biochemical values (Table 1) were suggestive of prerenal failure with normal LFT, ECG and Chest X-ray findings. Since he had no urine output over a six hour period of observation, he was shifted to the medical ICU. His CVP turned out to be as low as two cm of H_2O.

In view of raised ESR and insufficient renal functions in a febrile patient, who is an agriculturist by occupation, a review of diagnosis was made, with the possibility of leptospirosis with Weil's syndrome. He was initiated on an appropriate dose of crystalline penicillin (CP) 15 lakhs IV four times a day.

Table 1: Investigation on day I

Test	Values
Hb	10 gm%
PCV	28.4
TC	8600 cells/ cumm
DC	P-92 L-5 E-3
ESR	120 mm/hr
RBS	130 mg/dl
B. Urea	136 mg/dl
S. Creatinine	3.87 mg/dl
Na+	128mmol/L
K+	3.5 mmol/L
Urine spot Na+	20
Urine spot K+	26

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On the second day, he was noted to be more tachypnoeic, and had oliguria despite adequate hydration. A Nephrology review was sought for the worsening RFT's (Table 2); infusion of Furosemide was started (5mg/ hr), to which he responded well by the third day. He had worsening tachypnoea with florid bilateral alveolar infiltrates in chest X-ray, with clear costophrenic angles; Kerley B lines were absent (Fig. 1), suggestive of acute respiratory distress syndrome.

Table 2: RFT results

RFT	30 Jan	31 Jan	2 Feb	3 Feb	4 Feb	5 Feb	7 Feb	8 Feb	9 Feb
B. urea	136	147	237	234	192	157	67	50	42
S.creatinine	3.87	3.09	5.5	4.61	3.32	1.89	1.06	0.97	1.08

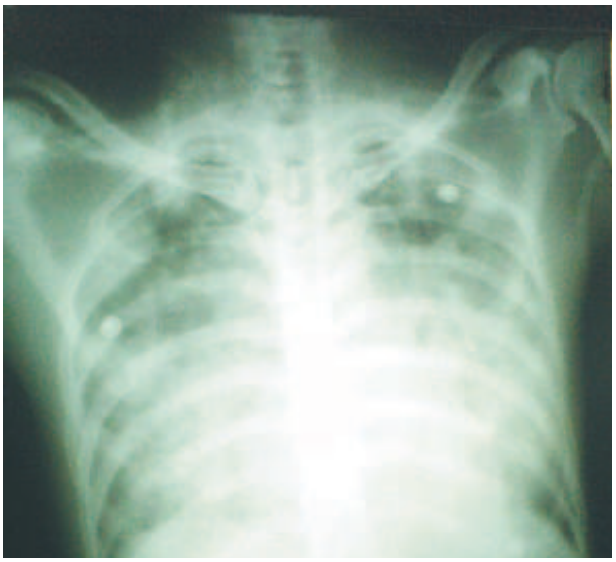

Fig. 1: Chest X-ray on second day with bilateral infiltrates

His arterial blood gas analysis (ABG) (Table 3) showed features of ARDS with PaO / FiO_2 179 and PaO_2 ~ 60 mm Hg on the third; a need for prophylactic ventilation was considered but deferred. He was continued on IV furosemide infusion and crystalline penicillin with other supportive measures.

Table 3: ABG analysis on the third day

Tests	Values
pH	7.435
pCO_2	19.9 mmHg
pO_2	62.8 mmHg
sO_2	90.6
HCO_3	13.5 meq/L
FiO_2	35%
PaO / FiO_2	179

The clinical diagnosis of Leptospirosis was confirmed by a positive antilepto antibody IgM (ELISA) on the third day.

He started showing signs of improvement by the fourth with decrease in tachypnoea and better chest X-ray and ABG (Table 4). He was further continued on IV antibiotics and other supportive measures and was shifted out of ICU on the fourth day with improving urine output and RFT's (Table 2).

Table 4: ABG values on fifth day

03 Feb	ABG values
pH	7.556
pCO_2	22.4
pO_2	100.6
$sO_{2\%}$	89.3
HCO_3	20.1
FiO_2	209

In the ward he showed rapid improvement with clear chest, near normal chest X-ray (Fig. 2) and RFT's (Table 2). He was discharged in a stable state on the ninth day with a diagnosis of Leptospirosis – Weil's syndrome and ARDS.

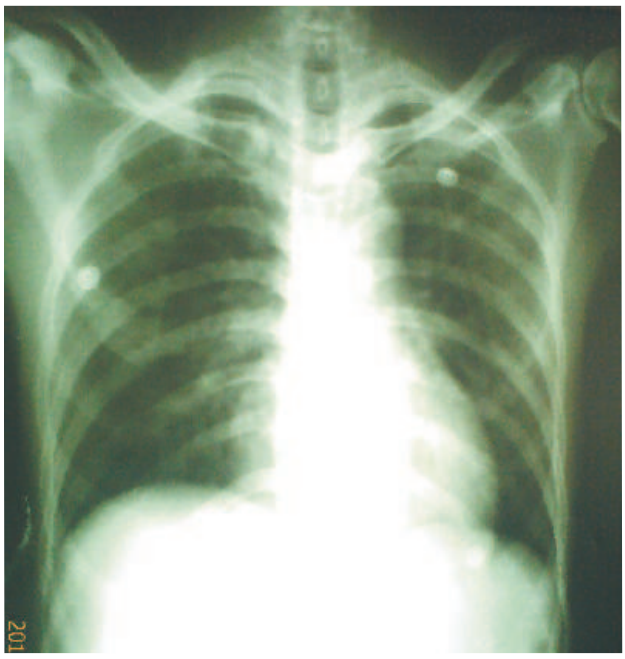

Fig. 2: Clear chest X-ray by seventh day

Discussion

Approximately 10% of patients diagnosed with leptospirosis develop signs of Weil's disease. The classic definition of Weil's syndrome include severe leptospirosis presenting with jaundice, renal failure, and pulmonary haemorrhage. Mortality rates among these patients are high despite care in an ICU.

A haemorrhagic diathesis is the cause of pulmonary lesions: it may occur in the lungs, pleura, or pericardium, and in severe infections there may be acute haemorrhagic lobar pneumonia. The most common radiographic abnormalities are increased non-segmental peripheral pulmonary densities, as seen in our patient. Other features include linear atelectasis, particularly at the lung bases. Pleural and pericardial effusions may occur and are often haemorrhagic. There is little or no correlation between the extent of the lung involvement and the severity of the disease or the prognosis. Cardiomegaly is due to circulatory stress and anemia rather than directly to leptospirosis.

Acute respiratory distress syndrome (ARDS) is associated with diffuse alveolar damage (DAD) and lung capillary endothelial injury. The early phase is describedas being exudative, whereas the later phase is fibroproliferative in character. Early ARDS is characterized by an increase in the permeability of the alveolar-capillary barrier leading to an influx of fluid into the alveoli. This barrier is formed by the microvascular endothelium and the epithelial lining of the alveoli. Hence, a variety of insults resulting in damage either to the vascular endothelium or to the alveolar epithelium could result in ARDS. The main site of injury may be focussed on either the vascular endothelium (eg. sepsis) or the alveolar epithelium (eg. aspiration of gastric contents)[3,4].

Severe leptospirosis manifests as pulmonary oedema leading to acute respiratory distress syndrome and polyuric acute renal failure (ARF). The aetiology of leptospirosis-induced pulmonary oedema is unclear[5]. Lung oedema clearance is largely affected by active sodium transport out of the alveoli rather than by reversal of the Starling forces. It was found that leptospirosis profoundly influences the sodium transport capacity of alveolar epithelial cells and that impaired pulmonary fluid handling can impair pulmonary function, increasing the chance of lung injury.

Abnormal chest radiographs are seen in 67% to 23% of patients. Resolution of radiographic abnormalities is usually complete in 7 to 10 days. In about 10% of patients there may be a relapse 6 to 14 days after radiographic clearance. It is emphasized here that radiographic pulmonary abnormalities may be seen without any clinical chest symptoms and that the radiographic findings cannot be used to determine severity or the rate of recovery.

Conclusions

- There are incidents of ARDS setting in following sepsis being considered to have poor prognosis, but Leptospirosis with Weil's syndrome is one scenario where the patient shows improvement if treated early.

- Due to early treatment and good supportive care and multi disciplinary approach, ventilator support as well as dialysis support could be deferred in this patient, without affecting the final favourable outcome.

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PUSHPAGIRI MEDICAL JOURNAL

✪ CASE REPORT

An unusual case of Duodenal perforation

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Abstract

A 10 year old girl was admitted with fever, generalized urticarial rashes and abdominal pain, after 2 days treatment from elsewhere. Plain X-ray of the abdomen taken on exacerbation of symptoms revealed features of bowel perforation. Per-operatively she was found to have a large duodenal perforation, which was closed. The cause could probably be corticosteroids from the referring hospital, used to treat the urticaria. The child was discharged after one week.

Key Words: Abdominal pain, Corticosteroids, Perforation, Duodenal ulcer.

Introduction

Perforation of bowel is known to occur in children following an acute appendicitis, acute intestinal obstruction, enteric fever etc. In these conditions it usually affects distal small bowel. Perforation of duodenum as such is very rare in children. We report such an unusual case of duodenal perforation.

Case Report

A 10 year old girl was referred from a local hospital with history of fever, generalised urticarial rashes, vomiting and abdominal pain. She had received antihistaminics, prednisolone and antispasmodics.

On admission she was febrile with tachycardia, normal blood pressure and some dehydration and had generalised urticarial rashes. Abdomen was soft with mild epigastric tenderness.

Her blood counts showed TC: 13700/mm^3, DC: P85, L13, E2; electrolytes were normal and LFT mildly deranged with S. bilirubin of 1.6 mg/ dl but SGPT of 9 IU/ dl. After admission, on the same day her abdominal pain increased, which was initially thought to be due to gastritis and abdominal colic, which commonly occur associated with acute urticaria.

After a few hours her pain decreased but plain X-ray abdomen showed gas under diaphragm (Fig.1). Abdomen became very tender with generalised guarding. The Paediatric surgeon was soon consulted, who immediately took up the patient for laparotomy. Per operatively it was found that duodenum harboured a big perforation on the anterior wall below the pylorus (Fig 2). Perforation edges were trimmed and closed with Graham's patch and peritoneal toilet was given. The child had an uneventful recovery after surgery and was discharged after a week. There was no family history of peptic ulcer disease or previous dyspeptic symptoms in this child, and no obvious cause for the acute perforation could be found out except for the oral steroids given for urticaria.

Discussion

Peptic ulcer disease in children and adolescents is rare. Peptic ulcers have been classified as primary when no aetiological factors are apparent and secondary when they result from disorders elsewhere in the body[1]. There is a strong correlation between Helicobacter pylori infection and primary peptic ulcer disease. Secondary peptic ulcer as in our patient usually results from stress, systemic illness or medications like nonsteroidal anti-inflammatory drugs and corticosteroids[2]. Zollinger Ellison syndrome and Crohn's disease also can result in secondary gastric ulceration. Other causes are Cushing's ulcer due to traumatic head injury and Curling's ulcer due to serious burn injuries. Secondary ulcers in older

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children are frequently single and deep instead of multiple superficial ulcers seen in the adult[3].

Various investigators have made varied observations regarding the distribution of stress ulcers in children[4,5]. Unlike primary peptic ulcer disease which presents with long standing complaints especially nocturnal, secondary ulcer presents acutely. Diagnosis is therefore more difficult and usually made when a catastrophic event such as perforation or haemorrhage occurs[3]. Such ulcers tend not to recur after healing if either the offending agent is removed or the underlying disease predisposing to mucosal ulceration is successfully treated. In case of urticaria as in our patient, there is a likelihood of histamine induced increased acid release also, in addition to the drug implicated. Probably that could have caused the sudden severe ulceration culminating in perforation of the bowel.

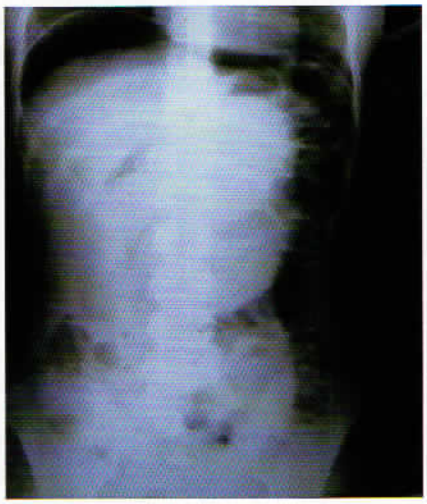

Fig 1: Plain X-ray abdomen erect showing gas under diaphragm

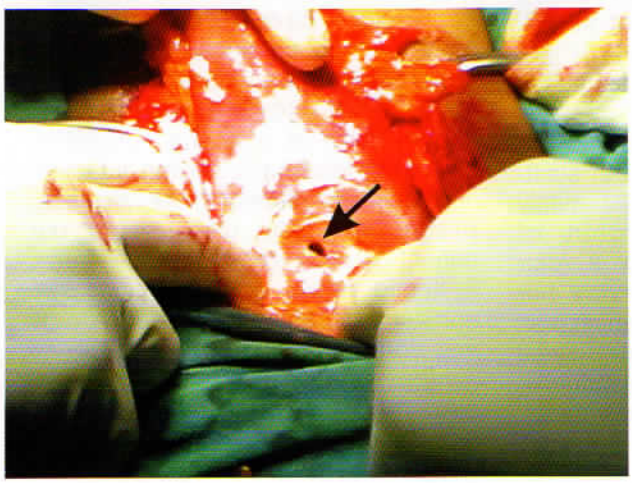

Fig 2: Per operative picture perforation of duodenum

Conclusion

- This case stresses the importance of being on the watch out for the symptoms of dyspepsia while using drugs like corticosteroids or NSAID and advice regarding giving the tablets after food only.
- H_2 blockers if used along with these drugs is also likely to reduce the chance of similar events.

Acknowledgement

We express our sincere thanks to Dr Vinod Kumar, DNB resident , Department of surgery for helping us with the photographs.

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✪ CASE REPORT

A case of Placental mesenchymal dysplasia:

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Abstract

Placental mesenchymal dysplasia is a rare entity of placentomegaly with vesicles[1]. It is often associated with IUGR and foetal demise[2]. About one third of the cases are associated with Beckwith Wiedemann syndrome. This case is reported due to its rarity, and as is it often misdiagnosed as molar pregnancy on both ultrasound and gross examination.

Keywords: Placental mesenchymal dysplasia, Cystic placenta, Beckwith Wiedemann syndrome, Pseudomolar pregnancy.

Introduction

Placental mesenchymal dysplasia (PMD) is a rare placental vascular anomaly which shows placental enlargement with vesicle formation. The chorionic plate vessels may be abnormally dilated and tortuous. It resembles partial molar pregnancy by ultrasonography and on gross examination. But there is absence of trophoblastic proliferation on histological examination.

Clinical presentation

A 34 year old lady ($G_2P_2L_1$), was admitted at 34 weeks of gestation. EDC was on 05/09/09. She had pregnancy induced hypertension (PIH), pedal oedema and oliguria.

Renal function tests showed elevated blood urea (60 mg%) and uric acid (7.8 mg%) levels. Lactate dehydrogenase level was also raised: 699 U/L. βhCG value was normal.

Ultrasonography: revealed a single live intrauterine gestation, cephalic presentation with a posterior placenta and adequate liquor.

Emergency caesarean section was done for uncontrolled PIH and a preterm female baby weighing 1.85 kg was delivered. The placenta was sent for histopathologic examination.

Gross structure of placenta: It was large and weighed 850 gm; umbilical cord was normally attached (Fig.1). Maternal surface showed multiple vesicles, the largest measuring 2 x 2 cm across (Fig. 2).

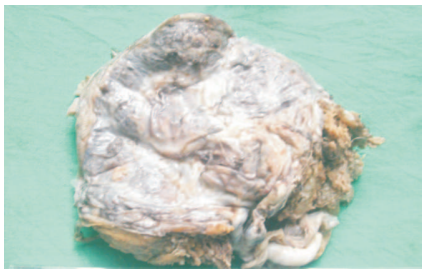

Fig. 1: Large placenta, foetal surface

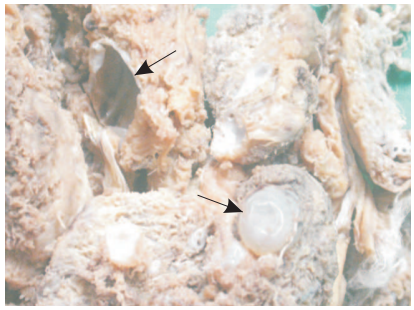

Fig. 2: Surface vesicles (arrows) on maternal surface

Microscopy

Showed marked enlargement of stem villi with cistern formation and thick walled blood vessels (Fig. 3). Normal villi were also seen scattered in between (Fig. 4); some small areas of chorangiosis were seen.

Trophoblastic proliferation seemed to be absent. Structure of the umbilical cord and membranes also appeared within normal limits.

Diagnosis: Placental mesenchymal dysplasia

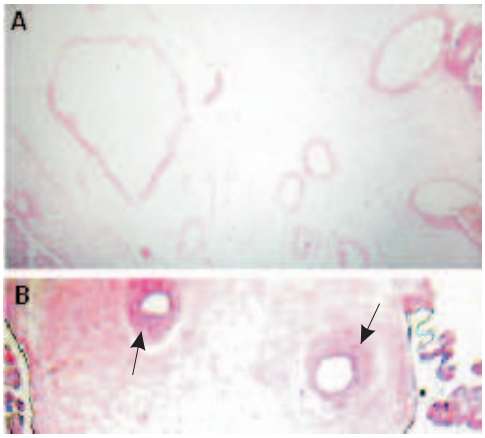

Fig. 3A: Enlarged stem villi & cistern formation
B: Thick walled vessels

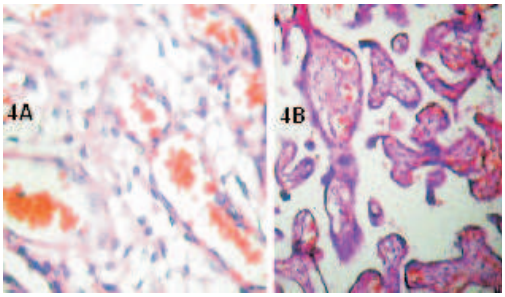

Fig. 4A: Chorangiosis
4B: Normal villi; no trophoblastic proliferation

Discussion

The true incidence of PMD is not known as it is under-diagnosed and under-reported. There is a definite preponderance in female foetuses (female:male = 3.6: 1)[3]. PMD is associated with Beckwith Weidemann syndrome (BWS) and foetal growth restriction. It can also occur with a normal appearing foetus. The components of BWS are macrosomia, exomphalos, macroglossia, omphalocele, gross visceromegaly, placentomegaly and increased susceptibility to childhood tumors[4]. PMD and BWS are considered a spectrum of phenotypic changes with a common etiology.

Androgenetic mosaicism provides an aetiology for PMD[5], and may be a novel mechanism for BWS and unexplained intrauterine growth restriction. Preferential allocation of the normal cells into the trophoblast explains the absence of trophoblast overgrowth. PMD has also been reported in association with hepatic mesenchymal and pulmonary hamartoma[6,7].

Histological similarity between PMD and chorioangioma suggests a common embryologic origin[8] for both these anomalies. USG studies indicate that the circulatory imbalance is due to hypovascularization of the dysplastic lobules, which induces the progressive dilatation of chorionic vessels.

The underlying cause of PMD is currently unknown. Hypoxia and hypoperfusion of unknown etiology stimulate the fibroblasts to produce increased connective tissue. Increased production of vascular endothelial growth factor (VEGF) leads to angiogenesis and vascular malformations[9].

Immunohistochemical studies show that stromal cells of normal and dysplastic villi are immunoreactive for desmin[10], similar to an age-matched normal placenta. Heazellab, et al report[11] positive immunostaining for lymphatic endothelium; this abnormal lymphangiogenesis is considered a possible aetiology of PMD.

DNA ploidy analysis[12] of the abnormal villi in most cases demonstrated normal diploid constituency. Most cases are diagnosed by prenatal ultrasonography. The sonographic features are similar to those of partial moles. An increased level of maternal serum alpha fetoprotein is seen[13]. βhCG level is usually normal. In a latest study[14] chorionic villous sampling has been suggested in the prenatal diagnosis of PMD.

Conclusion

Placental mesenchymal dysplasia should be included in the differential diagnosis of cystic lesions of placenta by sonography, especially when a phenotypically normal appearing foetus can be identified. This may prevent unnecessary termination of pregnancies during the first half of pregnancy.

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PUSHPAGIRI MEDICAL JOURNAL

✪ REVIEW ARTICLE

Transradial angioplasty: A major shift in Interventional Cardiology

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Abstract

Coronary Artery Disease will take epidemic proportion by 2015 and will exceed infectious diseases as the most common cause of death in our country, predict experts. There have been numerous advances in coronary angiography since Hales performed the first angiogram in 1711 on a horse[1]. In humans, the femoral artery has traditionally been the preferred site of arterial access for coronary procedures. Though this route provides an easier vascular access, it is associated with a small but potentially serious incidence of vascular complications at the puncture site. A useful alternative approach is the transradial access. Radial approach to angioplasty has become increasingly popular since its initial use in 1989 due to its relative safety, very low rate of vascular complications, cost effectiveness, early mobilization and patient comfort than other approaches[2]. The objective of this article is to review the currently available information regarding the efficacy, safety, benefits and limitations of radial angioplasty. Research has provided evidence that the radial approach is safe in most populations and has many added benefits over femoral approach. More research needs to be conducted in order to best define the patients in whom this approach is most effective.

Keywords: Allen's test, Coronary angiography, Coronary angioplasty, Transradial angiography, Transradial angioplasty.

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The beginning of angioplasty…

In 1844, French Physiologist Claude Bernard used catheters to record intra-cardiac pressures in animals, coining the term "cardiac catheterization"[3]. The first human cardiac catheterization was performed in 1929 by Werner Forsmann, a German surgical resident, who postulated that catheterization of right heart via the venous system would allow safe access to cardiac chambers. Using himself as a subject, Forsmann anesthetized his own elbow, introduced a needle through his antecubital vein and inserted the catheter (65 cm). A subsequent X-ray documented the catheter's position in right atrium, a historic landmark in the development of angioplasty[1]. Cournard and Richards furthered this intervention in 1941 when they employed a catheter to measure the cardiac output, for which they were awarded Nobel Prize in 1956[1].

Numerous advances relevant to angioplasty were made in the 1950's and 60's. Mason Jones, a Paediatric cardiologist using catheter dye techniques to work on the aortic valve inadvertently catheterized the coronary artery of a patient, leading to the observation that the coronary arteries could tolerate contrast dye, thereby giving birth to the diagnostic coronary angiogram. Melvin Judkins perfected the technique of coronary angiography via the femoral route by introducing more advanced catheters in the late 1960's[1].

In 1963 Charles Dotter recanalized an occluded right iliac artery by passing a percutaneously-introduced catheter retrograde through the occlusion[4]. Recognizing the potential of his finding, he conducted the first transluminal dilatation in an 82 year old woman with popliteal artery stenosis with Judkins in 1967. Initial criticism of these techniques focused

on the need for large bore rigid dilators, and large shear forces to atherosclerotic plaque, which made the technique cumbersome with potential risk to the branch vessels. However Dotter's European peers improved upon these techniques and devised new methods for peripheral artery angioplasty, despite that his techniques were not received favorably in the United States for several years[1].

In mid-1970's, Andréas Gruentzig miniaturized the equipment to be used in coronary arteries. With Myler, he performed the first coronary angioplasty in a human in 1977. He tried retrograde passage of a balloon catheter through an arteriotomy made in the left anterior descending coronary artery distal to the stenosis, before placing the bypass graft. Newer devices that could be delivered through smaller guiding catheters[1] were introduced.

How is femoral angioplasty done??

Skin around the femoral artery is anaesthetized with Xylocaine. The artery is punctured with a needle and a 10 cm long sheath is positioned inside the femoral artery. A 110 cm long preshaped catheter, usually 2.3 mm in diameter is introduced through the sheath and negotiated through descending aorta into ascending aorta and then into the coronary artery. Through this catheter a balloon is introduced and positioned across the stenosis and the balloon is inflated to eliminate the stenosis. A stent is positioned at the site of stenosis to prevent recoil of the dilated vessel.

Femoral approach – at crossroads…

The femoral route is popular, as puncturing the accessible and large calibre femoral arteries is relatively easy, and most coronary catheters are pre-shaped to facilitate procedures performed in this route. However it is associated with small but potentially serious complications, like pseudoaneurysm formation at the puncture site, AV fistula, arterial occlusion, nerve injury and most seriously, retroperitoneal bleed. These morbidities are usually not life-threatening, but often prolong hospitalization and sometimes require blood transfusion or surgical repair. Transfemoral approach may be unsuitable in some patients due to severe aorto-iliofe-moral obstructive disease, abdominal aortic aneurysm, groin infection or gross obesity.

Transradial approach…

Transradial access is an excellent alternative to femoral puncture. This artery has a superficial course; there are no nerves or veins of significant size near the usual site of puncture. The hand's dual arterial supply from radial and ulnar arteries adds an extra level of safety to the arterial puncture, should any thrombotic or traumatic arterial occlusion occur. It has been proved that in critically ill patients who had a prolonged cannulation of the radial artery, incidence of ischaemic damage to hand is minimal despite frequent occurrence of arterial occlusion[5].

History of Radial angioplasty…

In 1989 Lucien Campeau attempted the first radial artery approach postulating that it would be free of significant vascular complications. Campeau studied this approach in 100 patients using French 5 introducer sheaths and pre-shaped catheters[6]. Although radial artery cannulation as difficult, the impediments could be overcome with experience. Few complications, like radial artery aneurysm, haematoma, and compartment syndromes arose, proving that benefits outweigh the risks of the procedure.

Following Campeau's report, studies were conducted in patients in whom femoral approach was difficult or contraindicated due to advanced arteriosclerosis[7,8]. Otaki followed with 40 patients, all with indications for coronary angiography, easily palpable radial and ulnar arteries, and a normal Allen's test[9]. One patient was converted to brachial approach due to inability to advance the catheter. In the remaining 39 patients, selective left coronary angiography was done using a left Judkins catheter; the saphenous vein graft entered successfully using right Judkins or Amplatz catheters. In five patients (13%), the radial pulse remained acutely diminished, but there were no complaints of pain; bleeding at the puncture site occurred in one patient (3%) and subcutaneous bleeding around the site in five patients (13%).

In 1995, Kiemeneij et al[10] conducted transradial artery angioplasty using 6F introducer sheaths with new 6F guiding catheters. At that time, there was a trend towards using smaller PTCA guiding catheters. This evolution toward smaller equipment made the radial artery a suitable access site for PTCA. In 100 patients with collateral blood supply to the right hand, PTCA was attempted using 6F guiding catheters and rapid exchange balloon for exertional angina (87%) or nonexertional angina (13%). Angioplasty was attempted on 122 lesions (type A 67 [57%], type B 37 [30%], and type C 18 [15%]). Coronary cannulation was successful in 94 patients. The six unsuccessful interventions had successful PTCA through the femoral artery (n=5) or the brachial artery (n=1). Average minimal luminal diameter was increased from 0.9 ± 0.3 to 2.0 ± 0.5 and diameter stenosis was reduced from 74% ± 11% to 24% ± 11%27. The authors speculated that early withdrawal of the sheath immediately after the angioplasty, and aggressive anticoagulation may be important factors in the prevention of radial artery thrombosis.

How is transradial procedure done???

We use the right radial artery whenever possible as it was nearest to where the operator stands while facing the cardiac monitors. Before attempting transradial access, it is important to ascertain that the modified Allen's test is normal (positive), thus confirming an adequate collateral arterial supply from the ulnar artery (Fig.1). The majority of patients should have apositive Allen's test; in a study by Benit et al in 1000

patients undergoing cardiac catheterisation, 73% had a normal Allen's test[11].

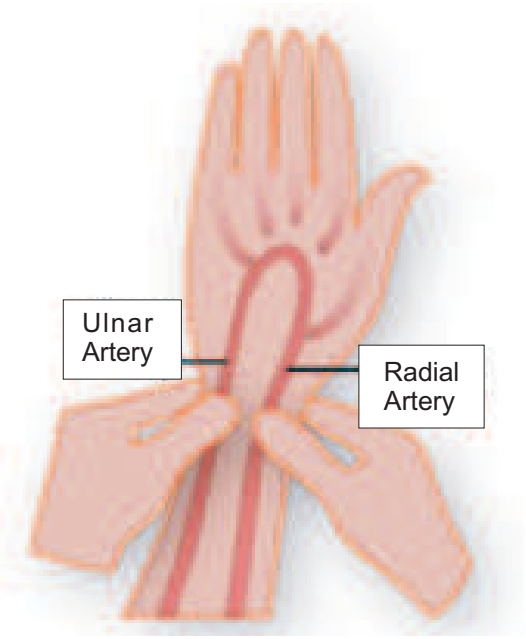

Fig. 1: Allen's test

The wrist is sterilized and draped, hyperextended over an arm board, and the skin anaesthetized with about 2 ml of 1% lignocaine. The radial artery was punctured 1 cm proximal to radial styloid process with a 20 G jelco needle and an 11 cm sheath is inserted into the artery using the Seldinger technique. Through the radial sheath side arm, a cocktail consisting of dilzem (5 mg) and nitroglycerine (100 mic) to reduce radial vasospasm, and heparin (5000 U) to prevent artery occlusion.

The coronary catheters are advanced into the aortic root over a 150 cm long 0.035" guide wire under fluoroscopic guidance (Fig. 2). Once the procedure is completed, the radial sheath is removed in the lab, pressure is applied over the puncture site and haemostasis is achieved (Fig. 3).

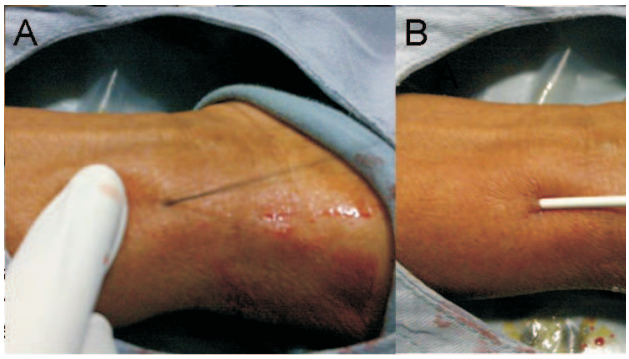

Fig. 2: A - 0.021 straight wire passed into radial artery
B - Sheath passed over the wire into the artery

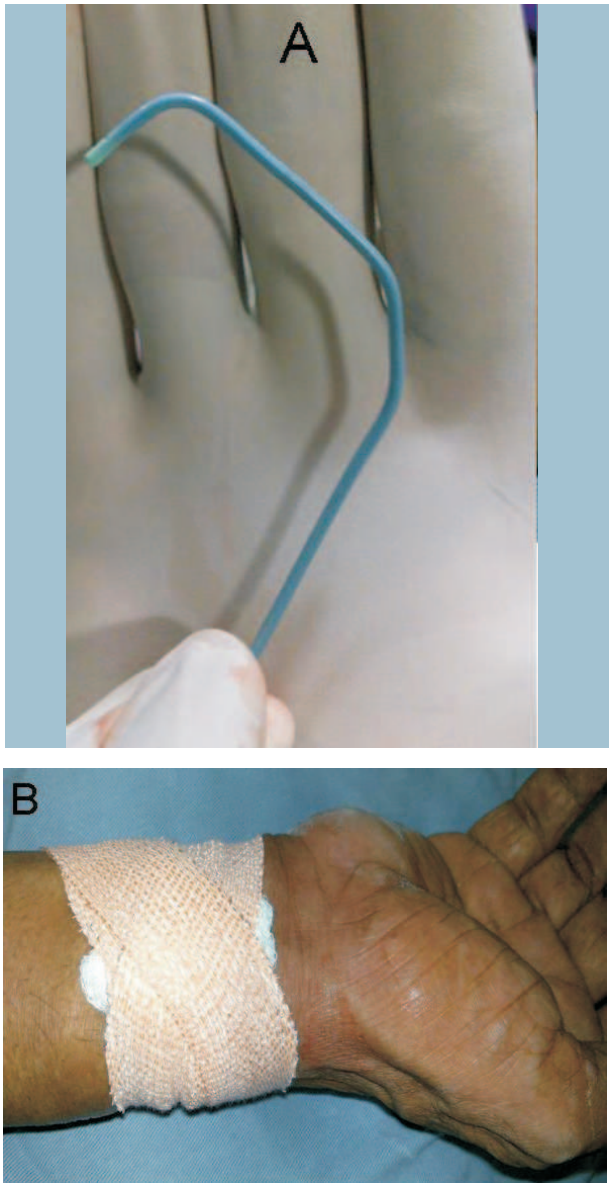

Fig. 3: A - Catheter (2 mm diameter) for angiogram
B - Sheath removed and haemostasis achieved

Advantages of transradial procedures….

1. Truly an OP Procedure: Patients can go home four hours after radial angiography, making it truly a "day case" procedure. Come in the morning, have angiogram and go home by afternoon or evening.

2. Groin region not "handled": Both women and men would rather have a procedure through the wrist than the groin. It is a lot more comfortable to have shaving and cleaning at wrist.

3. No need be in bed after test: After femoral angiography, patients have to lie flat in bed, fairly motionless, for at least eight hours (sometimes overnight). After radial angiogram, patients can walk straightaway.

4. Boon for back pain patients: Most people with back pain find it difficult to lie motionless for more than a few minutes, as changing position brings comfort. Imagine asking such a patient to lie down for 12 hours!

5. Urinary catheterization unnecessary: After angiography though femoral route, patients have to lie down urinary catheterization may be needed. As patients undergoing radial angiography can walk immediately after the test, there is no need for urinary catheterization.

6. Procedure can be done even if the patient is on anticoagulation: In 2006, Lo and colleagues reported on the safety of transradial right and left heart catheterization in 28 consecutive patients who were anti-coagulated to an INR of 2.5, showing low bleeding and thromboembolic risk[24].

7. More suitable in ACS & Primary angioplasty: TRI can be advantageous in patients with acute coronary syndrome (ACS) where aggressive antithrombotic and antiplatelet therapy like glycoprotein 2b 3a receptor antagonists is often instituted. Mann et al compared the use of radial and femoral access sites for PTCA in 142 patients with ACS, and found identical 96% primary success rate. The use of abciximab did not differ significantly (15% in radial group, 10% in femoral group). However, there was no access site bleeding complication in radial group, as compared to femoral group (4%)[12]. Transradial primary angioplasty for acute myocardial infarction patients also appeared to be feasible and safe in selected patients, with the main clinical advantage of reducing severe access site bleeding[13].

The downside of transradial procedure:

1. Radial approach failure: occurs in 1-9% of cases; the main causes are failed radial puncture, anatomic variations of the radial artery (Fig. 5,6) and small calibre vessels[14-18]. Yokoyama et al performed ultrasonography of the radial artery in 115 patients before transradial procedures, and found anatomic variations in 11 patients (9.6%): tortuous arteries with maximum angulation of more than 45^0, stenosis, hypoplastic radial arteries and radioulnar loops. Despite these, transradial access was successful in the majority of patients, except for those with hypoplastic arteries[19].

2.Radial artery spasm: related to circulating catecholamines and vessel trauma is a major limitation of this approach, occurring in up to 10% of cases. These difficulties required more operator experience and materials better suited for the radial artery route[22]. It has been demonstrated clearly by Kiemeneij that administration of an intra-arterial vasodilating cocktail (0.8 mg verapamil), prior to sheath insertion reduces the incidence and severity of radial artery spasm in patients undergoing these procedures[23].

3. Failure of selective coronary ostium catheterization: as a result of major tortuosities of brachial and subclavian arteries (Fig. 6,7) or major aortic arch dilatation.

4. Presence of an aberrant right subclavian artery anomaly (ARSA): is a major cause of particular problems for the right radial artery operator (Fig. 8). It is the most common congenital aortic arch anomaly, with a

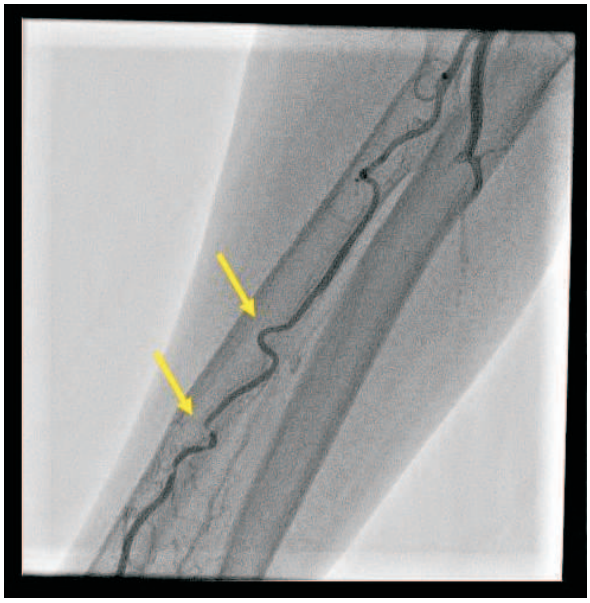

Fig. 4: Extreme tortuosity of radial artery

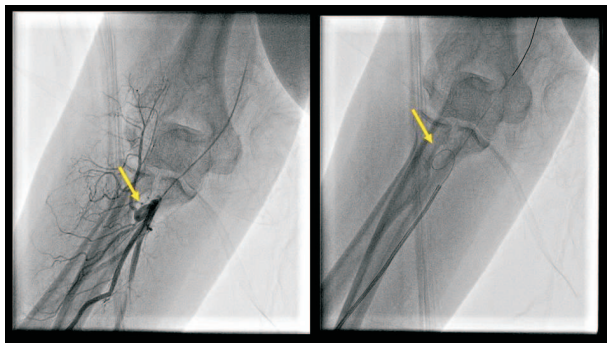

Fig. 5: A 360^0 loop in radial artery; the wire has negotiated the loop

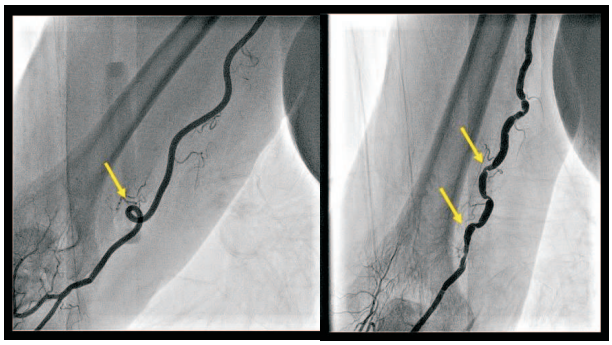

Fig. 6: Loop in brachial artery

Fig. 7: Tortuosity of brachial artery

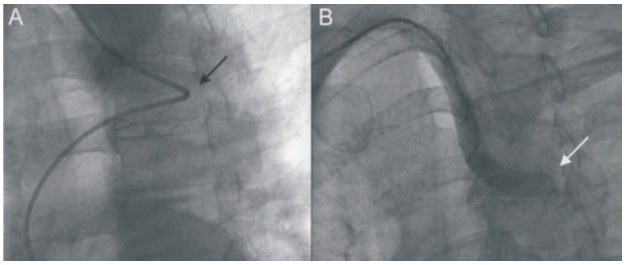

Fig. 8: Aberrant right subclavian artery: Characteristic angle of catheter in left anterior oblique view. Angiography ostium of ARSA in descending aorta

reported prevalence of 0.4-2%. The presence of an ARSA makes cannulation of the coronary ostium, especially the left, difficult and in some cases, impossible. In their retrospective study of 3730 transradial patients, Abhaichand et al reported finding an ARSA in 11 patients (incidence of 0.4%); however, the transradial procedure was completed successfully in ten of those patients by selecting appropriate catheters[20].

5. Radial artery occlusion: was found in 5% of patients at hospital discharge, and was still present in 3% of patients at one month follow-up. However, there were no clinical symptoms associated with these, due to the adequate collateral supply from the ulnar artery. Therefore radial artery occlusion after transradial access is not considered to be a major event[14].

6. Increased radiation exposure to the operator: may result from routine use of transradial approach. Lange and von Boetticher reported an increase in radiation exposure by radial approach, in a randomized comparison to femoral approach[25].

Conclusions and Implications for long-term use

To conclude, radial angiogram is being considered as the gold standard for evaluation of CAD and radial angioplasty is gaining recognition in India as it is safer and has fewer complications. Given data being presented recently on the safety and efficacy of the transradial approach for more complex lesions (eg. bifurcation), peripheral disease, coronary bypass graft angiography, as well as potentially right and left heart catheterization and primary angioplasty during acute myocardial infarction, it is likely that the indications for radial artery access to coronary angioplasty will continue to grow. The transradial technique is gradually gaining popularity, and is in fact, the primary mode of access in some cardiology centres. Our own experience demonstrates transradial access for coronary angiography or angioplasty to be a safe, effective and elegant alternative to transfemoral access, and is suitable for a wide variety of patients. Also, the patient is in and out of the hospital, the same day and may return to work after few hours, almost certainly the next day. It is as simple as going to the dentist to have a tooth extracted!

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PUSHPAGIRI MEDICAL JOURNAL

✪ TECHNICAL REPORT

Leptin – a multifunctional protein

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Abstract

Leptin is a 16 kDa circulating protein hormone produced by fat cells[1]. The word leptin is derived from the Greek word *leptos,* meaning thin. It plays a key role in energy intake and expenditure. The *Ob (lep*) gene, (*Ob* for obese and *lep* for leptin) is located on chromosome 7 (seven) in humans[2].Leptin has a key role in the long term maintenance of weight homeostasis. Studies on mutant, obese mice by Jeffrey M Friedman and his colleagues of Rockfeller University (1994) led to the discovery of this adipose derived hormone. This discovery revolutionized the understanding of nutritional physiology, and further research showed it to be an integrative hormone in diverse systems like neuroendocrine axis, immune functions, haematopoiesis, endothelial proliferation and brain development[1]. The present paper tries to highlight the role of leptin as an integrative hormone in addition to our current understanding about leptin in regulating appetite and energy expenditure.

Historical background

Researchers from Jackson laboratories (1950) discovered two recessive mutations in mice, obese *(ob/ ob)* and diabetic *(db/ db)*, both of which resulted in syndromes of hyperphagia, low energy expenditure, morbid obesity, insulin resistance and neuroendocrine abnormalities. Later Coleman suggested that *ob* gene encoded for a humoral factor which decreases appetite and increases energy expenditure, whereas *db* gene encoded for its receptor[1].

The discovery of 'leptin' led to understanding of the missing link, as to how this regulatory mechanism acts on the effector organs (like the brain) to maintain energy balance. Now it is understood that this adipose derived hormone serves both as a 'sensor of energy' and as a 'signal to hypothalamic targets' for regulation of appetite and metabolism[5].

Soon after *ob* gene discovery, its expression as 4.5 kb mRNA transcript in adipose tissue was also unraveled. Leptin receptor *(ob-R)* was isolated from mouse choroid plexus by Tartaglia et al (1995).

The first report of morbid childhood obesity due to frame shift mutation of ob gene was from a Pakistani family (with consanguinity) in 1997. The first case of human obesity due to mutations leading to deletion of intracellular and transmembrane domains of *ob-R* were reported in a French family of Kabalian origin by Clement et al in 1998; three sisters homozygous for this mutation had early onset obesity, impaired linear growth and hypothalamic amenorrhea[1].

Structure of Leptin

Leptin in humans is a 146 amino acid sequence containing four helix bundles connected by disulfide bonds[3]. The three dimensional structure is shown in Fig. 1.

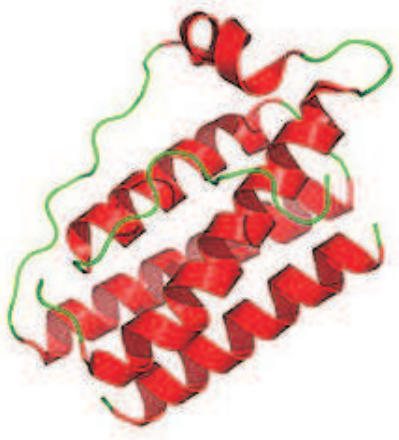


Fig. 1: Structure of Leptin[3]

Source

In addition to white adipose tissue, leptin is produced by brown adipose tissue, syncytiotrophoblast, ovaries, skeletal muscle, stomach, mammary epithelial cells, bone marrow, pituitary gland and liver[2].

Plasma levels, transport and clearance

Levels of leptin are higher in obese than in lean individuals; the values are higher in females than in males.

An acute rise in its levels within hours after a meal is seen in rats, but not in humans. Starvation and reduction in body weight decreases leptin levels in both. The levels rise in the course of the day and peak at night.

A strong positive correlation has been noted between insulin levels and leptin. Insulin directly stimulates leptin mRNA expression. Table 1 lists the factors which alter leptin levels in serum.

Table 1: Factors that influence serum leptin levels

Increase in levels	Decrease in levels
Over feeding	Fasting
Obesity	Testosterone
Insulin	Β adrenergic agonist
Glucocorticolds	Thiazolidinediones
Acute Infection / sepsis Endotoxins Cytokine Interleukein Tumor necrosis factor (TNF) Leucocyte Inhibiting factor (LIF)	Smoking
Glucosamine	Cold exposure (brown fat)

Leptin secreted by adipose tissue does not appear to undergo post translational modification. It circulates as a protein of molecular weight 16kDa. About 5-20% of it is bound to plasma proteins. It is distributed to many organs and gets cleared by kidneys. Leptin can cross the blood brain barrier.

Cellular mechanism of action

Leptin binds to its receptors on the target tissues, which leads to activation of **JAK/ STAT** pathway and its transcriptional regulation[4] (Fig. 2). Leptin receptor exists as a dimer linked an enzyme Janus Tyrosine Kinase (JAK) in the intracellular portion. Binding of leptin to the extracellular portion of the receptor alters its conformation, enabling phosphorylation and activation of JAK. This in turn phosphorylates STAT (Signal Tranducer and Activator of Transcription) proteins in cytoplasm. Activated STAT proteins act as transcription factor initiating new protein synthesis.

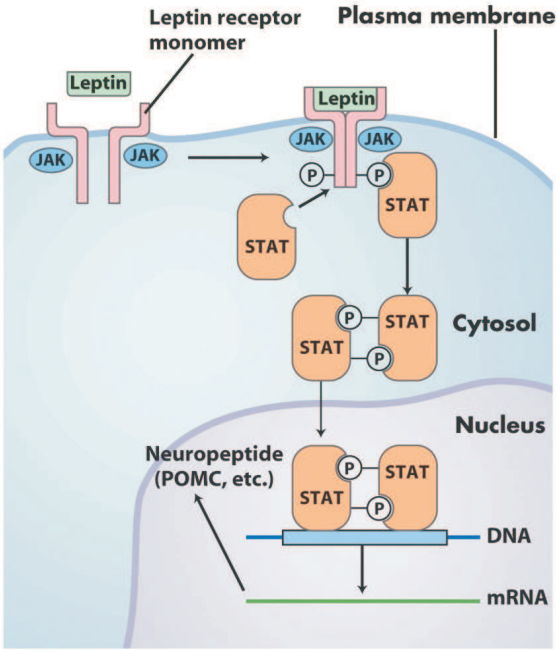


Fig. 2: Cellular mechanism of leptin via the JAK/ STAT pathway

Functions of Leptin

➢ **Role in energy homeostasis**

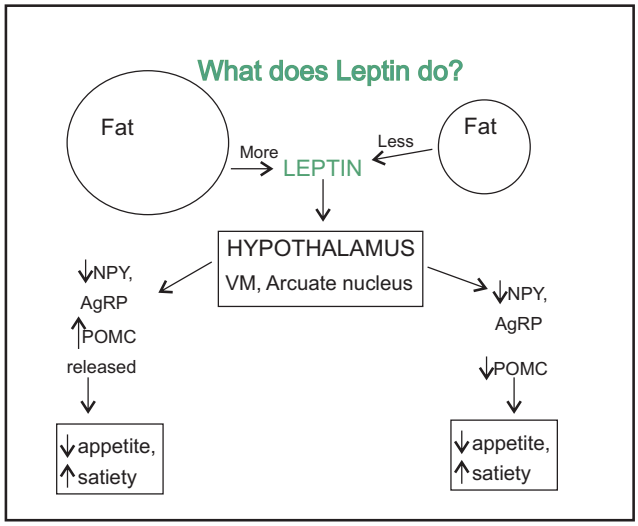
Leptin regulates energy intake and expenditure, by acting on the receptors at multiple sites of hypothalamus, especially arcuate and paraventricular nuclei. Circulating plasma leptin levels are in proportion to the body fat.

Leptin acts by two mechanisms:

(1) It binds to neuropeptide Y (NPY) produced by the neurons in the arcuate nucleus of hypothalamus, and reduces the activity of these neurons; this leads to satiety. Neuropeptide Y facilitates increase in food intake, and decreases energy expenditure.

(2) It suppresses the production of AGRP (agouti related peptide), which is an antagonist that acts on MC4 (melanocortin 4) receptor, a hypothalamic receptor for αMSH (melanocyte stimulating hormone). αMSH and CART (cocaine – amphetamine regulated transcript) are anorexogenic peptides produced from POMC (pro opio melanocortin) secreting neurons of hypothalamus. Both inhibit food intake and increase energy expenditure. NPY also directly stimulates the secretion of αMSH and CART. Thus leptin now has signaled to the brain that the body has had enough food (Fig. 3).

In the obese, the sustained high value of leptin leads to leptin desensitization. This leptin resistance in the obese prevents the body from receiving the satiety feeling subsequent to eating[4].



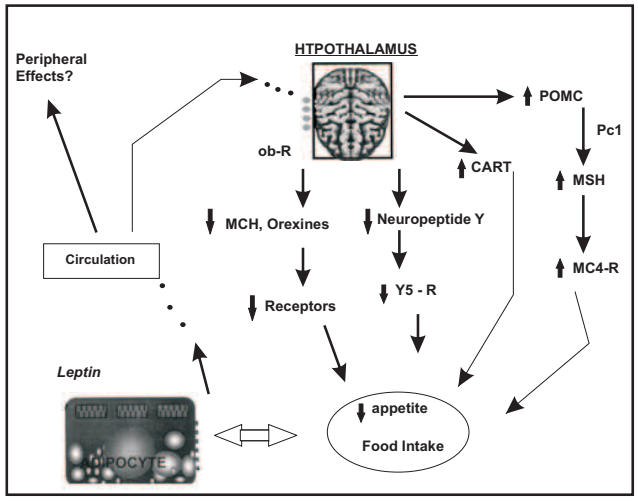


Fig. 3: Mechanism of action of Leptin in Hypothalamus[1,2]

➢ Reproductive system

In mice low leptin levels delay the onset of puberty. Such levels decrease GnRH and thereby FSH and LH levels[8]. This leads to amenorrhea in anorexic persons. Obese mice that cannot produce leptin are infertile.

Leptin is also produced by placenta, so high levels are seen during pregnancy. There is also evidence that leptin plays a role in hyperemesis gravidarum, polycystic ovarian syndrome and bone growth.

➢ Circulatory system

Leptin regulates haemopoiesis in the foetus; it stimulates erythropoiesis, lymphopoiesis and myelopoiesis. It also promotes angiogenesis by increasing vascular endothelial growth factor (VEGF) levels. Also it modulates the activities of T cells. High leptin levels reduce nitrous oxide (NO) and increases the production of superoxides. This damages the vascular endothelium, and could be the cause of increased cardiovascular complications in obesity[14].

➢ Respiratory system

Leptin induces the production of surfactant by type II pneumocytes[2].

➢ Endocrine system

Leptin regulates lipid and glucose metabolism by an action independent of its effect on appetite and body weight. It stimulates lipolysis, gluconeogenesis and glucose metabolism. It also stimulates sympathetic activity in adipose tissue, adrenal glands, kidney and hind limb muscles.

Leptin has been reported to regulate the levels of GH, TSH, GnRH and glucocorticoids[8].

➢ Nervous system

The plasma concentration of leptin determines its entry into the CNS. Leptin regulates neuronal and glial tissue growth[1]. A recent study by Dr Sudha Seshadri states that high leptin levels are associated with a lower incidence of Alzhemier's disease[15].

Recent advances

Leptin can be useful in the treatment of:

- *Breast cancer*

A class of anticancer drugs called EGFR (epidermal growth factor receptor) inhibitors which are not used now can be effective in obese persons. In obese patients leptin and IGF-1 stimulates the migration of cancer cells in breast. EGFR inhibitors prevent this stimulation[16].

- *Diabetes mellitus*

A leptin regulated gene IGF BP2 (insulin like growth factor) is found to have antidiabetic effect[17].

- *Osteoporosis*

Stimulation of leptin serotonin pathway increases the bone mass in the body. This explains why obese persons are less osteoporotic[17].

Future perspectives

Trials are underway to assess the efficacy of human recombinant leptin in the treatment of obesity. For this purpose, it needs to be administered in large and frequent doses, owing to its low circulating half life, low potency, and poor solubility. Due to the occurrence of inflammatory response in the skin to leptin injections, drop outs in the trial were frequent.

These problems could be alleviated by **Fc-leptin fusions**, which take the Fc fragment from the immunoglobulin gamma chain as the N terminal fusion partner with leptin. This makes the Fc - leptin fusion highly soluble, more biologically potent and prolongs serum half life. This enables Fc - leptin to become a potential drug in the treatment of obesity in humans. More extensive testing is being done on the use of Fc - leptin and the results are awaited[1].

Future studies would aim at identifying the molecular basis of defective leptin in obesity.

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PUSHPAGIRI MEDICAL JOURNAL

✪ TECHNICAL REPORT

Taking stock of Health Research*

"Between the health care we have and the care we could have, lies not just a gap, but a chasm."

(IOM Report, Crossing the Quality Chasm)

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Erosion of public trust in Science and Research

Mutual trust between the government officials, health experts, public and media is needed in order to advance the cause of global health, science and research. In her hardhitting book Betrayal of Trust, Laurie Garrett writes: "Over the last 20 years trust has frayed and our global public health system has been systematically destroyed. The impact has been felt by average citizens, as a blow to both their personal health and their pocket books". This broken trust has to be restored.

The Government, public institutions and private companies often present simplified explanations and do not reveal the full facts when communicating health issues. Rather than admitting their uncertainty in the decision-making process, they prefer to give the public reassuring advice. There is a growing awareness that this is the wrong approach. Political credibility and public trust are rapidly lost if the public believes it has not been given the full facts, especially on the risks that affect them.

While advances in information and communication technologies create opportunities for people to have more access to information than ever before, the challenge is to ensure that they are enlightened and empowered rather than getting drowned and disenfranchised by this revolution. There are many incidents that have eroded public trust and confidence in science and research in recent years. Highly publicized cases of scientific fraud, misconduct and malpractice have only added to the public's suspicion. Increased industry funding of scientific research in universities and other public institutions, academic pressures to "publish or perish" and insufficient accountability have led to questions about whether a research system can be relied on to regulate itself and serve society's needs. The growing interdependence and blurred interface between science, business and industry have raised questions about ethical conflicts between scientific values, profits and personal gain. These tensions have, in turn, raised concerns about the funding of science, peer review, scientific transparency, the ownership of knowledge, and fair sharing of the products of research. Complicating matters further is the confusion that arises when the experts cannot agree on what the results of research mean.

A health research system should build public trust in itself and its products by effectively communicating benefits as well as risks and uncertainties. Unfortunately, this ability to communicate with the public is one of the weakest attributes of most governments and health researchers. After all, it is the lay public (as taxpayers and philanthropists) who foot a large part of the bill for research. Health research is a multidisciplinary activity which exists at national, regional and global levels and it requires large scale public investment. And with the public's support much can be accomplished. Given the importance of linking health research and its application to public health, representatives of civil society should participate in setting the research agenda, in major health policy decisions and in the design,

* Adapted from WHO report on **Knowledge for Better Health, Geneva 2004**

Continued from page 44, PMJ Vol 1, No.1

implementation and evaluation of public health programmes.

More recently, the field of HIV/AIDS research has demonstrated the positive impact of engaging the public in the research process. But such co-operation between funders, the research community and civil society has neither been easy nor timely and it is still the exception rather than the rule. For example, public concern and consternation over HIV treatment trials in developing countries contributed to the development of initiatives to inject resources into global AIDS programmes, and to a global debate about drug patents, drug prices and access to medicine. This, in turn, led to important first steps to making anti-retrovirals available to millions of people who could not afford them before.

Financing health research

The discrepancy between expenditure on health activities and health research by the public and private sectors contributes a great deal to the world's health problems. Such a gap and other inequities in health research leads to inaccuracies in assessing the disease burden of populations or population groups, thus contributing to continued disparities in health. The Commission on Macroeconomics and Health underscored one of the key problems by concluding in 2001 that there were no economic incentives for private sector investment to research on diseases that affect the least-developed countries. Though it recommended increased investments to redress this gap and promoted more research on neglected diseases, the health inequality between developed and developing countries remains the single greatest public health problem.

Inequities in setting research agenda

Given that most developing countries do not have an adequate number of researchers or adequately equipped Research Institutes, they cannot ensure that the research that has been conducted meets their needs. Health research in developing countries is often the result of collaborative partnerships where the foreign donor agency or funder usually has more power in deciding the research agenda. This can skew research into areas that are not priority health problems for the local population.

Biomedical and Clinical research in both developed and developing countries are increasingly being funded and controlled by pharmaceutical and biotechnology companies. This may result in a situation where the drug maker's product portfolio rarely addresses the health priorities of the developing country where the research is being carried out. Another concern is that such collaborations divert already extremely limited qualified staff away from research on more nationally relevant problems.

Some progress, however, has been made. WHO's Ad Hoc Committee on Health Research Relating to Future Intervention Options outlined a five-step priority setting approach to decide how health research funds should be allocated in key areas of concern to developing countries. The Council for Health Research and Development and the Global Forum for Health Research subsequently refined and applied such priority setting tools.

Gender bias in health research

Clinical research has generally excluded female subjects from study populations because it is believed the menstrual cycle introduces a potentially confounding variable. Women are also excluded because of fears that experimental treatments or drugs may affect female fertility and expose fetuses to unknown risks. The consequences of interpreting research results based on studies only involving men as universally valid, without convincing evidence that they apply to women, may be harmful to women (Fig. 1).

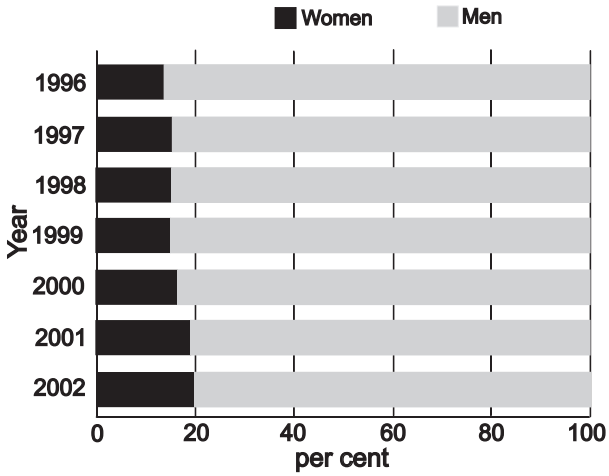

Fig. 1: Membership of WHO expert advisory panels by gender, 1996–2002

Although the proportion of women among medical students and faculty members at all levels in the world has increased steadily in recent years, their representation in decision-making bodies such as research funding committees and research advisory boards has not increased accordingly. Women also tend to be under-represented on the editorial boards of scientific journals. There is also differential treatment of female scientists in terms of career opportunities, salary, and obtaining research funds and post-doctoral fellowships.

Inequities in knowledge publication

More than 90% of scientific publications in health research are published by researchers in the developed world. There is widespread systematic bias in medical journals against diseases that dominate the least-developed regions of the world (Fig. 2).

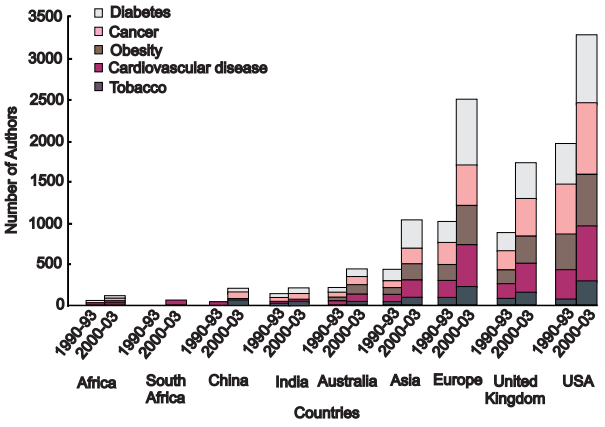

Fig. 2: No. of authors from various regions and published papers on chronic diseases / risk factors

An improvement in the representation of Scientists from developing countries on the editorial boards of major Medical Journals may improve the attention given to health challenges in these countries.

Divide in access to information

The peer reviewed scientific and health-care literature exists in the form of journals. Access to local, regional and international journals is especially important for researchers and systematic reviewers. Researchers in rich countries enjoy relatively easy access to research information but for many researchers in resource-poor environments, access to available research is far from easy. Internet access remains poor and few researchers or institutions in developing countries can afford the high cost of journal subscriptions (print or electronic). The divide in access is exacerbated by the massive increase in the number of scientific articles on health published each year.

Generating new knowledge Vs assimilating 'already known'

Research to date has focused on the generation of new knowledge but has tended to neglect the role and contribution of existing knowledge. This neglect has led to inefficient use of limited resources for research and missed opportunities for achieving health gains.

Knowledge depends as much on the evaluation of existing research as it does on the generation of new research. New research should ideally be interpreted within the context of an existing body of scientific knowledge. Despite their central role in a knowledge-based health system, and despite the skill and time they require, systematic reviews do not attract the same level of academic recognition or public attention as primary (especially biomedical) research. They are largely performed by researchers who volunteer their time outside their main work activities. As a result, the number of published systematic reviews is still relatively small, the coverage of different diseases and other aspects of healthcare are uneven, and few reviews are related to diseases with a high global burden.

Lack of openness and accountability

The diversity of funding sources for research, and the settings in which research takes place, calls for across-the-board policies that provide appropriate guidelines on making research results known. Publication may not be pursued because the results are negative or neutral, or because the trial was stopped before completion.

With increasing interest in commercialization of research findings, sometimes coupled with limited government funding for research, scientists are often the recipients of research grants from the commercial sector. In some cases, they may not have complete control on how the research results are used.

Ethics of research in developing countries

While the fundamental principles of ethical health research, such as community participation, informed consent, and shared benefits and burdens, remain sacrosanct, other issues, such as standards of care and prior agreements, merit greater debate. To sum up, the key challenge is how to effectively manage the “global standard” and “local context” interface.

Reorient research to strengthen Health systems

“Knowledge for Better Health” by WHO (2004) reviews the current state of global health research, and concludes that:

Much more investment is needed for a new,“ innovative approach” to health research.

Health research must be managed more effectively if it is to help strengthen health systems and build public confidence in science.

Stronger emphasis should be placed on translating knowledge into action to improve public health by bridging the gap between what is known and what is actually being done.

The ultimate objective is to facilitate the development of a culture of learning, problem solving and innovation to strengthen health systems, improve health outcomes and equity, and build public confidence in Science and Scientists.

(To be continued)

PUSHPAGIRI MEDICAL JOURNAL

✪ TECHNICAL REPORT

Nanotechnology Towards Healthcare

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Abstract

Nanotechnology is shaping the world atom by atom. Yet, this futuristic technology is not in the awareness of people of all kinds. This article serves to give general information about Nanotechnology, its application in medicine and its toxicological issues. Nanoparticles are smaller particles of size around one billionth of a meter (10^{-9}meter) and Nanotechnology is the study of matter around this size scale. To put this size in perspective, a sheet of paper is about 100,000 nanometres (nm) thick, the flu virus is roughly 2000 nm and mycoplasma is 200 nm in size. Or, to look at it another way, 1 nanometre is approximately 1/800th of a human hair or 1/70th the diameter of a red blood cell. The approaches to nanomedicine range from the medical use of nanomaterials, to nanoelectronic biosensors, and even possible future applications of molecular nanotechnology. Current problems for nanomedicine involve understanding the issues related to toxicity and environmental impact of nanoscale materials.

Key Words: Quantum dots, SPION, Scintillator, Fluorophores, Luminescence, CNTs, Dendrimers, Fullerenes, Buckyballs, Nanodrug delivery, AFM, Biomimetics

Introduction

Though the word *Nano-technology* is relatively new, the existence of functional devices and structures of nanometer dimensions is not new, and in fact such structures have existed on earth as long as life itself. It is not clear when humans first began to take advantage of nanosized materials. It is known that in the fourth-century A.D. Roman glassmakers were fabricating glasses containing nanosized metals. An artifact from this period called the Lycurgus cup is made from soda lime glass containing silver and gold nanoparticles. The colour of the cup changes from green to a deep red when a light source is placed inside it. Photography is an advanced and mature technology, developed in the eighteenth and nineteenth centuries, which depends on production of silver nanoparticles sensitive to light

In 1857 Michael Faraday published a lengthy paper in the '*Philosophical Transactions* of *the Royal SocieQ',* which attempted to explain how metal particles affect the colour of church windows. A catalyst for the development of the modern field of nanoscience and technology was the discovery of particles smaller than the atom: subatomic particles. The work of G. J. Stoney and J. J.Thompson led to the discovery of electrons and the development of quantum physics, ie. the field of particle physics. This work led to enquiry into thenature and substance of small particles. In the 1920s, Irving Langmuir introduced the concept of a monolayer, which is a layer of material one molecule thick. Over the next half century, the development of various scanning microscopes enabled visualization and even manipulation of nanosized structures.

In 1960 Richard Feynman presented a visionary andprophetic lecture at a meeting of the American Physical Society, entitled ***"There is Plenty of Room at the Bottom,"*** where he speculated on the possibility

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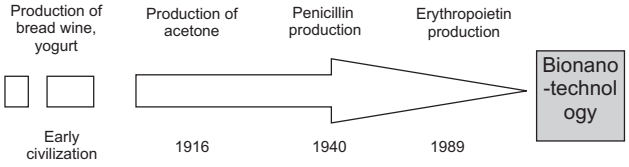
and potential of nanosized materials. He was awarded Nobel Prize in physics in 1965 for his contributions to quantum electrodynamics.

Nano meter scale structures are also present in naturally occurring substances. The abalone, a mollusk, constructs very strong shells having iridescent inner surfaces by organizing calcium carbonate into strong nanostructured bricks held together by a glue made of a carbohydrate-protein mix. Cracks initiated on the outside are unable to move through the shell because of the nanostructured bricks



(Courtesy: Plenty of room for biology at the bottom: An introduction to Bionanotechnology, Ehud Gazit)

At nanometer scale, manmade structures often show novel properties and match typical sizes of natural functional units in living organisms. This allows them to interact with the biology of living organisms.

Nanomedicine will be an essential tool to address many unaccomplished clinical needs of today and in the future. It exploits the improved and often novel physical, chemical and biological properties of materials at the nanometer scale. Nanomedicine has the potential to enable early detection and prevention of diseases. The application of nanotechnology in medicine will progress through three phases as proposed by Robert Freitas Jr in his book “Nanomedicine”.

Phase 1: refers to addressing medical problems by using nanostructures:
Phase 2: anticipates advances in molecular medicine and biotics;
Phase 3: long term, molecular machine systems and nanorobots for diagnosis and therapeutics[1].

New diagnostic tests making use of nanotechnology to quantify disease-related biomarkers could offer an earlier and more personalized risk assessment before symptoms show up. Nanotechnology could improve in vitro diagnostic tests by providing more sensitive detection technologies or by providing better nano-labels that can be detected with high sensitivity once they bind to disease-specific molecules.

Targeted delivery agents will allow a localized therapy which targets only the diseased cells, thereby increasing efficacy while reducing unwanted side effects. Thanks to nanotechnology, pluripotent stem cells and bioactive signaling factors will be essential components of smart, multi-functional implants which can react to the surrounding micro-environment and facilitate site-specific, endogenous tissue regeneration. Imaging and biochemical assay techniques will be used to monitor drug release or to follow the therapy progress.

Classification

Depending on the core material nanoparticles can be generally classified into organic or inorganic nanoparticles[2].

A. Inorganic Nanoparticles

Inorganic nanoparticles have a central core, usually of metal, that defines the properties of the particle, with a protective organic coating on the surface. These properties may be optical, magnetic or electronic (eg. gold nanoparticles, ceramic nanoparticles). The outer layer protects the core from degradation and usually is used to form bonds with other agents.

B. Organic Nanoparticles

They use organic molecules as major building materials. They can be conjugated with other agents. (eg. polymer nanoparticles, carbon nanotubes (CNTs), dendrimers, fullerenes, buckyballs etc).

Synthesis of Nanoparticles

Nanoparticles are synthesized mainly by two routes - 'bottom-up method' and the 'top-down method'[3]. *'Bottom up'* involves arranging small components into complex structures, atom by atom or molecule by molecule, which could include molecular self-assembly. DNA has been used as template for synthesis[4]. *'Top down'* approach involves creating smaller devices by using larger ones to assemble them.

Relevance in healthcare

The application of nanotechnology in healthcare is very vast ranging from imaging (nanoparticles serve as contrast agents/ fluorescent dyes) to biosensors and assays. Nanomaterials have been studied as potential materials for artificial molecular receptors. This field can revolutionize the conventional drug delivery techniques.

The novel targeted nano drug delivery techniques using multifunctional nanoparticles (MFNPs), [ie. Nanoparticle (metallic, polymeric or fluorophore) loaded with drug and contrast agent bound to a suitable ligand Fig.1], help in the imaging, early detection and treatment of diseases.

The drugs are either dispersed throughout the particle [nanospheres] or confined in an aqueous or oily cavity, surrounded by a single polymeric membrane [nanocapsule][2]. The small size of nanoparticles enables the drug to pass through cell membranes which helps in improved uptake.

Nanodelivery system alters exposure time by altering clearance. The nanomedicine increases the specificity by actively targeting diseased sites and tissues. This process is performed by attaching ligands that only bind to specific receptors to the nanoparticle containing a specific drug that allows for targeted therapeutics. Drug release can be controlled on a predetermined schedule, such as release can be triggered by certain molecules, microorganisms or energy radiations of particular wavelengths. These systems will result in reduced and more efficient drug use with improved bioavailability and fewer side effects resulting in more specific effects. Research is ongoing into the use of engineered viral nanoparticles as multifunctional devices for drug delivery[8]. Examples include the adenovirus and the cowpea mosaic virus[9,10].

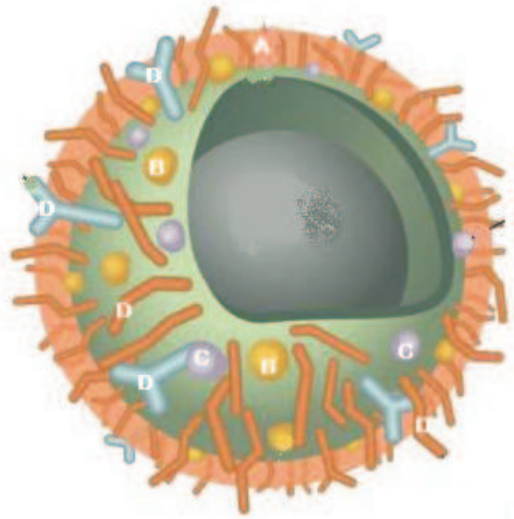


Fig.1: Multifunctional nanoparticles:
A - Drug delivery vehicle B - Therapeutic drugs
C - Imaging agents D - Site specific targeting ligands

Applications in Medicine

I. Implants

Implantable devices range from blood-pressure sensors to insulin pumps and intracranial devices. Biomimicry or biomimetics, is the process of using the way in which nature successfully produces something to create a man-made material. For example, nanopatterned polymer scaffolds that mimic the way in which minerals are deposited are used to make bone and teeth implants.

II. Early Diagnosis

Targeted delivery of scintillating materials (material which exhibit luminescence when excited by ionizing radiation) based on Gadolinium, Yttrium etc or Super Paramagnetic Iron Oxide Nanoparticles (SPIONs) could facilitate their accumulation in metastatic cancer cells and enhance the sensitivity of MRI. The specificities of luteinizing hormone releasing hormone (LHRH) and luteinizing hormone/ chorionic gonadotropin (LH/CG)-bound SPIONs have been tested in human breast[11].

III. Intraoperative imaging

Near-infrared (NIR) imaging using quantum dots are used to light up abnormal tissue so that it can be treated surgically without changing the look of the surgical field. Recent publications by a team have demonstrated the use of NIR fluorescence-guided Sentinel Lymph node Mapping (SLN mapping)[12]. This technology may eliminate the need for radioactive and coloured tracers, permit real-time image guidance, and assist the pathologist in tissue analysis.

IV. Tissue healing and wound care

Various nanoparticles, including those made of silver[13] are being investigated in the area of wound healing. Nanoparticles aggregates are being developed as wound dressings. This wound dressing material has the ability to control the release of active compounds over periods of up to 30 days to promote wound healing.

V. Wound infections

Controlled drug release is being applied to wounds via the use of nanoparticles. A group of researchers have designed a drug molecule that releases an antibiotic only in the presence of a specific infection; they envisage a dressing impregnated with various antibiotics, with actual release of only the one specific for the infecting organism[14]. Other investigators have applied nanoporous silver powders to wounds. These powders have been shown to be effective against Methicillin Resistant Staphylococcus Aureus MRSA (eg, Acticoat; Smith & Nephew, London, UK[15].

VI. Haemostasis

The use of a self-assembling peptide that forms a nanofiber barrier to achieve haemostasis in seconds has been described. Once applied to open wounds, the peptides self-assemble into a nanoscale protective barrier gel that seals the wound and halts bleeding. Once the injury heals, the nontoxic gel is broken down into molecules that cells can use as building blocks for tissue repair. This process has important implications for all forms of surgery[16].

VII. Improved tactile feedback

Gold nanoparticles have been used to create devices that have touch sensitivity comparable with the human finger; this would enable a laparoscopist to get an idea of the firmness of tissue, which could be useful in trying to decide whether tissue is grossly abnormal, rather than having to wait for repeated frozen sections[17].

VIII. Nanotechnology in Regenerative medicine

Regenerative medicine deals with the *in vivo*

regeneration or the *in vitro* generation of a complex functional organ consisting of a scaffold made out of synthetic or natural materials that has been loaded with living cells. The functionalisation of such a porous scaffold with different biomolecules (depending on the targeted cells) or the entrapment of nanoparticles, such as growth factors, drugs or genes, could enhance the success of tissue engineering.

IX. Microsurgery

Smart instrument surgical tools, such as scalpels, forceps, grippers, retractors, and drills, are being embedded with miniature sensors[18] to provide real-time information and added functionality to aid surgeons. A nanosurgeon potentially could perform an operation on a single cell without harming the cell[19]

X. Nanotweezer

Voltages are applied to electrodes attached to carbon nanotubes; this leads to opening and closing of their free ends[20]. The mechanical capabilities of the nanotweezers have been demonstrated by their grabbing and manipulating submicron clusters and nanowires. These devices could be used by nanosurgeon to move and manipulate objects within cells.

XI. Precision Lasers

Precision lasers help us to target a specific organelle inside a single cell, and destroy it, without disrupting the rest of the cell[21,22]. Researchers have destroyed a single mitochondrion within a mouse cell and has cut a single nerve in a flat.

XII. Nanorobotics

This concept is a futuristic potential application of nanoscience. These robots could operate independently or under direction within the human body, monitoring, and healing diseases.

XIII. Nanodevices used in medical field:

Nanotubes: Carbon rods, with a diameter of one nanometer, which may be single walled or multiwalled, are used in drug and gene delivery[5].

Dendrimers: These are man-made molecules that have a tree-like; these regularly developing branches emanate from a core[6]. The branching creates a large surface area to which various ligands can be attached.

Nanoshells: Layered colloids with a nonconducting nanoparticle core[7] covered by a thin metal shell to which ligands can be attached. The thickness of this shell is adjusted to absorb infrared light at specific wavelengths, which would enable the nanoshell to attach to a specific tumour cell. Infrared light then applied allows for killing or other interventions of the nanoshell-tumour entity.

Nanopores: Tiny pores in a membrane that are single-molecule detectors; for example, they may allow the passage of single strands of DNA and, thus, make DNA sequencing more efficient.

Quantum dots: Semiconductor quantum dots (QDs) are nanometer-sized crystals with unique photochemical and photophysical properties that are not available from either isolated molecules or bulk solids. In comparison with organic dyes and fluorescent proteins, these are brighter, more stable and can be excited for multicolour emission with a single light source[34]. They are used in various applications, including as fluorescent dyes.

Nanotoxicology

In 2005, Oberdorster et al defined nanotoxicology as the safety evaluation of nanoengineered structures and nanodevices[23]. Nanoparticles can be inhaled, ingested, injected, or absorbed through the skin where they are distributed through lymphatics. Their actions in vivo are determined by the particular properties of the nanoparticle involved, as shown by Ryman-Rasmussen et al[24]. The greater surface area per mass makes a nanoparticle more biologically active. In addition, dose-dependent cytotoxicity has also been reported[26].

Quantum dots have been shown to penetrate easily intact porcine skin at occupationally relevant doses within the span of an average length work day[27,28]. Other properties that influence nanotoxocity include shape, chemical composition, aggregation, solubility, and the presence of other functional groups or chemicals. Both pro inflammatory and antioxidant activity have been demonstrated[23]. In addition, cytokine production and cell death have been reported. More research is needed, especially because a few reports have disputed these initial findings[29,30].

As continued research into these interactions continues to take place, some researchers have advocated reactive oxygen species generation and oxidative stress as test markers to compare various nanoparticle toxicities[31]. Limited clinical experience with different nanoparticles in their various forms makes it difficult to characterize any particular chemistry[32]. Nanoparticles with different morphologies made of non-biodegradable materials provided invaluable information on their self-assembly and physicochemical properties, but were rarely tested *in vivo*.

Nanotechnological products are being evaluated under the Critical Path Initiative, which was designed to speed the provision of new technologies to patients, but because nanotechnology and nanotoxicityare still in their infancy, the FDA gives each product individual consideration. Along with the FDA, the Environmental Protection Agency (EPA) is also taking steps to evaluate the implications and applications of the impact of nanoparticles and

Ethical considerations

Lenk et al[33] identified four main areas of ethical concern:

- Risk assessment in medical research, diagnosis, and therapy.
- Questions of personal and human identity; for example, surgery at the cellular level that alters DNA might lead one to question whether one is the same human being.
- Enhancement by possible nanotechnological implants, for example, the ability to see infrared light and whether this is ethical.

"Nano-ethics" does not necessarily introduce brand new ethical problems; particles do not necessarily become problematic in a unique way just because they are smaller. However, discourse on the potential of nanotechnology that is rational, fair, and participatory needs to take place to form the basis for informed, responsible societal and political decisions[34].

Conclusions

The agricultural revolution took centuries. The industrial revolution took decades. Molecular nanotechnology will change human civilization more than the agricultural or industrial revolution. The cell repair machines of molecular nanotechnology will not only prevent the natural causes of death, but most death by trauma as well. Artificial molecular machines can perform repairs far faster than the natural healing process. The research in nanotechnology can find out the potentiality of science to its more faithful place and handle technologies miracles to leverage the quality of healthcare by developing cost effective systems. The toxicology of nanomaterials should be also simultaneously investigated.

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PUSHPAGIRI MEDICAL JOURNAL

✪ TECHNICAL REPORT

Material management in hospitals - An overview

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Any organization has several resources, which are **m**anpower, **m**oney, **m**oment (time), **m**achinery and **m**aterials. Management is the application of scientific tools to accomplish the right thing done by the right personnel in the right manner at the right time. It also implies optimal planning and utilization of the resources within the frame work of technology and environmental factors, so as to provide services of acceptable quality (consumer satisfaction) and reasonable amount of profit.

The fast developing Indian economy has placed before the hospital administration a big challenge and a great responsibility. Good healthy economic practices are important for identification of cost effective technologies, allocation of resources and their optimal utilization. Due to the increase in specialization, changing technology and increase in the expectation of consumers and employers, the hospitals require better co-ordination and organizational adaptability. The administrators' expertise is integrated, structuring the perception among staff and consumers, so that changes can be effected without destroying the organizational integrity. Hospital's desire to update technology and competition among the health organizations should always be weighed against the benefits of the organization and the quality of health care delivery.

The objective of material management is to provide the right material at the right place at the right time in the right quantity at the most economical price. Hospitals can apply the various techniques of management to stress these resources in employing the quality and quantity of healthcare without economic loss.

Every health organization requires a continuous stream of materials and supplies for providing quality care to patients. The efficiency of a hospital partly consists in maximizing the quantity of patient care per unit cost while maintaining satisfactory levels of quality and consumer satisfaction. In many organizations many of the resources are scarce and play a key role because 30-40% funds are spent for materials and 40-60% funds are spent on manpower. The importance lies in the fact that any significant diligent restriction of the material cost will go a long way in improving the returns of investment. Administrative personnel are involved in identifying the materials, studying their demand, estimating, procuring, stocking and controlling their release in an optimal manner and in providing quality services to the consumer/ patient at a minimum cost, with a goal at better accountability, co-ordination and performance.

The **operative goals** of an administrator are:

1. Optimum material acquisition
2. Optimum size of inventory
3. Optimum inventory turnover rate
4. Good vendor relationship
5. Material cost control
6. Effective issue and distribution
7. Evaluation of losses and pilferage

There are two kinds of costs associated with materials. These are cost of materials like drugs and other materials including their taxes, and opportunity cost of capital or simply the interest on money blocked in materials, salaries and wages, storage cost rent, property taxes, insurances, material transporting and cost deterioration, evaporation, breakages and pilferage. Ordering cost like cost of stationery and telephones, salary and wages of purchasing personnel are also included under cost on materials.

Significant cost reduction can be affected by applying scientific

methods of material management. Cost (price) of material can be reduced by effective purchasing negotiation and cost price analysis. Inventory carrying cost and ordering cost can be brought down by effective inventory management. Significant costs restriction is possible by integrating various subsections of purchasing, store keeping etc.; close monitoring is done for an integrated approach to the management of materials.

Integrated material management

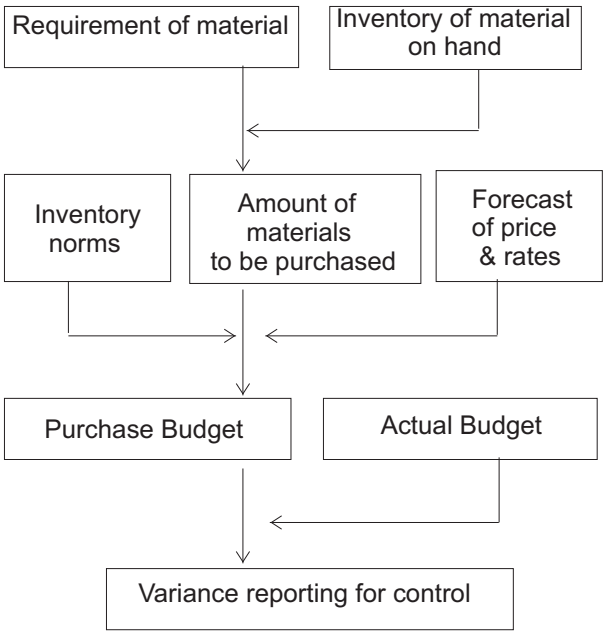
The reason for bringing all the materials related activities under one common head, namely the material manager, is to permit uninterrupted flow of materials from suppliers. The areas which come under the integrated material management are:

- Material planning/ material requirement planning
- Purchasing
- Receiving and incoming inspection for quality control
- Store housing/ warehousing
- Inventory control
- Material handling transportation including logistics and physical distribution management
- Scrap and surplus control and disposal
- Cost reduction techniques like value analysis
- Forecasting and market analysis

Material planning and budgeting

An accurate, well thought services [in quality and quantity] forecast should be the starting point for planning. The annual service forecast can be converted to quarterly service plan to take care of variations in the service forecast.

Flow chart showing the budgeting process



The above chart gives the outline of budgeting process. In ordering for materials like dyes, equipments etc., computers can be used to print out orders with desired quantities, prices and delivery periods. Computers also help in providing information regarding printing requisitions or outstanding orders. Based on this information purchasing can expedite actions in house and /or chaser of vendor for expediting supplies.

Purchasing

Purchase is the last goldmine of profits. It is one of the important functions of administration. The goals of purchasing are to purchase at right price, right quality, right quantity, right contractual terms, right time, right source, right materials, right place, right mode of transportation, right attitude with techniques such as value analysis, material intelligence, purchase research, SWOT [strength, weakness, opportunity and threats] analysis, purchase budget, lead time analysis etc. For obtaining these 'rights', sourcing of right vendors becomes paramount. One of the very important functions of purchasing is vendor department. Having developed the vendors, their constant evaluation is also necessary to weed out vendors who do not perform in terms of quality and delivering period and those who do not quote competitive prices or do not quote at all. Various type of vendor rating plans are available in material management, but the weighted point method is the most popular and also the one where the computers can be used to generate information, which is of immense use to the purchaser. Weighted point method of vendor evaluation is made by the administrator using evaluation criteria. Each of the factors is given a relative weightage depending on their importance. These factors are the percentage of shipment accepted, quality rating percentage on schedule, delivery dating, average price per unit material, lost price and actual price, price rating etc. A composite performance index can be determined and the vendor comparisons can be made. Outsourcing (in the premises or outside the hospital) is an indirect method of purchasing.

Buffer (safety) stock is a stock which is kept to cater for uncertainties in consuming rate or lead time of the material. The safety stock is calculated by multiplying the difference between minimum and maximum lead units with the monthly consumption of the item. In other words, the longer the lead time the more the safety stock. Lead time is the average duration of time in days from the initiation of purchase requisition, to the time the material takes to the reach hospital stores, inspection, time taken to stock and made ready for issue to the consumer. There are two components in lead time, namely the administrative lead time (internal lead time) and delivery lead time (external lead time). Administrative lead time includes time required for raising the purchasing of the requisition for container enquires, obtaining quotations, making comparative statements, scrutiny and approval. Placement of purchase orders and its reaching the supplier, arrival of

inspection of stores and checking up ledger of stores are also administrative lead time. The delivery lead time is the time required by the supplier to get the materials ready and its transportation and clearing.

Receipt and inspection

The role of receiving section is to ensure that right quantity of material in accordance with the order is received from the vendor. Inspection ensures that quality requirements are met. These activities consume a lot of time especially when the quantities involved are large. Use of computer in documentation of receipt and inspection therefore results in reduced lead time and reduced inventories.

Caduceus system, a modern information system is meant to deliver improvements in the ability of hospital facilities and network with other healthcare organizations to optimize the processes and work flows associated with hospitals' materials management information systems and reduce the costs related to inventory and supply chain management (SCM).

Storekeeping

A normal store of a major hospital may have thousands of items costing lakhs of rupees. The manner in which these stocks are stored and information on that stock status determines the efficiency of stores. It is not merely “keeping” stocks or materials but it is “managing” them. Stores management is envisaged as a dynamic function involving preservation of material, proper accounting, ensuring proper layout and housekeeping, physical stock verification, financial audit and support services to the purchase department.

Inventory control

Inventory control is a “scientific system which indicates as to what to order, when to order, how much to order and how much to stock so that purchasing cost and storing cost are kept minimum.” Inventory control therefore means an optimal utilization of the money available with the hospital, avoiding unnecessary building up of stocks.

Inventory analysis and cost reduction

A high degree of control of inventories of each item is neither practicable considering the work load involved nor worthwhile since all items are not of equal importance. Therefore analysis has been made effective by carrying out “overall analysis, category analysis and individual item analysis.”

Over all analysis is done by a large bird's eye view of total inventory over a period of time to find out trends of inventory organizations. This type of analysis is very useful for top managers to have an idea of the inventory behaviour.

Sometimes it is found that even if the overall stock position is fairly satisfactory, the stores carry higher inventory in some categories and low in some other categories resulting in over stocking or under stocking for different categories of stock. In order to avoid such situation, the management should fire inventory level of each category item according to various conditions like lead time, nature of items, stock exhaustion date etc. This method is called category analysis/value analysis.

The items can be classified according to their use, price, lead time etc. Analysis of each item is called item analysis. Item analysis is usually done by ABC analysis or VED analysis or a combination of both.

ABC analysis

It is based on the 'vital few and the trial many.' A higher degree of attention is focused on the vital few which affects the result significantly. 'A' items are those whose cost is high. 'B' Items are the intermediate items less costly. 'C' items are least costly. It could be seen that 70% money spent by hospitals are for 10% of items in the inventory whereas 10% of the money is spent on about 70% of items and the remaining 20% of money is spent for 20% of items. This system reduces both stock out and inventory investment.

There are certain policies to be adopted by the organizations for A, B and C items.

The policies for “A items” may be as follows:

- Tight control should be exercised
- To be purchased more frequently to reduce the capital lock up in the inventory
- To be purchased on exact requirement basis
- Annual or six monthly contract should be made (running tenders)
- Experience to be involved to have the delivery lead time shortest
- Order quantities, re-order level, safety stock should be meticulously developed
- Should not depend on one source of supply
- Review of items so far as consumption is concerned should be more frequent
- Waste control also should be tightened like safety stock to be maintained
- Stock report should be frequently communicated to the top management.

The policies for “B items” are

- Moderate control be exercised
- Order quantities, re-order point, safety stock should be fixed barring expert's revision once a year
- Minimum safety position and safety stock position to be followed
- Personal checking by the store-keeper is adequate.

For “C items” the policies that can be followed are:

- Ordinary control to be exercised
- Large supply stock to be maintained
- Annual order or six monthly order be placed
- Checking by ordinary clerk and counter checking by store keeper is sufficient

Combined "ABC" & "VED" Analysis

	V	E	D
A	√√√	√	X
B	√√√	√√	X
C	√√√	√√√	√√√

√	Items to be purchased
X	Items not to be purchased

VED Analysis

"V" stands for items those are very essential, "E" for essential items and "D" for desirable items, regarding the items to be purchased. All items which are very essential (V) are to be purchased irrespective of its cost. Essential items (E) are purchased based on the cost. Desirable items may be purchased based on the financial status at that point of time.

Conclusion

To summarize, the relevance of the adoption of scientific material management in hospitals is discussed; certain common terminologies in material management like inventory control are explained, and discussion on a few areas of material management is covered. All who are material managers may resort to practicing methods of scientific material management to achieve their aims and objectives, and to avoid pilferages and wastages.

Writing does matter!.... Art of writing a scientific paper

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Type "how to write a scientific paper" into any of the search engines and you will be drowned in a deluge of articles from the cyberspace telling you ***how to*** and ***how not to do*** it! There are any number of books offering similar guidelines. So why another epistle of the same genre? Well, this is an attempt at summarizing several of such commentaries gathered while trawling the web and the print media. While the specific recommendations vary, the basic theme remains the same in all of them.

"Publish or perish" has become the survival mantra of the scientific world - whether it is for advancement of careers or obtaining funds for sustaining research or other academic pursuits. This has resulted in a spate of articles of all hues crowding the mail boxes of publishers. Some would be of great scientific value, many are downright worthless in quality and content, while the majority are of average caliber. Good writing style and attention to detail can help salvage many lackluster papers, otherwise destined for the waste basket. Most of the scientific writings are often unpalatable for the average reader and are only read by people who have a specific interest in them. Further, writing a journal article could be a Herculean task for someone whose first language is not English. Many medical journals are crammed with lengthy, unclear prose which is likely to baffle the readers, even those familiar with the subject. The better a paper is written, the more readers it will attract and more citations it will receive. This is where the right style matters!

Style has been interpreted as a manner of expression in language. Jonathan Swift the famous author felt style was *"proper words in proper places".* Matthew Arnold, poet and literary critic, declared *"have something to say and say it as clearly as you can"*. Specifically style also denotes custom regulations in spelling, capitalization, punctuation, formatting and display. The JAMA style book states that a scientific journal should have consistency of style and an accuracy of reporting that the readers trust. The rules the journal adopts should be simple and encourage clear, explicit writing. The primary function of a scientific paper is to convey an idea or a finding convincingly. The standard format of title, authors, abstract, keywords, introduction, materials and methods, results, discussion, references does impose restrictions on writing style. But these are flexible enough for the paper to be written in an informative as well as interesting way.

Title is undoubtedly the most important part of the entire paper. If the significance or relevance of the paper is not obvious from the title, the reader is not going to proceed any further. This is akin to window shopping, one does not venture inside, unless the display is compelling. Could be a catch 22 situation…. longer title may be more informative, but many readers only quickly scan through the headings and might not comprehend the meaning. Short ones may be attractive, but could be too puzzling. Clever use of catch phrases could be useful, but not at the cost of content.

Abstracts could be either free form or structured, the latter is often the norm in scientific journals. It is the abstract which dictates whether one should read *any further or skip!* The article could be a gem by its own merit, but runs the risk of being ignored unless the abstract conveys the gist of the paper lucidly.

Listing of authors should be strictly according to instructions given. **Choice of key words** is another important aspect which could improve accessibility while doing a literature search. **Introduction** is again of paramount importance and should give a general overview and put the work done in perspective. This is not synonymous with literature review. **Methods** section should be precise and specifically describe work done - nothing more, nothing less. **Results** should be presented in a coherent structured manner. Logical sequence than chronological order is preferred. **Discussion** must project a lucid interpretation of results and demonstration of their relevance convincingly, or else the very purpose of the paper is lost. Literary flamboyance in discussion often implies that the paper cannot stand on its own. **References** are essential, but being dragged through every publication that is related to the topic can be very tiresome. Try and use original research, meta analyses, evidence based guidelines and systematic reviews wherever possible and use proper format for quoting them.

Some tricks of the trade:

Good writing need not necessarily be long. Keeping it **short and simple** impresses the editors and naturally attracts more readers. Readers of specialized journals may be put off by lengthy discussions of basics which are presumably common knowledge. Conversely, general journals may require more background explanation to enable the readers to follow what is being discussed ahead. Organize articles into neat little paragraphs each focusing on a particular aspect. Ideally such paragraphs should contain only about ten sentences. Avoid long sentences and minimize wordiness - using more words than necessary to convey the same meaning. Use as many words as you must and as few as you can.
Eg: *It has been found from several studies in the past that……* Change it to*: Earlier studies showed that….*

Another example of verbosity, as quoted by Dr Mark H Ebell:

One of the problems I have with writing is that I have a lot of ideas that are interconnected and so I try to put them into one sentence, which in turn tires the reader, because they have to read a long stretch of ideas without a break and which also tends to bog down the meaning when different ideas intermingle in one long run on sentence!

This may be rewritten as:

One of the problems with writing is that I try to put a lot of interconnected ideas into one sentence. This practice tires the reader, who has to read a long stretch of ideas without a break. It also tends to confuse meaning. The different ideas intermingle in one long run on sentence.

Yet another one: "*Because the differential diagnosis of abdominal pain is extensive and includes multiple disease entities that can be placed into broad categories of abdominal and extra abdominal disorders and subdivided as follows: abdominal disorders include four categories of intra peritoneal conditions {inflammatory, mechanical, malignancy, and vascular disorders} and a limited list of extra peritoneal conditions."*
More appealing would be:

Because the differential diagnosis of abdominal pain is extensive, it is helpful to organize it anatomically into abdominal and extra abdominal disorders.

Intra abdominal disorders can be intra peritoneal or extra peritoneal.
Intra peritoneal disorders can further be divided into four categories [inflammatory, mechanical, malignancy, and vascular disorders].

One of the pitfalls often quoted is a blatantly casual approach to choice and use of words. Strunk and White gave this sage counsel as early as 1959 - *"A sentence should contain no un necessary words, a paragraph no unnecessary sentences for the same reason that a drawing should have no unnecessary lines or a machine no unnecessary parts."* Very apt indeed. Make every word tell. Simplicity improves readability. Short words, short sentences, short paragraphs make the paper more appealing. However over simplification and mindless over writing are both taboos.

Why say " *only the individual who utilizes a durable covering for the lower extremity of the leg can ascertain the narrowly particularized and localized position where the internal surface of that footwear presses painfully against the surface of his/ her dermatological tissue"*, when *" none but the wearer knows where the shoe pinches"* will do? A word of caution though… cutting down on number of words should not withhold the meaning of what you write.

Avoid figures of speech and idiom

Also avoid foreign, technical or jargon words. Refrain from using slangs [phrases used in medical conversations] in scientific writing. Eg: *Blood glucose concentration* is scientifically "sweeter" than *blood sugar! Pleural fluid aspiration* is more appropriate than just *pleural tap!* And by no means say

worked up for fever when *investigated* or *evaluated for fever* would be proper.

Good writing also does not need an abundance of adjectives, adverbs, transitional adverbs or abstract nouns. They reduce easy readability. Showing off your proficiency in language time and again, may not be appreciated by the readers. Avoid "empty" phrases, which do not contribute to understanding.
Eg: *In order to call attention to the usefulness of….* could be changed to… *to emphasize the usefulness of…...*

Be "tense" specific: Results described in the paper should be in past tense, while results from already published papers [the established truths] are given in present tense. Future tense is meant for describing the proposals being planned ahead.

Passive voice is usually dull and uninspiring. Use active voice for greater impact.Eg: "*It has been proposed that MRI studies of the pancreas should be considered"* "*Order an MRI study of the pancreas*." surely is more direct. Customarily, a scientific paper is written in third person, though first person account may be appropriate at times.

Down with abbreviations!

Well known or standard abbreviations are acceptable eg: ECG, BP, CT, MRI. etc; But what will you make out of CD, ESLD, WD, HVOTO in a general interest journal *[for Crohn's disease, End stage liver disease, Wilson's disease, Hepatic venous outflow tract obstruction]?* Papers studded with unfamiliar abbreviations are quite exasperating and difficult to read.

Some more tricks:

Avoid repetition - say it well and say it once! In other words, echoing what has been already said again and again using literary acrobatics is superfluous… like this very sentence, which should have been deleted!
Stay away from nonstandard capitalization: *Abdominal Pain can be classified as Parietal and Visceral.* Diagnoses, tests and generic drugs are NOT capitalized: *Order a Complete Blood Count in a patient suspected to have Appendicitis and start Ciprofloxacin.* Correct: *Order a complete blood count in a patient suspected to have appendicitis and start ciprofloxacin*. However proper names [Crohn's disease] and brand names [Becosules] ARE capitalized.

Proof reading is a must. Avoid factual errors: *'Upper GI endoscopy was unremarkable and biopsies from the erosions at lower end of esophagus were taken to rule out H. pylori".* Obviously the findings cannot be unremarkable if there were erosions, and biopsies are taken to rule out esophagitis and not H. pylori [a factual error].
Avoid indirect or tortuous words and phrases: Eg: *It has been suggested that/ some might consider/ preliminary evidence suggests that…* Why not say *the data shows…*

Properly format your article:

Give double space. Adequate margins at least 1 inch on all sides. Insert page breaks after title page, abstract, body of paper and each table. Use hard line breaks [Enter] only for new paragraph. Label all tables [with numbers and caption above the table] and figures [with numbers and caption below the figures]. Do not wrap words around tables or figures or embed them in the manuscript. They should be conspicuous.
Use appropriate sub headings. Use a good font - Arial/ Tahoma/ Times New Roman etc.
Avoid double parentheses. Eg: *omeprazole was shown to be more effective in suppressing HCl production than ranitidine [Figure 4] [6].* Better statement would be *Figure 4 shows that omeprazole was more effective than ranitidine in suppressing HCl production [6].*

Numbers, percentages should be stated in the correct format:

5 mg/ml	and not	5mg/ml
5 percent		5 Percent
5%		5 %
5 to 10 grams		5 gms to 10 gms
5 years old		5 yrs

Typos or typographical errors, though unintentional as they are, should be avoided at all costs. Always run a spell check and meticulously scrutinize for factual errors, even if the sentence is grammatically correct. Be specific and do not make readers guess or presume what the author means. Ignoring the rules of punctuation is detrimental to the readability of the paper. Ideas can be conveyed with absolute clarity only if one bothers to put the right dots and markings between words in the right places.

Follow *instructions to authors,* be up to date by checking their current website. Get an issue of the journal and study it to get the feel of the format and style before submitting your manuscript.

To write well you'll have to revise, redraft, amend, alter the manuscript any number of times. Edit your own

paper well. Editors are often forced to maul your article because of poor English, lack of clarity or both. One suggestion has been to stay away from what is written for a certain period of time, critically look at it later and ruthlessly edit out those seemingly useless sentences or paragraphs. But most of us leave things until the last minute and then try frantically to meet the deadline. Requesting a trusted friend or colleague to impartially go through and criticize your writing would be another way of avoiding the knife later on. Medical authors, whose main business is not art and letters but science and sick people, should take more trouble and *must learn* to write better!

After all that sweat and grime at the end of a hard day's work, if your article is still rejected by the editor, do not lose heart… reformat and send it to the next suitable journal !

Source:

1. R.B.Taylor: The clinicians guide to medical writing: Springer Science and Business media Inc: New York 2005

2. Jagdeesh Kumar M: Writing skills and Review articles: http://www.tr.ietejournals.org. cited 25/01/10

3. Thomas E Cronin: The Write Stuff: Writing as a Performing and Political Art http://www.whitman.edu

4. Amin S bredan,Frans Van Roy : Writing readable prose : EMBO *reports* Vol 7 | No 9 | 2006

5. The Good, the Bad and the Ugly of Medical writing: Dr Mark H Ebell
http://www.fmdrl.org/index.cfm?event=c.getAttachment&riid=2290.

6. How to write a paper : George M Hall, Byword publishers 1996

7. J.W Howie. Writing and speaking in medicine. BMJ 1976,3,1113-25

8. Strunk Jr W, White EB. [1959] The elements of style. London, Macmillan.

✪ CME REPORT

Leprosy Management and Rehabilitation

T P Thankappan

From:
Pushpagiri Institute of
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& Research Centre
Tiruvalla - 689 101, India

Department of Dermatology, Leprology and Venerology conducted a CME programme on **Leprosy Management and Rehabilitation** on the 17th of January 2010. Registration began at 08.30 am; fifty one delegates registered for the programme. At 09.30 am the CME was inaugurated by Rev. Fr. Thomas Kodinattumkunnel, CEO, Pushpagiri Group of Institutions, in Lecture Hall no. 1 of the Academic block of Pushpagiri Medical College.
There were two Scientific sessions.

Scientific Session I was chaired by Dr G Sukumaran, the then Prof. and HOD of Medicine. The first paper on ***'Introduction to Leprosy Rehabilitation'*** was presented by Dr Jacob Mathew MS, from Chennai; he is a world renowned Reconstructive Surgeon in the field of leprosy. The second topic of the first session ***'National Leprosy Elimination programme***' was presented by the State Leprosy Officer, Dr Sreerekha Panicker MD (D&V).

Scientific Session II was chaired by Dr V Sreedevan, Professor & HOD of Dermatology of Medical College, Alappuzha. Dr G Nandakumar MD (D&V), MD Pathology, Associate Professor, Medical College, Thiruvananthapuram presented the topic, ***'Clinical diagnosis and Investigations in leprosy'.***

All three papers were authentic and up-to-date, and enlightened all those who attended the CME programme. Certificates were distributed to all the registered participants.

The programme came to an end by 17.00 hrs.

T P Thankappan MD
Professor and HOD

Dept of Dermatology, Leprology and Venerology
PIMS & RC

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✪ CME REPORT

Internal Medicine

G Sukumaran

From:
Pushpagiri Institute of
Medical Sciences
& Research Centre
Tiruvalla - 689 101, India

A CME Programme was conducted by the Department of General Medicine on 15th November 2009 in the Senate Hall of Pushpagiri Medical College Campus. A total of 160 delegates from the Alleppy, Kottyam, and Pathanamthitta districts participated in the CME.

The programme was inaugurated by our CEO Fr. Thomas Kodinattumkunnel, and was felicitated by Dr. A. S. Mathew and Dr. Ashok Philip Oommen. The speakers on each topic highlighted the updates in the concerned fields. The following seven Scientific Topics were presented:

1. **Fever with thrombocytopenia - A practical approach**
   Dr. C. S. Kesavan MD, Professor of Medicine, Pushpagiri Medical College, Tiruvalla.
   Chaired by Dr. Sunil Mathew, Physician, Taluk Hospital, Tiruvalla and
   Dr Thomas Mathew, Physician, St Thomas Hospital, Chethipuzha.

2. **Blood and Blood components - Rational use**
   Dr. Basanti Nair MD, Professor of Pathology, Pushpagiri Medical College, Tiruvalla.
   Chaired by Prof. M.O. Annamma, Prof. & HOD of Pathology, Pushpagiri Medical College.

3. **Anaemia in the elderly - A Clinical approach**
   Dr. P. Viswanathan MD, MNAMS, Professor of Medicine, Pushpagiri Medical College.
   Chaired by Dr. P.T Zachariah, Physician, Sahrudaya Hospital, Alapuzha.

4. **Syncope, an overview of Aetiopathogenesis - How and when to investigate**
   Dr. George Koshy MD, DM, DNB (Card) Asso. Professor, Pushpagiri Heart Institute.

G Sukumaran MD
Professor Emeritus

5. **Endothelium in health and disease**
   Dr. G. Sukumaran MD, Professor of Medicine, Pushpagiri Medical College, Tiruvalla
   Chaired by Prof. Lekha, HOD Medicine, TD Medical College, Alapuzha.

6. **X-ray Chest in Acute dyspnoeic patient**
   Dr. Sudheer MD, FRCR, Professor of Radiology, Pushpagiri Medical College
   Chaired by Dr. Benjamin, Senior Physician, Tiruvalla.

7. **Arterial Blood Gas analysis - a practical approach**
   Dr. R. N. Sharma MD, Professor of Medicine, Amrita Institute of Medical Sciences, Cochin.
   Chaired by Dr. P.P. Mohanan, Professor of Medicine, Medical College, Kottayam.

Dept of General Medicine
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The programme was very much appreciated by the delegates. Certificates of participation were issued to all delegates. The programme concluded at 16.00 hrs.

ACHIEVEMENTS

The Editorial Board of Pushpagiri Medical Journal feels honoured to congratulate the following eminent faculty members for their academic excellence, leadership quality and organizing capacity.

1. Dr Rajan Joseph Manjooran
   National President,
   Fellow Indian College of Cardiology (FICC)
2. Dr T U Sukumaran
   National President Elect , Indian Academy of Paediatrics, 2011
3. Sinu M Gopi
   First rank, Final MBBS in Mahatma Gandhi University (2009)

Also we congratulate the Pushpagiri MBBS graduates for their brilliant performance in PG Entrance Examinations

(A) Qualified in the All India Medical PG Entrance Examination (AIMPGEE), 2010

1. Reena Mary Abraham
2. Anju Sussanna Thomas
3. Ajith Kumar Pillai

(B) Cleared the First part of DNB examination, 2010

1. Afshana Sidhik
2. Amjed Nizamuddin
3. Anju Mathew
4. Anju Sussanna Thomas
5. Anu M George
6. Binu George Babu
7. Cerene Rose Jose
8. Dhanya Gopinathan
9. Jitha S
10. Leeba Elizabeth Babu
11. Merin Joselin George
12. Mohammed Jashin
13. Moncy Michael
14. Om Prakash
15. Poornima R Pai
16. Reena Mary Abraham
17. Rinu Ruth George
18. Santy Antony
19. Smrithesh Somakumar
20. Vandana Sudheer

(C) Qualified in the All Kerala Medical PG Entrance Examination 2010

1. Afshana Sidhik
2. Ajith Kumar Pillai
3. Anju Mathew
4. Anju Sussanna Thomas
5. Binu George Babu
6. Leeba Elizabeth Babu
7. Mohammed Jashin
8. Moncy Michael
9. Nithya George
10. Pearly P K
11. Reena Mary Abraham
12. Rinu Ruth George
13. Smrithesh Somakumar
14. Thaju Louis
15. Azad Abdul Salam
16. Fesmitha P S
17. Harish S
18. Meera Selvarajan
19. Navaf K M
20. Soumya V K
21. Varghese Thomas

✪ STUDENT CORNER

Innovators and Researchers amongst Pushpagiri MBBS students

The Editorial Board of Pushpagiri Medical Journal joins the Management, College authorities, all Faculty members and the Students Union in congratulating the brilliant, young, vibrant MBBS students who submitted research projects to the ICMR and who presented papers in the National and International Conferences on Students' Medical Research, in 2009.

A. Short Term Studentship (STS) Research program under the ICMR:

Of the 11 STS projects from Kerala State accepted by the ICMR in 2009, 6 had been from Pushpagiri MBBS students. We congratulate these students who conducted the studies, and the faculty members who spared time and took the pain in guiding them.

Name of Student	Name of Guide	Sanction no.
1. Amina Beevi S	Dr Lizamma Alex	21/KE/PIM-6/09-BMS
2. Joslin S Joy	Dr Manju George Elanjickal	21/KE/PIM-7/09-BMS
3. Kripa Susan Thomas	Dr Felix Johns	21/KE/PIM-8/09-BMS
4. Litty John	Dr Abraham Varghese V	21/KE/PIM-9/09-BMS
5. Rony George	Dr P Jose Paul	21/KE/PIM-10/09-BMS
6. Rosa Mariam Mathew	Mrs Nisha Kurian	21/KE/PIM-11/09-BMS

B. National Conference on Students' Medical Research:

In the second National Conference held in Govt. Medical College, Thiruvananthapuram in January 2009, the following 9 students from Pushpagiri Medical College had presented their Research papers:

1. Body mass index and total body fat to detect changes in physical activity patterns and adiposity in adolescence, by Amina Beevi Shahabuddin
2. Presence of asymptomatic deep vein thrombosis in critically ill patients, by Aneena Chacko
3. Incidence of post operative infections in patients receiving peri-operative blood transfusions, by Deepa M S
4. Prevalence of respiratory symptoms and diseases among tyre manufacturing factory workers, by Kripa Susan Thomas
5. Prevalence of absence of Palmaris longus muscle, by Libu Varghese
6. Effect of Insulin on serum Magnesium levels in Diabetics, by Litty John
7. Mean corpuscular volume in normal healthy adult population of Kerala, by Nissy Susan Varughese
8. Clinical and mycological study of Tinea versicolor, by S Nithya Priya
9. Correlation of clinical parameters with O_2 saturation measurements in acute bronchiolitis, by Rohini Sebastian

Of these, S Nithya Priya and Nissy Susan Varghese won the best paper award in the Oral presentation.

C. **MEDICON 2009** (The 2nd Asian & 3rd National Medical Students' Research Conference), conducted in Kasturba Medical College, Mangalore, from 24 - 28 June 2009:

Nine MBBS Students of Pushpagiri attended the Conference and presented their research papers.

1. Aneena Chacko
2. Anju Alex
3. Joel Jacob
4. Kripa Susan Thomas
5. Litty John
6. Nissy Susan Varughese
7. Rohini Sebastian
8. Rony George
9. S Nithya Priya

Among these, Aneena Chacko won the third prize for the oral presentation.

✪ BOOK REVIEW

Clinical Anatomy for Students: Problem Solving Approach

Neeta V Kulkarni

First edition: 2006 Reprint: 2008 ISBN: 81-8061-734-3

Publishers : JAYPEE BROTHERS Medical Publishers (P) Ltd.
B-3, EMCA House, 23/23B Ansari Road, Daryaganj, New Delhi 110 002, India.
Email: jaypee@jaypeebrothers.com Website: www.jaypeebrothers.com
Free online access: www.jaypeeonline.in

Lizamma Alex

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"Clinical Anatomy for Students: Problem Solving Approach" is a very comprehensive Anatomy textbook, blending Gross Anatomy with Developmental, Radiological and Applied Anatomy. The book reflects the general opinion of all Anatomy teachers that learning Anatomy extensively in the reduced duration of 9 months (as per the MCI stipulations of 1997) is an extremely difficult task for an average first year MBBS student. A first MBBS student is barely able to identify and pick up essential points from the text in many of the currently available books. Avoid unnecessary details is probably the best achievement of the author.

The book stresses on the Applied anatomy in depth, which sometimes necessitates a detailed explanation by an experienced teacher. This enables the undergraduate students to correlate cadaver anatomy with bedside clinics. Also this makes the book valuable for the postgraduate students and clinicians alike. The Clinical highlights could have been given in boxes, probably with a different colour.

The Clinicoanatomical Problems and Solutions at the end of each section give a clear guideline for the proper interpretation of the frequently asked long questions based on the clinical case presentations.

The Radiographs of the various regions in the body along with CT/ MRI images and contrast studies, given in the Annexure are mostly self explanatory. At least a few ultrasonographs could be included along with these.

The relevant developmental anatomy (along with picturesque demonstrations) integrated to the gross anatomy, enables the students to correlate the two easily. It also demands attention by all anatomists, that some of the traditionally followed Embryology textbooks are becoming too descriptive for an undergraduate.

The Osteology section towards the last part of the book seems too brief. It probably would have been better to include it in the corresponding region itself; the current presentation as such would make the student underestimate the importance of learning osteology.

The most cumbersome task of the author could be the way she condensed all the essential features into a single volume of textbook, without compromising on the subject content, thus facilitating a holistic approach to learning human anatomy. The illustrative figures in the book are generally quite simple for a student; a few of them require modification.

The paper of the book is good, but the publishers need to give it a firmer binding, so as to give the book an extended shelf-life.

I heartily appreciate the efforts of the author, especially so in the Kerala scenario, where hardly any Anatomy book has been published. I would strongly recommend this text for undergraduate as well as postgraduate medical students.

Lizamma Alex MS
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Vice Principal (Academic)

Department of Anatomy
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