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INDEX OF ARTICLES

1] Pre-natal diagnostic technique act-

2] A study of medical students' exposure to formaldehyde in gross anatomy dissection laboratory

3] Clinical study of respiratory distress in admitted children with special reference to mortality

4] Incidence of tuberculosis from study of fine needle aspiration cytology of lymphadenopathy

5] Study of 110 cases of arteriovenous fistula

Created for hemodialysis

6] Prevalence of refractive errors in children (age group 7-15 years) of rural and urban area of gujarat :a population based study

7] Axis determination: vector disc v/s perpendicular method

Recent resurgence of diphtheria among children- our experience
Bird flu: is panic justified?

8] Adipose tissue as an endocrine organ:

Adipose brain communication

9] Newborn screening for inborn metabolic disorders

10] Gene therapy in cancer

11] Placebo's in pain –

12] stem cell therapy ahead

13] Molecular basis of trans-differentiation of adult stem cells

14] Role of human chorionic gonadotropin testing in detection of early pregnancy viability and its complications

15] Early pregnancy detection tests

16] Probiotics, prebiotics and symbiotics

Case reports

17] Atypical presentation of thalassemia major

18] A rare case of origin of cystic artery arising from inferior pancreato-duodenal artery.

19] Intercostobrachial nerve ;Supplying the entire medial side of the arm

20] Cornelia de lange syndrome with rarest presentation of ring of 9th chromosome.

21] Pulmonary alveolar protinosis with agammaglobulinemia, a rare presentation.

22] WHO-Message of World health day 2006

1] PRE-NATAL DIAGNOSTIC TECHNIQUE ACT-

(REGULATION AND PREVENTION OF MISUSES 1996)

IS THE GOVERNMENT JUSTIFIED IN IMPLEMENTING THE LAW STRICTLY?

Dr.Pratik R.Patel-HOD Forensic Medicine, Aditya Joshipura V semester Smt

NHL Mun Med.College Ahmedabad

Female foeticide being an extremely common event in India, or shall we say CRIME, the government has acted actively to curb this offence.

The days are gone when there was waiting period of 9 months and result delivery .And then if it was a girl, she would be killed. Come 2006, the latest techniques provide an easy way out via USG. A sex determination test and you know whether it's a boy or a girl, and if the latter, easy abortion. Some gynecologists actively do this for financial up lift. So the government has pragmatically put into enforcement the PRE NATAL DIAGNOSTIC TECHNIQUES act (1996). Thereby it lays down specific criteria for the tests to be carried out during pregnancy, the relevant paperwork and the facilities required for the diagnostic center. Some salient features are:

- The center must have a qualified gynecologist or any experienced medical man who has attended more than 25 surgeries.
- The center must be registered with the government and a record of the tests carried out must be kept.

And most importantly:

- No tests for sex determination can be carried out under any circumstances.

Thus, the act forbids radiologists and gynecologists against this grave crime.

But the doctors haven't been called the most intelligent guys for nothing.

Even

Today, they subtly pass the information about the gender to future parents by pointing towards photographs of male/female cine stars or gods/goddesses

So, since recently the officials have started surprise raids at such centers to keep vigilance.

The punishment laid out ranges from sealing the sonography machine to monetary penalty to sending him to jail and even canceling his registration.

Recently doctors have cried foul over the too strict policies of the govt. and have launched an agitation for allowing themselves free of the "vice like grip" that has been apparently put on them. But, in the larger interests of the society the government is unrelenting.

Looking on, some of us who are reading this article will be put in a situation in the future whereby a decision would have to be made between short term financial gains and a greater, duty towards society. So, we must decide our objectives right now and act accordingly. Finally, the government is doing something except price hiking. We must support this if done in the right faith by the government. Or else our next generation will be completely masculinized and the generation after that might not even appear!

The editor wish to end with remark

MAA TUJE SALAM .

2]

A STUDY OF MEDICAL STUDENTS' EXPOSURE TO FORMALDEHYDE IN GROSS ANATOMY DISSECTION LABORATORY

Shah RK*, Trivedi BD**, Patel JP ***/ * M.S. (Anatomy) Tutor in Anatomy **MS (Anatomy) Professor & Head, *** MS (Anatomy) Assistant Professor in Anatomy, NHL Municipal Medical College Ellisbridge, Ahmedabad- 380 006

Abstract

The authors studied 112 medical students exposed to the formaldehyde during the dissection of cadavers. This was done to study the allergic effects of Formaldehyde on first year MBBS students of the Smt. NHL Municipal Medical College in Ahmedabad. The study was carried out during the first 15 days of their exposure to Formaldehyde. The acute allergic symptoms like eye burning, URT irritation, cough, lacrimations and headache were noted and found to be significant. These symptoms were also significantly related to time and place of occurrence. Medical schools should take more concrete measures to reduce students' exposure to formaldehyde.

Introduction

Formalin is a colorless irritant fluid which gives out pungent Formaldehyde vapours and is widely used in the medical field as fungicide, germicide, disinfectant and preservative. Formaldehyde is a hepten and Formaldehyde-protein complex may be immunogenic (6). The chemical is extensively used to preserve the cadavers in the Anatomy department. The primary route of exposure to formaldehyde is by inhalation. Formaldehyde is a gas at room temperature Formaldehyde is readily absorbed the lungs and gastro-intestinal tract and to a much lower extent through skin. It is water soluble and is usually absorbed through upper airways and nose (6).

The literature on Formaldehyde contains reports on dermatitis and asthma (3,5,8) on industrial exposure to Formaldehyde only a few mentions effects in medical students following exposure to Formaldehyde (1,4,7)

As exposure to Formaldehyde in Anatomy department is continuous and higher than other departments, the present study was done to assess the prevalence of allergic reactions to acute exposure to Formaldehyde.

Material and Methods

The study was carried out at Department of Anatomy of Smt. NHL Municipal Medical College. The study group consisted of newly admitted students of first year MBBS at the

college. Any student having prior history of cough, respiratory or skin disease was excluded from the study. Students who missed any of the dissection schedules were also excluded from the study.

The study was carried out during the first 15 days of their exposure to Formaldehyde. The responses from the students were collected and noted. All the symptoms were explained to the students beforehand for accurate response.

The average duration of exposure for students in the dissection hall was 10 Hrs/Wk. Usually after the dissection schedule is over the cadavers were submerged in the formalin tank and were taken out during the next dissection schedule.

Observations

Table 1. showing various effects seen in students after Formaldehyde exposure

Eye	%	Nose	%	Throat	%	Skin	%	CNS	%
Itching	8.04	Irritation	9.82	Irritation	1.79	Burning	-----	Headache	28.57
Burning	39.28	Dryness	8.93	Dryness	14.29	Shrinking & Hardening	-----	Nausea	3.57
Lacrimat- -ion	9.82	Running Nose	13.39	Coughing	11.6	Desquamation	-----	Vomiting	2.68
		Sneezing	8.04			Hair dryness	24.11	Drowsiness	10.71
								giddiness	5.36

Table 2. Comparison between Male and Female Students

Male		Female	
Total	85	Total	27
Affected	59	Affected	23
Percentage	69.41	Percentage	85.16

On comparison of various effects due to Formaldehyde exposure, about 57% students complained of eye symptoms, about 40% students complained nose symptoms, about 27% students complained of throat symptoms, about 24% of hair dryness and about 50% students complained about various CNS symptoms (Table 1).

Discussion:

The fluid is used to embalm the cadavers contains denatured spirit (methylated spirit) and glycerin along with Formaldehyde in various combinations. In thin body the glycerine content is increased whereas in fatty body it is decreased. Since no convincing data is available about the allergenicity of spirit of glycerin, the allergic manifestations detected may be attributed to Formaldehyde.

Total number of students who were found to be affected by any of the irritational effect of Formaldehyde was 82. Respiratory tract irritation, conjunctival irritation, headache, cough and hair dryness were found to be more pronounced after acute short exposure to formaldehyde vapor. This may be due to acute reaction of the mucosa to Formaldehyde in the form of increased rate of mucus production and increased ciliary activity. Prolonged exposure for constant period also leads to inhibition of mucous secretion resulting in delayed effects like chronic atrophic rhinitis (2).

Out of total 112 students selected for the study, 82 students were positive to have been affected by allergic effects of Formaldehyde. Among all the symptoms Eye soreness was found to be the leading and immediate effect to Formaldehyde exposure, the finding which is similar to other studies (4,9). This was followed by headache in 32 students and 27 students complaining of dryness of hair (Table 1).

On comparison between male and female students, 85.16% of female students were affected whereas only 69.41% of male students were affected. Again eye soreness was main symptom found leading in both the sexes (Table 2). It was also found that symptoms reappeared consistently in both the sexes during every exposure to Formaldehyde.

Though allergic or irritative symptoms could be shown to be significantly more to the acute exposure to Formaldehyde, incidence of eczema or asthma were not significant among this group (3,5). Further the basic allergic symptoms may exacerbate due to gaseous Formaldehyde exposure (7).

Conclusions:

- (a) Most of the effects reported including Ophthalmic and Pulmonary effects are more due to irritative and inflammatory response than allergic in nature.
- (b) Non occurrence of any kind of skin lesion may be attributed to common practice of wearing gloves now a days during dissection.

- (c) Steps to reduce exposure to individual and public at risk can help to reduce the morbidity, which includes protecting students (by providing gloves, goggles, and masks), good ventilation of dissection hall, periodic air sampling and health evaluation of employees for allergic manifestations.
- (d) Some sort of hypersensitivity (patch test) should be developed to identify individuals at high risk of exposure

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CLINICAL STUDY OF RESPIRATORY DISTRESS IN ADMITTED CHILDREN WITH SPECIAL REFERENCE TO MORTALITY

Dr. Rajiv Arora (3rd Year Resident) Dr. Satyapal Rathod (2nd Year Resident) Dr. (Mrs.) R.H. Bhavsar (Professor & Head)
(Pediatric department. N.H.L. Medical College, Ahmedabad 380006)

ABSTRACT

INTRODUCTION : Respiratory Problems are common in infants and Children. Respiratory distress is an important cause of death in pediatric age group.

OBJECTIVE : To know clinical profile and risk factors for mortality in children admitted with respiratory distress.

DESIGN : Prospective Study

TENURE : March 2005 – April 2006

SUBJECTS : Children between Age of 1 month and 12 year presented with respiratory distress having no past history of respiratory distress.

METHOD : 200 admitted children were enrolled, detailed history taken, clinical examination done and recorded in preformed Performa. SpO₂ was monitored constantly. Haemoglobin estimation and X-Ray chest of each child taken. All children were treated according to standard protocol. They were followed till discharge or death. The data analyzed to know socio-demographic variable, nutritional status, immunization status of children. Appropriate statistical tests were applied to study the significance of various risk factors and to know the predictors of mortality.

Results

During the study period 1338 children were admitted and out of these, 14.9% (200/1338) had respiratory distress. Total deaths were 80/1338. Of this 46 patients were expired due to respiratory distress. Proportional Mortality rate 57.5% (46/80) Overall case fatality rate was 23% (46/200).

Case fatality rate in children : Below 2 months was 57.14% (8/14).

Between 2 months to 59 months 21.53% (31/144)

Above 60 months 16.67% (7/42)

Case fatality rate in Males : 24.7% (24/97)

in Females : 21.3% (22/103)

Case fatality rate in children belonging to Urban Area :21.6 % (26/120)

Case fatality rate in children belonging to Rural Area :25 % (20/80)

Case fatality rate in children from low socio-economic status (Modified Prasad Classification III, IV, V) 23.% (42/180) and in children from high socio economic status (Modified Prasad Classification grade I, II) was 20% (4/20)

Case fatality rate in immunized children : was 18.7% (33/176) and in non immunized children was 54% (13/24)

Case fatality rate in under nourished children : (PEM Grade 1 to 4 according to IAP Classification was 26.% (23/88) and in children with normal nutritional status was 20.5% (23/112)

The Most common associated symptom in descending order were cough 78.26% (156/200), fever 74% (148/200), altered sensorium 34.50% (69/200), cyanosis 6.5% (13/200)

Most common sign was tachypnea 84% (168/200)

Case fatality rate in children with hypoxemia (SpO₂ <90%) was 37% (33/89) and in patients with normal SpO₂ (>90%) was 11.7% (13/111)

Case fatality rate in children having anemia (Hb <10 gm) was 29.25% (31/106) and in children with (Hb >10) was 15.96% (15/94)

Case fatality rate in children with abnormal radiological picture was 17.6 (21/119) and in children with normal radiological picture 18.5% (15/81)

Case fatality rate in children with primary respiratory cause of respiratory distress was 25% (12/72) and in children with non respiratory distress was 19.4% (14/72)

Conclusion

Case fatality rate due to respiratory distress in young infants <2 months was observed to be higher as compared to older children. (P Value <0.0005 significant).

The difference of case fatality rate due to respiratory distress observed in different gender, place of residence, socio-economic status were not significant.

Immunization was observed to be important determinant for protecting the child (P Value <0.0001, very highly significant).

Low SpO₂ level was attributed to higher case fatality rate (P Value <0.0001, highly significant).

Case fatality rate due to respiratory distress was higher in children with anaemia and the difference was highly significant. (P Value < 0.025)

No significant difference was observed between mortality in children with abnormal and normal chest radiographs.

No significant difference was observed between mortality in children having respiratory distress due to primary respiratory cause and respiratory distress due to non respiratory cause.

INTRODUCTION

In Developing countries childhood pneumonia is still a cause for high mortality. It is estimated that 13 million children age less than 5 yrs die world wide annually. Among them about 4 million children die due to pneumonia. Because of such high mortality subject was taken for study.

Respiratory distress is characterized by signs of increased work of breathing, including tachypnea, nasal flaring, and use of accessory muscles of respiration and inspiratory retraction.

Evaluation of respiratory performance was done by increased respiratory rate, increased respiratory effort, decreased level of consciousness and cyanosis.

Materials and Methods:

During the study period, children between 1 month and 12 years, admitted with complaints of difficulty in breathing of less than 5 days were enrolled for study.

History of fever, cough, respiratory distress, cyanosis and altered sensorium taken and recorded. Immunization status assessed by history given by the informant. Nutritional status assessment was done as per IAP classification. Socio-economic status was considered as per modified Prasad classification.

Axillary temperature was taken for 3 min. and fever was defined as axillary temperature more than & equal to 37.5⁰c. Respiratory rate was counted for 60 seconds in a quiet child. Tachypnea was considered as per W.H.O. Definition. Respiratory System examined for breath sounds and other foreign sounds.

All children were constantly monitored with pulse oxymetry. Haemoglobin estimation done and chest X-ray done in each child reported by radiologist. All children were treated according to standard protocol. They were followed till discharge or death. Data was analyzed & appropriate statistical tests were applied to study the significance of various associated risk factors for the mortality.

Results

◆ During the study period 1338 children were admitted, out of the admitted 14.9% (200/1338) had respiratory distress. Total mortality was 80 out of 1338, out of this these 46 patients expired due to respiratory distress. Proportional mortality rate was 57.5% (46/80) and Case fatality rate was 23% (46/200). The most common associated

symptoms in descending order were cough – 78.26%(156/ 200), fever 74% (148/200), altered sensorium 34.50% (69/200), cyanosis 6.5% (13/200). The commonest sign was tachypnoea 84% (168/200).

Table-1: Case Fatality Rate in Children with Respiratory Distress

<u>Parameter</u>	<u>Admission N=200</u>	<u>Death n=46</u>	<u>Case Fatality Rate</u>	<u>P Value</u>
AGE				
<i>< 2 Months</i>	14/200 (7 %)	8/21 (17%)	57.14	0.0050
<i>2 Months - 59 Months.</i>	144 /200 (72%)	31/46 (67%)	21.53%	
<i>> = 60 Months.</i>	42/200 (21%)	7/46 (15.20%)	16.67	
SEX				
<i>Male</i>	97/200 (48.5 %)	24/46 (52.17%)	24.71%	-0.50
<i>Female</i>	103/200 (51.5%)	22/46 (47.8%)	21.3%	
Residence				
<i>Urban</i>	120/200 (60%)	26/46 (56.25%)	21.6%	0.78
<i>Female</i>	80/200 (40%)	22/46 (47.80%)	25%	
Socio Economic Status (Modified Prasad Classification)				
<i>Class III/IV/V</i>	180/200 (90 %)	42/46 (97%)	23.3%	0.736
<i>Class I = II</i>	20/200 (10%)	4/46 (8.6%)	20%	

Immunization				
<i>Vaccinated</i>	176/200 (88%)	33/46 (71.73%)	18.7%	0.0001
<i>Unvaccinated</i>	24/200 (12%)	13/46 (28.26%)	54%	
Nutrition				
<i>Normal</i>	112/200 (56%)	23/46 (50%)	20.5%	0.35
<i>Undernutrition</i>	88/200 (44%)	23/46 (50%)	26.1%	
SpO2				
SpO2 <90%	89/200 (44.5%)	33/46 (71.31%)	37%	0.0000
SpO2 >90%	111/200 (55.5%)	13/46 (28.6%)	11.7%	
Haemoglobin (gm %)				
Hb<10	106/200 (53%)	31/46 (67%)	29.25%	0.025
Hb<10	94/200 (47%)	15/46 (32%)	15.96%	
Chest X-ray				
Abnormal	119/200 (59.5%)	21/46 (45.65%)	17.6%	0.878
Normal	81/200 (40.5%)	15/46 (32.60%)	18.5%	
Etiology				
Primary Respiratory Cause	128/200 (64%)	12/46 (69%)	25%	0.82
Non respiratory Cause	72/200 (36%)	14/46(30%)	19.4%	

◆7% (14/200) of the admitted children were below 2 months. Proportional mortality rate was 17% (8/46). Case fatality rate was 57.14% (8/14).

◆72% (144/200) of the admitted children were in the age group 2 months – 59 months. Proportional mortality rate was 67% (31/46.) Case fatality rate was 21.53 (31/44)

◆21% (42/200) of the admitted children were above 60 months. Proportional mortality rate in them was 15.21 (7/46) case fatality rate was 16.67% (7/42).

◆48.5% (97/200) were males among admitted children, proportional mortality rate in them was 52% (24/46) and case fatality rate was 24.7% (24/97) 51.5% (103/200) were females among admitted children, proportional mortality rate in them was 52% (24/46) and case fatality rate was 21.3 (22/103)

◆60% (120 / 200) of the admitted patients were from urban area and 40% (80/200) were from rural area. Proportional mortality rate in patients from urban area was 56.25% (26/46) and case fatality rate was 21.6% (26/120) The proportional mortality rate in children from rural area was 47.8% (20/46) and case fatality rate was 25% (20/80)

◆90% (180/200) of the admitted children were from low socio-economic status (Modified Prasad classification class III, IV, V) Proportional mortality and case fatality rate was 97% (42/46) 23.3% 41/180 respectively. 10% of the admitted children were from high socio-economic class (Modified Prasad classification class I, II). Proportional Mortality and case fatality rate was 8.6% (4/46) and 20% (4/20) respectively.

◆88% (176/200) of the admitted children were immunized appropriately for age. Proportional mortality rate in them was 71.73% (33/46) and case fatality rate was 18.7% (33/176). In the unvaccinated group, proportional mortality was 28.26% (13/46) but the case fatality rate was 54% (13/24).

◆Nutritional status of 56% (112/200) was adequate. Proportional mortality rate was 50% (23/46). Case fatality rate was 20.5% (23/112). 44 % (88/200) were undernourished with proportional mortality rate of 50 % (23/46) and case fatality rate of 26 % (23/88).

◆44.5 % (89/200) of the admitted children had signs of hypoxemia (SpO₂ <90%). The proportional mortality rate was 71.31% (33/46) and case fatality rate was 37% (33/89) in them.

◆ 55.5% (111/200) of the admitted patients had SpO₂ >90%. Proportional mortality rate was 28.26% (13/46) and case fatality rate was 6.5% (13/200) in them.

◆53% (106/200) of the admitted children's had anaemia (Hb<10 gm%) proportional mortality rate in them was 67% (31/46) and case fatality rate was 29.25% (31/106).

47% (94/200) did not have anemia (Hb> 10gm%). Proportional mortality rate in them was 32.60% (15/46) and case fatality rate was 15.96% (15/94).

◆59.5% (119/200) had abnormal radiological picture. Proportional mortality in them was 45.65% (21/46) and case fatality rate was 17.6% (21/119). 40.5% (81/200) had normal chest radiograph. Proportional mortality rate in them was 32.6% (15/46) case fatality rate was 18.5% (15/81)

◆Patients of respiratory distress having primary respiratory cause constituted 64% (128/200). 36% (72/200) had non respiratory cause of respiratory disease. The mortality in patients with primary respiratory cause of respiratory distress was 69% (32/46). The case fatality rate in same was 25% (32/200). The mortality due to non respiratory cause of respiratory distress was 30% (14/46) and case fatality rate was 19.4% (14/72)

Conclusion:

◆ The Case fatality rate due to respiratory distress in young infants <2 months was observed to be higher as compared to older children. (P Value <0.0005 significant).

- ◆ The difference of case fatality rate due to respiratory distress observed in different gender, place of residence, socio economic status had no significance.
- ◆ □ Good immunization status of children was observed to be an important determinant protecting the child. (P Value <0.0001 very highly significant).
- ◆ Low SpO₂ level was attributable to higher case fatality rate. (P Value 0.000 highly significant).
- ◆ Case fatality rate due to respiratory distress was twice in children with anemia. The difference was statistically significant (P Value <0.025)
- ◆ No significant difference was observed between mortality in children with abnormal and normal chest radiographs.
- ◆ No significant difference was observed between mortality in children having respiratory distress due to primary respiratory cause and respiratory distress due to non respiratory cause.
- ◆ Therefore rational use of O₂ supplementation, immunization, correction of anemia would be significant factors to reduce the mortality in children with respiratory distress.

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INCIDENCE OF TUBERCULOSIS FROM STUDY OF FINE NEEDLE ASPIRATION CYTOLOGY OF LYMPHADENOPATHY

Majal G Shah¹, Chetan M Dharaiya², Kanaiyalal J Patel³, Vilas J Patel⁴, Chilvana V Patel⁵, Nikesh R Agrawal⁶

1. MD (Path & Bact), Assistant Professor in Pathology, C.U. Shah Medical College, Surendranagar, Gujarat.
2. MD (Path & Bact), Tutor in Pathology, B. J. Medical College, Ahmedabad, Gujarat.
3. MD (Pathology), MD(Microbiology)
Assistant Professor in Microbiology, B. J. Medical College, Ahmedabad, Gujarat.
4. Associate Professor in Physiology, B. J. Medical College, Ahmedabad, Gujarat.
5. 3rd year Resident in Medicine, B. J. Medical College, Ahmedabad, Gujarat.
6. MD (P & SM), Assistant Professor in Community Medicine, B. J. Medical College, Ahmedabad, Gujarat.

SUMMARY

Fine needle aspiration cytology of 205 cases of lymphadenopathy were performed at the department of Pathology, C. U. Shah medical College, Surendranagar, Gujarat from August 2003 to July 2005. Smear were fixed in alcohol and stained by Hematoxylin & Eosin, Papanicolaou and Ziehl-Neelsen stain. There were 140 cases of tuberculous and 65 cases of reactive lymphadenitis. Third decade is the most common affected age group in tuberculosis. Acid fast positivity is seen in 47.8%

cases of tuberculous lymphadenitis and it is particularly higher when only cheesy and necrotic material aspirated (71%). Fine needle aspiration cytology of superficial lymph nodes assisted with Ziehl-Neelsen (Z-N) stain is an investigation of great utility in the diagnosis of tuberculosis.

Key words : Lymph node aspiration, Tuberculosis incidence, Z-N stain.

Introduction :

Fine needle aspiration cytology (FNAC) provides an alternative to excision biopsy for lymph nodes and is easy procedure for collection of material for cytomorphologic and bacteriologic examination. The use of FNAC in the diagnosis of tuberculous lymphadenitis is being described increasingly, as described by many authors¹⁻⁵. The diagnostic findings are epitheloid cell granulomas with or without multinucleate Langhan's giant cells and caseation necrosis. However, in case presenting with cold abscess, well formed epitheloid granulomas may not be present, and in such cases acid fast staining of the smear is of great help. In developing countries such as India, tuberculosis is rampant; tuberculous lymphadenitis constitutes to be one of the most common types of lymphadenitis⁶⁻¹⁰. The present study was undertaken to evaluate the role of FNAC in tuberculous lymphadenitis.

Material and Methods :

From August 2003 to July 2005, fine needle aspiration cytology of 205 cases of lymphadenopathy were performed at Pathology Department, C. U. Shah Medical College, Surendranagar. FNAC of the enlarged lymph node was performed with informed consent of the patient following thorough clinical examination. Aspirations were performed using 20 to 24 Gauze needle and disposable 10 ml plastic syringe with a detachable syringe holder. In all the cases, alcohol fixed smears were made and stained with Hematoxylin & Eosin and Papanicolaou Stain, and for each case an additional slide was kept unstained for further required stain as needed. Tuberculous aspirates were diagnosed on FNAC by polymorphous picture of the smear, with no evidence of malignant cells and the characteristic features were epitheloid cell clusters, caseation necrosis with or without typical Langhan's giant cells. In all cases, where the cytological diagnosis was of granulomatous disease, Ziehl-Neelsen staining for acid fast bacilli (AFB) was performed. Furthermore the clinical characteristic of lymph node were studied and correlated to cytological finding to ascertain the incidence of tuberculosis in the community at large.

Results :

Table I. Incidence of reactive v/s tuberculous lymphadenopathy in male and female

	Male	Female	Total	%
Reactive Lymph node hyperplasia	41	24	65	31.7
Tuberculosis	76	64	140	68.3
Total	117	88	205	100

Table II. Incidence of tuberculous lymphadenopathy in relation to age and sex

Age group (in yrs)	Males	Females	Total	Percentages
0-10	13	12	25	17.85
11-20	17	11	28	20.00
21-30	24	25	49	35.00
31-40	09	07	16	11.42
41-50	05	04	09	06.43
51-60	05	04	09	06.43
≥61	03	01	04	02.85
Total	76	64	140	100

Out of the 205 cases, 140 cases were of tuberculous in nature and 65 cases were reactive in nature (Table I). Thus, tuberculous lymphadenopathy forms the largest group of the patients. The age of the patient in tuberculous lymphadenitis range form 1.5 year to 75 year. The majority of the cases in first four decades of life (84.27%), with a pick age range of 21-30 years (35%). Its incidence declined with advancing age (Table II). Out of the 140 cases of tuberculous lymphadenopathy, 76(54.3%) cases were reported in male and remaining 64 (45.7%) cases in female with the male: female ratio being 1.18:1 (Table II). The cervical group of lymph node was involved most commonly in present study (112 cases, 80%). The most common picture on cytologic examination was the presence of epitheloid cell clusters with or without Langhan's giant cell with necrosis and caseation, or smear with only necrotic material consisting of diffuse granular debris containing acid fast bacilli in Ziehl-Neelsen stain. Out of the 140 cases of tuberculous lymphadenopathy, AFB was found in 67 (47.8%) cases. The morphology of tubercle bacilli in smear was as short and stumpy rods. The AFB positivity rate was particularly high when only cheesy or necrotic material was aspirated (71%). Among the 65 cases of reactive lymphadenopathy, the age of the patient, range from 2 years to 70 years, thus showing wide range of distribution of cases from early life to advance age. 41 (63.1%) cases were reported in male and remaining 24 (36.9%) cases in female with male: female ratio being 1.7:1. Clinical characterization of lymph node was done, and on correlation with the cytological findings we came to the assertion that lymph node size was less than one cm in 76% cases of reactive lymphadenopathy, where as it was over one cm in size in 87% cases of tuberculous lymphadenopathy. 90 % cases of reactive lymphadenopathy showed discrete lymph nodes; where as 61% cases of tuberculous lymphadenopathy had matted lymph nodes.

Discussion :

This study was undertaken to evaluate the role of FNAC in tuberculous lymphadenitis. Although the symptoms and sign may indicate the probable etiology of lymphadenopathy, the clinical diagnosis has pitfalls. Therefore, a morphologic diagnosis is required before starting anti tuberculosis therapy. FNAC which has recently become a diagnostic technique for various pathologic lesions is particularly useful in developing countries, including India where facilities for biopsy are not readily available in peripheral areas. The lesion arising in lymph node can be found in patient ranging from early to advance age. In our study youngest patient was 1.5 years old and oldest was 75 years of age which is fairly comparable to a study of Steel BL et al¹¹ of 1,103 patient where youngest patient was 1 year old and oldest being 90 years. In our study maximum

numbers of cases were in the third decade of life followed by second and first decade of life. The incidence was decreased after thirty years of age. It may be due to the development of immunity in older patients. These findings are comparable with that of Gupta SK et al¹². Male predominance with 1.18:1 sex ratio was noted by us in cases of tuberculous lymphadenitis, these results are comparable with the findings of Rajsekaran S et al¹³ and Bailey TM et al¹. Rajsekaran S et al¹³ and Bailey TM et al¹ described 1.3:1 and 1.4:1, male: female ratio respectively in tuberculous lymphadenitis. Correlation of the clinical characteristic of lymph glands to cytological impression was also observed. In our study, reactive glands were mostly less than 1 cm in size (76%) where as tuberculous glands were over 1 cm in size in majority of cases (87%) which was in concordance with Bedi RS et al¹⁴ and Ahmad SS et al¹⁵. Matted lymph nodes were seen in 61% cases of tuberculous lymphadenitis where as discrete lymph nodes were seen in 90% cases of reactive lesions, similar findings were observed by Bedi RS et al¹⁴ and Tilak V et al¹⁶. Bedi RS et al¹⁴ and Tilak V et al¹⁶ found matted lymph nodes as one of the characteristic features of tuberculous lymphadenitis. In our study, we found 140 (68.29%) cases of tuberculous lymphadenitis. Ahmad SS¹⁵ found 38%, Tilak V et al¹⁶ found 38.8% cases of tuberculous lymphadenitis. The higher rate of tuberculous lymphadenitis at our region is due to very lower socioeconomic status, higher rate of illiteracy, incomplete treatment, drug resistance and increasing incidence of HIV. Among 140 cases of tuberculous lymphadenopathy, 67(47.8%) cases showed acid fast positivity. These figures come in close comparison to a study of Ahmad SS et al¹⁵. Maximum AFB positivity rates (71%) was found in smear containing purulent material on aspiration. These findings correlate with findings of other authors^{1,14-16}, who also found highest yield of tubercle bacilli in purulent material. Negative mycobacterial examination does not exclude the possibility of tuberculosis because for bacilli to be demonstrated in smear, there number should be 10,000 to 100,000 / ml of material¹⁷. If the number is less than this, the bacilli may not be detected in smears.

Conclusion :

FNAC coupled with Ziehl-Neelsen staining for AFB is a very useful diagnostic tool in the diagnosis of tuberculous lymphadenitis. It can be performed as an out patient department procedure. The procedure is easily accepted by patient & is cost effective. There is no need of anesthesia and speedy results are obtained. An accurate diagnosis can be mad even in most remote areas, where other sophisticated diagnostic tools are not available. It serves as a complimentary diagnostic procedure to histopathological examination.

The present study made it clear that the FNAC is the best investigation one can ask for with a good accuracy which can be achieved with greater experience and expertise.

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STUDY OF 110 CASES OF ARTERIOVENOUS FISTULA CREATED FOR HEMODIALYSIS

Dr. Asit Patel*, Dr. Archana Dalal**, Dr. Ajay Munshi***
Dep. Of surgery Smt NHL Mun medical college Ahmedabad 380006

AIMS & OBJECTIVES :

Repeated hemodialysis is the mainstay of the treatment of chronic renal failure [CRF].

Arteriovenous fistula (AV Fistula) is the most convenient & safe mean of undergoing hemodialysis. This study is aimed to assess the success & failure rates, duration of patency of fistula, immediate complications of the procedure & cost-effectiveness. We have included the patients, who underwent this procedure from May 2002 to May 2004 at Dep. Of surgery Smt NHL Mun medical college , Ahmedabad.

MATERIALS & METHODS :

Commonest site selected was radial aspect of wrist & lower forearm on nondominant upper limb. If the nondominant limb is not suitable for creating AV fistula (i.e. due to thrombosis of veins or repeated venepunctures), dominant upper limb was selected. Fistula was created under local anaesthesia i.e. a cocktail of 5 cc Xylocaine 2% & 5 cc Bupivacaine, infiltrated at the operative site. About 4 cms. long incision was put. Cephalic vein was dissected free from facial coverings & all tributaries were ligated using 3/0 silk. Radial artery was dissected & all its branches were secured with 3/0 silk. Vasa vesorae of Radial artery were also dissected off the artery. During dissection, radial nerve was safeguarded. We anastomose the Radial artery & Cephalic vein in side-to-side manner with 7/0 Prolene & ligate the Cephalic vein just distal to the anastomosis. Just before starting anastomosis, 5000 units of heparin was given intravenously.

RESULTS :

According to the methods of anastomosis, the patients were categorized in 3 groups-

METHOD	PATIENTS	PERCENTAGE
Side-to-side anastomosis	27	24.54%
End-to-side anastomosis	10	9.06%
Side-to-side anastomosis with ligation of vein just distal to anastomosis	73	66.38%

We had given intravenous heparin (5000 units) to all the patients about 10 minutes before starting the anastomosis. In initial 50 cases, heparin in the same dose was continued 8 hourly for 3 days. Rest of the patients were given only one shot of heparin preoperatively.

Amongst initial 50 patients, 15 patients required re-exploration within 24 hours of initial procedure due to bleeding from incision site & swelling. In 7 patients, the bleeder was found & secured. 8 patients were found to have diffuse oozing & presence of clots. The clots were evacuated & localized pressure was applied which stopped the bleeding. All these 15 patients had maturation of fistula. Because of this complication, we abandoned the protocol of “3 days heparin therapy” & shifted to single shot preoperative heparin (5000 units) which did not cause such complication.

Out of 110 patients, 9 patients required re-operation due to failure of initial procedure. In all these patients, re-operations were carried out at the level of elbow. The opposite forearm was not selected in view of thrombosis of superficial veins due to repeated previous venepunctures. All these patients underwent side-to-side anastomosis.

INITIAL PATENCY	NO. OF PATIENTS	PERCENTAGE
Fistula working at first Instance	101	91.81%
Re-operation required	9	8.19%
Total	110	100%

In 17 patients, fistula was created at mid-forearm level due to thrombosis of vein at wrist level.

Maturation of AV fistula occurred within 15-20 days. After this time, hemodialysis was successfully done in all patients.

The follow up of the patients ranged from 4 to 24 months (mean 14 months). Out of 110 patients, 85 were males & 25 females with age ranging from 25-78 years (mean 51.5 years).

Male	85	87.28%
Female	25	22.72%
Total	110	100%

7 patients failed to develop maturation of AV fistula even after re-operation. Our failure rate was 6.36%. In 10 patients, the fistula got thrombosed after 15 months. 20 patients were lost to follow up after 4 months. In rest 73 patients, the fistula is still working satisfactorily after 24 months.

DISCUSSION:

In our series, the procedure of AV fistula was cost-effective. The cost of the procedure ranged from 800-1000 rupees. This procedure was carried out on an outpatient basis except for the patients who required medical treatment of complications of CRF i.e. severe anemia, breathlessness, metabolic encephalopathy etc. Moreover, this procedure alleviates need of repeated insertions of catheters in major vessels like Subclavian & Femoral vessels. Thus this procedure is safe & well acceptable to the patients.

AV fistula created at wrist for hemodialysis gives good results in form of high reflux fistula³. There is no difference in state of patency with administration of postoperative heparin¹. In cases of very small veins of upper extremities which are unsuitable for anastomosis with an artery, prosthetic conduits like “U graft” or stent- graft expandable balloon device can be used which also give excellent results⁵. In patients, if the upper extremity veins are thrombosed – as in AIDS or in patients who are chronically drug abusers; lower extremity saphenous vein transposition AV fistula (SVTAF) is a successful alternative⁴. These patients are prone to develop infections & so use of prosthetic grafts should be avoided⁴. The Brachial artery – transposed Basilic vein AV fistula has been used in preference to a prosthetic graft as the complication rates are higher with prosthetic grafts².

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PREVALANCE OF REFRACTIVE ERRORS IN CHILDREN (AGE GROUP 7-15 YEARS) OF RURAL And URBAN AREA OF GUJARAT :A POPULATION BASED STUDY

Dr. Vivek Trivedi *& Dr. Sandip Zalawadiya* Dr. Janardan V. Bhatt ** Dr Tapaswi Pawar***, Dr Bhavana Kupmavat*** Interns , * Intern dictors ** Prof. at Nagar School of Optometry and Associate prof. of physiology, ***Assit.prof. of P&SM Smt NHL Mun Medical college Ahmedabad 380006

AIM: To assess the prevalance of refractive error and related visual impairment in school-aged children in the rural population of the Prantij village of Sabarkantha district and compare the result with similar study done at Urban area in Ahmedabad in Gujarat.

METHOD: Random selection of village-based clusters was used to identify a sample of children 7 to 15 years of age. From February 2006 through April 2006, children in the

25 selected clusters were enumerated in a door-to-door survey and examined at a rural eye center. The examination included visual acuity measurements, ocular motility evaluation and examination of the anterior segment & media. Myopia was defined as spherical equivalent refractive error of at least -0.50 D and hyperopia as +2.00 D or more.

RESULTS: A total of 452 children from 500 households was enumerated, and 417 (92.3%) were examined. The prevalence of uncorrected, baseline (presenting), and best corrected visual acuity of 20/40 or worse in the better eye was 2.7%, 2.6%, and 0.78%, respectively. Refractive error was the cause in 61% of eyes with vision impairment, amblyopia in 12%, other causes in 15%, and unexplained causes in the remaining 13%. A gradual shift toward less-positive values of refractive error occurred with increasing age in both boys and girls. Myopia in one or both eyes was present in 4.1% of the children. Myopia risk was associated with female gender and having a father with a higher level of schooling. Higher risk of myopia in children of older age was of borderline statistical significance ($P = 0.069$). Hyperopia in at least one eye was present in 0.8% of children, with no significant predictors.

CONCLUSIONS: Refractive error was the main cause of visual impairment in children aged between 7 and 15 years in rural India. There was a benefit of spectacles in 70% of those who had visual acuity of 20/40 or worse in the better eye at baseline examination. Because visual impairment can have a significant impact on a child's life in terms of education and development, it is important that effective strategies be developed to eliminate this easily treated cause of visual impairment.

Key words: Refractory errors, Rural and urban area, correction of errors

Introduction:

REFRACTIVE ERROR is one of the most common causes of visual impairment around the world and the second leading cause of treatable blindness. Few population-based data on refractive error are available from India, but some are available for children attending school. Data obtained only from children going to school cannot be reliably used to plan eye-care services, however, because they are not representative of the population at large, particularly in India, where a significant proportion of school-aged children do not attend school.

Method:

FIELD OPERATION

Fieldwork was performed between July 2006 and August 2006, proceeding in a cluster-by-cluster sequence. All field operations within a particular cluster, including clinical examinations, were generally completed within a 1-week period, before moving on to the next cluster.

Each cluster was mapped to identify all houses by three field investigators, followed by a household-to-household enumeration of eligible children. A community leader was contacted

before the mapping by the field investigators to explain the purpose of the survey and to seek his or her support. Family members living and eating in the same premises were defined as a household. The study's purpose was explained to the man or woman of the household during the enumeration. The name, age (completed years), gender, years of schooling, and name of the school were collected for each child 7 to 15 years of age. Also, data on the schooling level of parents and whether eligible children were absent from the community were collected. The number of eligible children in each household and their availability were verified by querying neighbors.

A card with the scheduled date for the eye examination was given to the man or woman of the household for each eligible child. Children with spectacles were requested to bring them on the day of the examination. Written informed consent for the examination was obtained from the man or woman of the household after explaining the eye examination procedures. Those who refused to participate in the study were contacted at least three times on separate occasions before they were deemed to be non participants—twice within the 1-week period when the team was in the cluster and again toward the end of the study. Children who could not keep the scheduled date were given another date within the same week or were offered an examination near the end of the study. Age was verified before the examination process was initiated. Those who were found ineligible were offered an eye examination but were not considered to be study participants.

CLINICAL EXAMINATION

Examinations were generally performed during standard clinic hours on Saturday and Sunday.

In brief, the examination included distance visual acuity measurements, ocular motility evaluation. Visual acuity was measured. The right eye was tested first and then the left, both with (presenting visual acuity) and without glasses (uncorrected visual acuity), if the child brought them. Ocular motility was evaluated at both 0.5 and 4.0 m. Subjective refraction was performed in children with uncorrected visual acuity of 20/40 or worse in either eye.

The principal cause of visual impairment of 20/40 or worse was assigned after completion of the ocular examination, using a seven-item list (refractive error, amblyopia, corneal opacity due to trachoma, other corneal opacity, cataract, retinal disorder, other causes). Refractive error was recorded as the cause of visual impairment in eyes improving to 20/32 or better with refractive correction. Amblyopia was considered the cause of impairment in eyes with best corrected visual acuity of 20/40 or worse and no apparent organic lesion.

Children whose vision improved with refractive error correction in either eye were prescribed and spectacles were advised. Children needing medical or surgical treatment were referred to the rural eye center for treatment.

DATA MANAGEMENT AND ANALYSIS

Prevalence of visual impairment (visual acuity 20/40 or worse) and blindness (visual acuity of <20/200) was calculated for uncorrected visual acuity, baseline (presenting) visual acuity, and best measured visual acuity. The latter measurement was based on subjective refraction obtained in those with reduced uncorrected visual acuity.

Myopia was defined as a spherical equivalent refractive error of at least -0.50 D and hyperopia as +2.00 D or more. A child was considered an emmetrope if neither eye was myopic or hyperopic, a myopic if either or both eyes had myopia, and a hyperope if one or both eyes had hyperopia, so long as neither eye had myopia. Age-specific prevalence of myopia and hyperopia were estimated. In addition to these two variables, the years of schooling of the father, as a surrogate for the socioeconomic status of the family, and years of schooling of the child were also included in the regression model. The father's schooling was categorized to correspond to distinct grade level achievement: none, 1 to 5 years, 6 to 12 years, 13 to 15 years, and more than 15 years. Pair-wise interactions between regression model variables were assessed simultaneously, using EPI 2002 by chi-square test and were considered significant at $P < 0.10$.

Result:

A total of 500 households were identified in 25 clusters, of which 256 (51.2%) provided 452 eligible children between 7 and 15 years of age. In households with eligible children, 47.4% had one such child, 33.7% had two, 14.9% had three, and 4.0% had four or more. The largest household had seven eligible children.

Of these 452, 417 were examined—a participation rate of 92.3%. Examination response across the 25 clusters ranged from 81.2% to 98.3%. Girls had a better overall examination response rate: 93.3% compared with 91.4% in boys. Although there were differences in response rates across ages and gender, the distribution of the examined population was not significantly different from that of the enumerated population.

Approximately half of the examined children were attending school, including 84% of 7-year-olds. Twenty-four percent of children had never been in school. Three fourths (78%) of fathers had no formal schooling: 8% had 1 to 5 years, 13% 6 to 12 years, and 2% had 13 years or more. Ninety percent of mothers had no schooling.

VISUAL ACUITY

Uncorrected and baseline visual acuities (determined at initial examination) were available in 409 (98.0%) children. Uncorrected visual acuity of 20/32 or better in at least one eye was found in 406 (97.3%), corresponding to 11 (2.7%) with acuity of 20/40 or worse in both eyes. One (0.23%) child had visual acuity of 20/200 or worse in the better eye. One (0.23%) had less than 20/200 in the better eye and was therefore blind according to the definition used in India.

Twenty-three children had spectacles at initial examination, six (26.1%) with baseline visual acuity of 20/40 or worse in at least one eye, including one child with visual acuity less than 20/200 in the better eye. Among those with uncorrected visual acuity of 20/40 or worse in both eyes, ten (9.2%) were wearing glasses. Because so few children were wearing glasses, baseline acuity was essentially the same as uncorrected visual acuity. In 11 (2.6%) children, acuity was 20/40 or worse in both eyes, including one (0.23%) child who was blind, with acuity less than 20/200 in the better eye. The additional case of blindness with baseline acuity was because the one child with visual acuity of less than 20/200 in both eyes with spectacles had uncorrected visual acuity better than 20/200 in the better eye when the glasses were removed.

Best corrected visual acuity measurement was available in 409 (98.1%) children, of whom 11 (0.78%) had visual acuity of 20/40 or worse in both eyes. Accordingly, 1.8% of all children examined had improved baseline visual acuity to 20/32 or better in at least one eye with prescription glasses.

OTHER OCULAR ABNORMALITY

Eyelid abnormalities (mainly blepharitis) were observed in 6 eyes of 4 (0.93%) children. Conjunctival abnormalities were present in 38 eyes of 21 (5.1%) children, including 31 eyes in 16 (3.9%) children with Bitot spots. Corneal abnormalities were observed in 3 eyes of 2 (0.39%) children. Pupillary abnormalities were noted in 3 eyes of 2 (0.37%) children. Lenticular abnormalities were present in 3 eyes of 2 (0.37%) children, including 1 child with a pseudophakic eye and another with traumatic aphakia.

CAUSES OF VISUAL IMPAIRMENT

In more than half of the children, the reduced visual acuity was because of refractive error. Amblyopia, satisfying the predefined criteria, was the cause of uncorrectable vision impairment in another 65 (15.5%) children. In another 24 eyes of 16 children, the criteria were not met, but it was concluded that amblyopia was the most likely cause of vision impairment. Corneal opacity and scars were the other significant causes of visual impairment.

COMPARATIVE ANALYSIS OF PREVALANCE OF REDUCED VISUAL ACUITY IN A RURAL STUDY POPULATION (AGE GROUP 7-15 YEARS) OF PRANTIJ AS AGAINST TO URBAN STUDY POPULATION OF AHMEDABAD CITY.

	<i>PERCENTAGE OF RURAL POPULATION N1=417</i>	<i>PERCENTAGE OF URBAN POPULATION N2=100</i>	<i>P Value</i>		
<i>PARTICIPATION RATE</i>	92.3%	85.1%	<0.05		
<i>VISUAL ACUITY OF 20/40 OR LESS IN UNCORRECTED VISION OF ONE EYE</i>	2.6%	4.9%	N.S.		
<i>VISUAL ACUITY OF 20/40 OR LESS IN UNCORRECTED VISION OF BOTH EYES</i>	0.78%	2.6%	N.S.		
<i>CORRECTION OF REFRACTIVE ERROR USED BY CHILDREN AGE GROUP 7-15 YEARS (SPECTACLES USED)</i>	5.3%	26.8%	<0.05		
<i>PREVALANCE OF MYOPIA IN AGE GROUP 7-15 YEARS</i>	4.1%	7.4%	N.S.		
<i>PREVALANCE OF HYPEROPIA IN AGE GROUP 7-15 YEARS</i>	0.78%	7.7%	P<0.05		
<i>PREVALANCE OF BLINDNESS (VISUAL ACUITY OF < 20/200 IN THE BETTER EYE)</i>	0.18%	1.6%	N.S.		
<i>REFRACTIVE ERROR AS A CAUSE OF VISUAL IMPAIRMENT</i>	8.5%	66%	N.S.		

N.S.=difference is not significant statistically

DISCUSSION:

This is a population-based cross-sectional survey of school-aged children between 7 and 15 years of age in a rural and urban population of Gujarat in India. Five- and 6-year-olds were finding it very difficult to comprehend the visual acuity test—particularly, those without prior schooling experience. Because many of these visual acuity measurements would not have been accurate, a decision was made to exclude children of these ages from the study sample.

Flood conditions that were prevailing in Gujarat during this time contributed to this possibility. The major occupation in Sabarkantha district is agriculture, which was seriously affected by the flood. To help households survive financially, children 13 years of age and older may have temporarily moved to cities with their fathers to look for work, where, through manual labor, they could contribute to the sustenance of the household. In other cases, entire households may have relocated to cities—particularly those with children in this employable age range. Although not representing incomplete enumeration of children with residence remaining in Sabarkantha district, it would have contributed to the deficit of children 13 to 15 years of age.

The overall examination participation rate was 92.3%, with participation the lowest among older children. Again, older children were more likely to be unavailable for examination, even though they may have been enumerated. To improve the participation rate in this age group, the field team revisited households toward the end of the study. However, this had limited success in increasing response rates. The combination of migration, under enumeration, and lower examination participation among 13- to 15-year-olds may have introduced biases that could have affected study results in some unsuspected way.

Baseline (presenting) visual acuity of 20/40 or worse in at least one eye was found in 4.9% of the study population, which decreased to 2.5% with best corrected vision. For visual acuity 20/40 or worse in the better eye (i.e., both eyes), the respective percentages were 2.6% and 0.78%. With uncorrected visual acuity, 2.7% had acuity worse than 20/40 in the better eye. These findings illustrate the potential benefit of spectacles in 70% of the children who had bilateral vision impairment and in 50% of those with visual acuity of 20/40 or worse in at least one eye.

The prevalence of baseline visual acuity of 20/40 or less in the better eye in the urban population in Ahmedabad, 4.9%, was nearly double the 2.6% found in the rural population of Sabarkantha district. Although with best corrected vision the prevalence of impairment was similar in urban and rural populations, blindness remained nearly twice as high in the rural population as in the urban population with both baseline and best corrected visual acuity. The burden of visual impairment in both urban and rural populations was mostly due to refractive error. The prevalence of uncorrected visual acuity of 20/40 or less in the better eye because of refractive error was 1.9% in the rural population, compared with 5.6% in the urban population of Ahmedabad. The difference in visual impairment at initial examination between these urban and rural populations would have been even greater, approaching a threefold difference, had not a higher percentage of children in the urban population had correction for refractive error—26.8% versus 5.3% in the rural population. These data highlight the need for refractive error correction in school-aged children in India.

The overall prevalence of myopia of -0.50 D or worse in this study was 4.1%, which is higher than the 1.2% reported in children 5 to 15 years of age from rural Nepal, but less than that reported from China (16.2%), Chile (6.8%), and Ahmedabad (7.4%). Myopia was associated with female gender and older age, which was also found in Ahmedabad and China. The association of myopia with the father's schooling was found in both this and the Ahmedabad survey. Children from families led by parents with higher levels of educational attainment,

and probably greater resources, may experience more pressure to study, entailing near work, which in turn could cause the onset of myopia.

The prevalence of hyperopia of +2.00 D or more was 0.78%, less than the 1.4%, 3.5%, 16.3%, and 7.7% reported in children 5 to 15 years of age from Nepal, China, Chile, and Ahmedabad, respectively. Review of age-specific data indicates that this low prevalence is not explained by the exclusion of 5- and 6-year-olds in this rural population. There were no significant associations of age or gender with hyperopia. The age-related shift from hyperopia to myopia was not as prominent in our study population as in the urban population in Ahmedabad, which could be related to the increased intensity of schooling in the urban population compared with that in our rural population.

Notable differences in the prevalence of myopia, hyperopia, and astigmatism were found between this rural population and the urban population in Ahmedabad. Because of the cross-sectional nature of these studies, it is possible to comment only on the association between refractive error prevalence and possible risk factors, and not on the more specific causes. Observed differences in the schooling of both children and parents, specifically fathers, represents one possible explanation for the differences in refractive error between the rural and urban populations studied. The association of myopia with the father's educational level may represent an environmental effect, as well as a genetic one if fathers with myopia are more likely to have higher levels of schooling. Although the influence of environment on myopia, separate from genetic influences, cannot be addressed using these data, the apparent importance of schooling intensity on the prevalence of myopia is clearly highlighted by these studies.

Refractive error was shown to be the leading cause of visual impairment among rural children 7 to 15 years of age, accounting for 68.5% of impairment, with amblyopia included. (To estimate the complete burden of refractive error, refractive error-related amblyopia should also be taken into account.) Data from the Sabarkantha survey suggest that 0.18% of rural school-age children are blind (baseline visual acuity <20/200 in the better eye) and another 2.4% are visually impaired (baseline visual acuity 20/40–20/200 in the better eye), but that these proportions can be reduced to 0.13% and 0.65%, respectively, with the use of refractive correction. The findings in this survey are comparable with the ones obtained in the current study.

From a public health perspective, vision screening is an appropriate strategy to reduce vision impairment. Most of this impairment is caused by refractive error, for which treatment is simple, effective, and inexpensive. A few factors should be considered, however, in establishing screening programs: First, vision screening should take place only if adequately trained personnel are available who can perform refraction of reasonable quality in children identified with vision impairment. Second, provision of good-quality and affordable spectacles should be an integral part of the vision-screening program. Third, an attempt should be made to include all school-aged children, not just school-attending children, because many of the children in developing countries do not attend schools. Fourth, target populations should be prioritized using available population-based data on the age distribution of refractive error.

CONCLUSION and implications:

Significant proportion of children of rural area had uncorrected refractory errors warrant urgent action to correct the visual error by providing adequate spectacles. This will further help to improve his/her school and social participation and psycho social development. As the defective vision is obstacle to learning process and are prone to road accident. It also help to prevent the further deterioration of vision and blindness and irreversible changes in retina and macula.

Many children with severe visual disability can benefit greatly from optical correction .Services for refractory error correction , provision of low cost [free?] spectacles and low vision care must be provided on large scale in the country and it should reach to rural area if our program for vision 2020 is to make successful. Many NGOs are working in this field can play significant role .Epidemiological studies are required to identify the refractory errors quantum and efforts are to be focused on in time correction of refractory errors to prevent irreversible visual loss and primary prevention of blindness . In this context , Information, education and communication amongst people in primary health care play pivotal role in prevention and early detection of refractory errors. Primary teacher , parents are also to be educated and made aware of early detection of refractory errors. This education can be intervened with other health education programs i.e. education of breast feeding, lactation, and nutrition and immunization programs.

In conclusion, significant visual impairment due to refractive error was found among school-aged children living in a rural district of western India. Because most refractive error can be easily corrected with spectacles and because visual impairment can have a detrimental impact on education and development in a child's life, cost-effective strategies to eliminate this easily treatable cause of visual impairment are warranted.

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AXIS DETERMINATION: VECTOR DISC V/S PERPENDICULAR METHOD

Dr. V.P.Bhatt , Dr. Chinmay Shah Department of Physiology. P.D.U. Medical College Rajkot.

Introduction:

Electrocardiogram is a record of electrical impulses from the Heart on to graph paper. These electrical impulses are recorded as a wave or deflections that spread from the Heart to the body surface area.¹ Direction of electrical forces in the Heart is represented by Axis of ECG. It is important to determine the mean direction of current flow during depolarization of ventricles in every 12 lead E.C.G. The normal QRS axis in the adult points downward and to the left. The normal axis ranges between 0 to 90°, although normal range can vary from -30° to + 110°. An abnormal QRS axis may occur with hypertrophy of ventricles, myocardial infraction, conduction block in ventricles and multiple other causes.

In this respect, **various objective methods** especially for axis determination are developed. E.g. Quadrant method, Right reaches left leaves method and perpendicular method for determination of ECG axis. Out of all, perpendicular method is most accurate method for determination of QRS axis. Recently I came across the **new method**: Vector disc² for determination of ECG axis. In present study we had tried to cases the accurate of method and we had compared this new method with perpendicular method of axis determination.

Material and Method:

The study has been carried out at Department of Physiology, P.D.U. Medical College Rajkot. Randomly selected 50 ECG was studied. We had Collected ECG of All Subject from Department of Medicine Without inquiring detail about Patient Disease to Prevent Bias in Axis Determination.

QRS axis of each ECG was determined by both methods.

Perpendicular method: As Routinely done with the Help of Graph and Scale³

Vector disc method²: The principle employed in this model is based on Hexaxial reference, which is shown in the center of disc. Six circles represent positive and negative zones of standard limb leads in order of L1, L2, L3, aV_E, aV_L, and aVF. Clear area represent zone of negativity and colored area represents zone of positivity.

For axis determination standard limb leads of the electrocardiogram are inspected starting from lead I. the needle is moved over the model considering the positive and

negativity of each area. The ultimate position of the needle will read the axis in frontal plane.

Result:

When axis were determined by both method. They are of following degree in different ECG by both methods was seen.

Degree	By perpendicular method	By Vector disc method
+0° - + 30°	5	5
+30° - + 60°	4	4
+60° - + 90°	14	14
+90° - + 120°	6	5
+120° - + 150°	1	2
+150° - + 180°	9	9
- 60° - - 90°	6	6
- 120° - - 150°	5	5
	50	50

Discussion:

As with the **conventional, Perpendicular method**, determination ECG axis is accurate but it is long procedure, time consuming and requires graph paper and other instrument for determination of axis. To carry all these with a person is cumbersome and so not followed routinely.

In case of **vector disc**, It is very easy, very quick, less time consuming and also nears accurate for determination of axis. One can carry vector disc anywhere he wants. So it can be used routinely for the purpose of axis determination.

Study shows that there is no difference in result except only one. In determination of axis by vector disc, which suggest **accuracy of vector disc**, though study with more number of ECG is necessary.

Thus, vector disc can be used routinely for determination of ECG axis. In different disease of Heart.

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RECENT RESURGENCE OF DIPHTHERIA AMONG CHILDREN- OUR EXPERIENCE

**Dr Ritesh C Shah, Dr A S Shah, Dr R N Joshi, Dr B S Shah Department of
Pediatrics, Smt NHL Mun. Med.college Ahmedabad.**

Introduction: Diphtheria is the first infectious disease to be conquered by vaccine. It is an acute toxic infection caused by C.Diphtheria. It affects superficial layers of skin and respiratory tract membrane resulting in local inflammation by producing a potent polypeptide exotoxin. The aims and objectives of this study are to study percentage of cases of diphtheria, to study duration of symptoms before treatment and outcome and to study relation between complications and cause of death in patients of diphtheria.

Methods: Total 25 cases of diphtheria admitted in year 2005 were studied. Patients with positive throat swab for Gm stain and special stain (Macune Albright strain) confirmed by culture report were taken as cases. All patients received ADS in proper doses as and when available at the earliest. All patients were treated on the standard line of treatment.

Results: Out of total 2742 admissions during the year 2005 there were 25 cases of diphtheria while during the year 2004 only 11 cases were there (out of 2831 admissions). 18 patients out of 25 cases were not vaccinated. Highest number of cases was in preschool age group. Fever and oropharyngeal membrane were the most common symptoms. Mortality was highest in patients who presented 6 days after the appearance of symptoms (8 out of 9). 80% of patients in this study had complications amongst which myocarditis (13 pts) and mechanical obstruction (7 pts) were major. 16 patients were expired (64%). All 13 patients who got myocarditis were expired.

Conclusion: There is a trend of significant increase in cases of diphtheria Majority of cases were unvaccinated. Late presentation and patients with myocarditis are very high-risk patients.

Recommendations: there is urgent need for refocusing on immunization and completion of immunization before school days. Aggressive management of cases of myocarditis in ICU. There is need for prospective study to be undertaken

Bird flu: IS PANIC JUSTIFIED?

Dr. Sheetal Vyas, Associate Professor, Department of Community Medicine
Dr. Jyotiben S Deokule, Professor and Head, Department of Microbiology

1. Influenza :

1.1 Introduction:

It is an acute respiratory infection caused by influenza viruses A, B and C and characterized by sudden onset of chills, fever, malaise, muscular pains and cough. It manifests in several forms ranging from sub-clinical infection to pandemics. The disease occurs in form of epidemics in between the pandemics. The periodicity of epidemics is irregular due to circulation of many strains.

1.2 Causes of rapid spread:

The factors contributing to rapid spread of the disease are as follows-

1. Short incubation period
2. Large number of sub-clinical cases
3. High proportion of susceptible.
4. Short duration of immunity
5. Absence of cross immunity

1.3 Epidemiology

At present there are three influenza viruses which are in circulation namely Influenza A (H1N1),

A (H3N2) and B. Whenever there is epidemic of influenza children and old people observe highest mortality. Epidemics are more common in winters due to overcrowding as transmission of infection from one person to other person is due to droplets which are generated while sneezing, coughing and talking. Incubation period is ranging from 18 Hours to 72 Hours.

1.4 Antigenic Shift and Drift

Influenza A virus has mainly two antigens Haemagglutinin or 'H' antigen and Neuraminidase or 'N' antigen. H antigen initiates infection following attachment of virus to the susceptible cells and N antigen is responsible for release of virus from the infected cells. Antigenic shift means sudden and complete major change in antigenic components because of genetic recombination of human influenza virus with animal or avian virus. Antigenic drift means gradual change over a period of time because of point mutations.

1.4 Influenza Pandemics

Pandemics are caused by type A virus and usually result from unpredictable recombination of human, swine or avian antigens. In past epidemics of influenza occurred in 1918 (H1N1, Spanish Flu), 1957 (H2N2, Asian Flu), and 1968 (H3N2, Hong Kong Flu).

2. Avian Influenza

Avian influenza is an infectious disease of birds caused by type A strains of influenza virus. All known subtypes of influenza A virus circulate amongst wild bird species. Out of 16 known subtypes of H antigens in birds 3 are circulating in the humans namely H1, H2 and H3. Two out of 9 subtypes of N antigens are circulating in the humans which are N1 and N2.

All 16 HA and 9 NA subtypes of influenza viruses are known to infect wild waterfowl, thus providing reservoir of influenza viruses in bird population. While all birds are thought to be susceptible to infection with avian influenza virus, many wild bird species carry these viruses without any apparent signs of harm. Other bird species including domestic poultry develop disease when infected with avian influenza viruses.

2.1 Characteristics of avian influenza in birds

The virus causes two distinct forms of disease - one common and mild, the other rare and highly lethal. The mild form is expressed as ruffled feathers, reduced egg production or mild effects on respiratory system. Highly pathogenic form of avian influenza is characterized by sudden onset of severe disease, rapid contagion and mortality rate that can approach 100% within 48 hours. The virus not only affects respiratory tract but also involves multiple organs and tissues resulting in massive internal hemorrhages and hence also named as Chicken Ebola.

2.2 Outbreaks of avian influenza

All outbreaks have been caused by viruses of H5 and H7 subtypes. Not all virus strains of H5 and H7 subtypes are highly pathogenic but most are thought to have the potential to become so. Some species of migratory waterfowl are now thought to be carrying the H5N1 virus in its highly pathogenic form and introducing it in the new geographic areas located along their flight routes. Apart from being highly contagious among poultry, avian influenza viruses are readily transmitted from farm to farm by movement of live birds, people (especially when shoes and other clothing are contaminated), contaminated vehicles, equipments, feed and cages. Highly pathogenic viruses can survive in bird faeces for 6-35 days with more survival period at low temperatures.

2.3 Control of avian influenza in birds

The logistics of recommended control measures are more straightforward when applied to large commercial farms but difficult where birds are raised in small backyard. The suggested control measures are-

- Rapid culling of all infected or exposed birds
- Proper disposal of carcasses. The carcasses fall in category two of hospital waste and should be disposed by incineration or deep burial.

- Quarantine and rigorous disinfection of farms
- Implementation of strict sanitary measures
- Restriction of movement of live poultry both within and between countries
- Vaccination of poultry in high risk areas provided that quality assured vaccines are used. Poor quality vaccines pose a risk for human health as they may allow infected birds to shed viruses while still appearing to be disease free.

3. Human exposure and infection

The domestic birds usually roam freely as they scavenge for food and often mingle with wild birds or share water sources with them. On the other hand domestic birds enter household and share areas where children play or sleep. Poverty exacerbates the problem in situation where a prime source of food or income can not be wasted and households frequently consume poultry when deaths or signs of illness appear in flocks. This causes high risk of exposure to the viruses during slaughtering, defeathering, butchering and preparation of poultry meat for cooking. Moreover, deaths are not reported as they are considered common in adverse weather conditions. The frequent absence of compensation to farmers for destroyed birds further works against those reporting of outbreaks and may encourage owners to hide their birds during culling operations.

3.1. The role of migratory birds

Scientists are convinced that migratory water fowl are carrying H5N1 virus. Evidence regarding this appearing in mid 2005. The die-off space of more than 6000 migratory birds infected with highly pathogenic H5N1 virus which began at Qinghai Lake nature reserve in central China in late April 2005 and probably unprecedented. Scientific studies have found that viruses from the most recently affected all of which lie along migratory routes.

3.2. Countries affected by outbreaks in birds

The outbreaks began in South- East- Asia in mid 2003 and have now spread to a few parts of Europe. Nine Asian countries have reported outbreaks, namely- republic of Korea, Vietnam, Japan, Thailand, Cambodia, the Lao People's Democratic Republic, Indonesia, China and Malaysia. In July-2005, the virus spread beyond its original focus beyond Asia to affect poultry and wild birds in the Russian federation and Kazakhstan.

4. The disease in human

Influenza viruses are highly species specific. Since 1959, instances of human infection with an avian influenza virus have occurred on only 10 occasions. Of the hundreds of strains of avian influenza viruses, four are known to cause human infections namely- H5N, H7N3, H7N7 and H9N2. Human infection is mild except with H5N1 which is of concern because of two main reasons- firstly as it has caused higher number of cases of severe disease and secondly it has crossed species barrier on at least 3 occasions in recent years- Hong Kong 1997, Hong Kong 2003 and current outbreaks which began in December 2003. H5N1 influenza virus, if given enough opportunities will develop characteristics it needs to cause pandemic. The virus has

met all the prerequisites for start of a pandemic save one: an ability to spread efficiently and sustainably among humans. Moreover studies of human cases determined that contact with live poultry was source of infection and there are very limited evidences of person to person transmission. Each additional human case gives the virus an opportunity to improve its transmissibility in humans, and thus develop in to a pandemic strain.

4.1 Transmission of disease to Humans

Following modes of transmission have been identified :

1. Close contact with dead or sick birds
2. Slaughtering, defeathering, butchering and preparation for consumption of infected birds.
3. Exposure to chicken faeces.
4. Yet unknown environmental factor.
5. Role of peri-domestic birds like pigeons or use of untreated bird faeces as fertilizers.

However further research is needed to better define the exposure circumstances, behaviors and possible genetic or immunological factors that might enhance likelihood of human infection.

4.2 Assessment of possible cases:

While assessing possible cases, following things are kept in mind:

1. Inquiry about direct contact with infected birds or their faeces
2. keeping high index of suspicion for those showing influenza like symptoms

4.3 Clinical Features

Most human cases have unusually aggressive clinical course with rapid deterioration and high fatality. Incubation period for H5N1 avian influenza is longer than seasonal influenza ranging from 2-8 days and may be upto 17 days. World Health Organization currently recommends incubation period of 7 days for field investigations and monitoring of patient's contacts. Initial symptoms include a high fever, usually with a temperature higher than 38 C, and influenza like symptoms. Diarrhea, vomiting, abdominal pain, chest pain and bleeding from nose and gums have also been reported as early symptom in some patients. Few patients may present without respiratory symptoms and may have encephalitis, fever and diarrhea as main symptom. There is usually development of manifestations of the lower respiratory tract early in the illness. Difficulty in breathing develops around 5 days following the first symptoms. Respiratory distress, a hoarse voice and crackling sound when inhaling are commonly seen. Sputum production is variable and sometimes bloody. Almost all patients develop pneumonia. Acute respiratory distress develops at around 6th day and range is 4 to 13 days. Respiratory failure has been observed after 3 to 5 days of onset of symptoms. Another common feature is multi-organ dysfunction involving kidney and heart. There may be associated lymphopenia, leucopenia, elevated aminotransferases, thrombocytopenia and disseminated intravascular coagulation.

4.4 Role of anti-viral drugs

Two drugs in the neuraminidase inhibitor class namely, oseltamivir (Commercially known as Tamiflu) and Zanamivir (Commercially known as Relenza) can reduce the severity and duration of seasonal influenza. An older class of anti-viral drugs amantidine and ramantidine could potentially be used against pandemic influenza but resistance to these drugs can develop rapidly.

Oseltamivir (commercially Known as Tamiflu) should be prescribed as early as possible ideally within 48 hours. As mortality associated with the disease is high and prolonged viral replication occurs in it, administration of drug is considered even in those presenting late in illness. Dose in adults and adolescents of more than 13 years age is 150 mg/day, given as 75 mg twice a day for 5 days. It is not recommended for children less than 1 year of age. Treatment may be prolonged to 7 to 10 days in those not showing clinical response. In severe infection with H5N1 virus the dose and duration of treatment may be increased keeping in mind that daily dose of > 300 mg may be associated with severe side effects. Serial clinical assay to monitor viral load, drug susceptibility and drug levels has to be carried out.

4.5 Countries with Human cases in current outbreak

Human cases have been reported from six countries- Cambodia, China, Indonesia, Thailand, Turkey and Viet Nam. Altogether, more than half of the laboratory confirmed cases have been fatal.

4.6 Reasons for Panic and no panic

Reasons for panic are-

- The antigen H5 in H5N1 virus is totally new for human population hence no herd immunity is existing at present .
- This causes mostly serious infection with systemic complications.
- The Case Fatality rate is very high.
- It has crossed species barrier several times.
- No vaccine is available which can provide protective immunity.
- Treatment is also not very effective and not available readily.
- Migration of birds (Waterfowls) is natural and universal phenomenon.
- Domestic ducks now excrete large quantities of highly pathogenic virus without showing signs of illness and are now acting as silent reservoir of virus
- Virus circulating now are more lethal and survive longer in the environment
- H5N1 has expanded host range

Reasons for no panic are-

- Till now H5N1 has caused very few human cases
- The disease is rare
- Only those in direct contact with poultry are affected
- Person to person transmission is not observed

So it is an impending pandemic.

4.7 Why are the pandemics such dreaded events

Influenza pandemic can rapidly infect virtually all countries. Once international spread begins, pandemics are considered unstoppable, caused as they are by a virus

that spreads very rapidly by coughing and sneezing. As infected people can spread virus before they become symptomatic, it adds to the risk of international spread via asymptomatic air travelers. Severity of disease and the number of deaths caused by a pandemic virus vary greatly. Pandemics can cause large surges in the number of people requiring or seeking medical or hospital treatment, temporarily overwhelming health services. High rates of worker absenteeism can also interrupt other essential services. Based on past experience, a second wave of global spread should be anticipated within a year. As all countries are likely to experience emergency conditions during a pandemic, opportunities for inter-country assistance are nil.

4.8 Warning signals of a pandemic

Clusters of patients with clinical symptoms of influenza, closely related in time and place, detection of cases in health workers caring for H5N1 patients are warning signs of human to human spread of disease. In such situation field investigation of every possible case and sharing viruses with WHO reference laboratories should be carried out.

4.9 Status of Vaccine

Vaccines effective against a pandemic virus are not yet available. Besides that no vaccine is expected to be widely available until several months after the start of a pandemic. Further the vaccine needs to closely match the pandemic virus hence large-scale commercial production will not start until the new virus has emerged and a pandemic has been declared. Current global production capacity falls far short of the demand expected during a pandemic.

4.10 Can a pandemic be prevented?

No one knows with certainty. The best way to prevent a pandemic would be to eliminate the virus from birds but it can not be achieved. By early 2006 WHO will have stockpile of antiviral medicines sufficient for three million treatment courses which could be used prophylactically near the start of pandemic to reduce the risk that a fully transmissible virus will emerge or at least delay its international spread. But the world is ill prepared to defend itself during a pandemic.

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ADIPOSE TISSUE AS AN ENDOCRINE ORGAN: ADIPOSE BRAIN COMMUNICATION

Dr Janardan V Bhatt MD Med, MD Phys, PhD Phys ;Editor, Prof.of physiology at Nagar school of optometry and Associate prof. of Physiology Smt NHL Mun. Med.College Ahmedabad 380006

Abbreviations: AGRP=Agouti-related peptide, ASP=Acylation stimulating protein, C1q=complements 1q,CART:Cocaine-and amphetamine-regulated transcript, CRH= corticotrophin-releasing hormone,IL6=interleukin 6,IRS= insulin receptor substrate, JAK=janus kinase, MCH=melanin concentrating hormone, MSH=Melanocyte stimulating hormone,MCP=Monocyte chemo attractant protein ,NPY=Neuropeptide Y ,PI3K= phosphatidylinositol 3-kinase protein tyrosine phosphatase ,SOCS=Suppressor of cytokine signaling ,STAT=Signal transducer and activator of transcription, TNF=Tumor necrosis factor

The adipose tissue is a significant portion of our body weight. Body weight is not constant but in dynamic pool of total metabolism of food stuff i.e. carbohydrates, proteins and fats i.e. body energy fuels. The body weight is maintained by complex balance mechanisms of intake and out put of energy fuels. Normally the healthy person maintains constant body despite wide variation in intake of food. In one scientific investigation it was found that average woman gain 11 Kg weight between the ages of 25 and 65. It was further calculated that the total food intake of a woman over the 40 year period is more than 18 metric tons [18000 kg]. In this experimental set up the error in food intake over the energy expenditure that they produce the weight gain is less than 0.03%. You will just say amazing! mechanism of regulation of weight . Due to recent epidemic of obesity especially the child hood and adolescence obesity craving for need of slimming, figure and beauty, there is enough motivation among the medical scientists to discover mechanism and management of obesity.

Since long the adipose tissue was considered as physiologically and biochemically as silent /inert organ and only known function was storage i.e. for storage of excess of energy in the form of triglycerides in adipocytes.

Recent breaking news about adipose tissue is, that it secret number of proteins which act as hormones, cytokines known as adipokines.

If the body weight is to be maintained constant, there has to be some communication between brain / hypothalamus and adipose tissue.

And yes the recent observations have proved the fact that brain and adipose tissue communicate and transfer the signals by adenosines. It is also found that these adipokines are closely related to the severity of adiposity.

In fact the adipose tissue is a versatile organ system necessary for survival. However, dysregulation of adipose signaling in the brain and peripheral organs clearly leads to obesity a major metabolic abnormalities, and insulin resistance, diabetes and dyslipidemia.

Leptin, adiponectin and to some extent resistin offer potential mechanisms to explain how adipose tissue is able to modulate glucose and lipid metabolism under various physiologic and pathologic states.

Adipocyte hormones could become important markers of disease prevention as well as potential therapeutic targets for obesity and related diseases.

Before we proceed to endocrines and adipokines of adipose tissue, let us revise our knowledge of regulation of food intake. It was BK Anand et al who proposed the role of

hypothalamic neurons in regulation of food intake. This hypothesis was later found to be conclusive for establishing the two centers in hypothalamus i.e.

A] Feeding centre

B] Satiety centre ventro medial nucleus of hypothalamus

Stimulation of feeding centre lead to feeding behaviors and destruction of the centre lead to anorexia. Contrarily, if the neurons of satiety centre are stimulated, the animal stop eating while if this area is destroyed there is hyperphagia.

The evidences suggest that satiety centre function by inhibiting the feeding centre.

It appears that the feeding centre is chronically active and its activity is transiently inhibited by the activity of satiety centre after the ingestion of food. BUT the mechanism is not as simple as it looks. For example a rat with lesion in satiety centre there is hyperphagia with weight gain [the classical hypothalamic obesity], but later on achieve a plateau state and maintain a new weight gain by same feeding regulation. The probable explanation for this phenomenon is neuro plasticity. We have just begun to learn the neuro transmitters secreted by these hypothalamic neurons. Many of the transmitters are peptides and known as neuro peptides. One such neuropeptide is known as neuro peptide Y [NPY]. NYP secreting neurons are located in arcuate nuclei and project to Para ventricular nuclei. The activity of the cell bodies of NPY neurons are increased during feeding and decrease during satiety. The action of NPY is coupled with G Proteins via receptor i.e. Y1, Y2, and Y5. It has been found that Y5 increase food intake while Y2 is inhibitory. The recent clinically significant observation is that accumulation of Malony COA in the tissue inhibit food intake with loss of weight by decreasing the activity of NPY neurons. If the non toxic inhibitor of fatty acid synthesis may increase level of Malonyl CoA and achieve weight control. Another group of Lateral hypothalamic neurons secret two neuro peptides Orexin A and B and increase food intake and interestingly mutation of gene of receptor of orexin is associated with Narcolepsy in dogs. Recently, lots of interest is generated about a neuro peptide Gherin. Gherin is produced by stomach also found in hypothalamus. It binds with a receptor called Growth hormone secretagogue [GHS]. Its action is increase body weight.

It also observed that in mammals there is Melanin concentrating hormone MCH secreting neuron in lateral Hypothalamus and it increase food intake.

There are another group of neuro peptides which decrease food intake i.e. Pre opio melano cortin POMC and alpha MSH Secreting neurons found in hypothalamus and they decrease food intake via MC4-R receptor. A mutant strain of mice called agouti over produces agouti protein and inhibit the action of MC4R and causes obese mice strain. Still a novel peptide called CART [cocaine and amphetamine regulated transcript] decrease food intake. Similarly two known peptides CRH and ACTH also decrease food intake. Catecholamine also suppresses the appetite and decrease weight is by many mechanisms and one is by increasing the basal metabolic rate. Clinically used amphetamine and related drugs act by releasing nor epinephrine in brain. Serotonin is also play role but more complex depending upon the type of receptor. In mice if the gene for 5HT2C receptor is knocked out, the mice is obesity. Majority of tricyclic antidepressants are associated with increase body weight .The most commonly used drug for gaining weight cyprohaptidine is anti serotonin. While majority of SSRI [selective serotonin reuptake inhibitors] sertraline ... decrease body weight. To day most effective drug for treatment i.e. Sumatra was introduced as SSRI antidepressant, but later on found to be good appetite suppressant.

Like any homeostatic mechanism, in body weight regulation there is

A] Sensory/ afferent mechanism

1] Glucostat neuron Glucose sensor

2] Gut hormones and other gut afferent

3] Lipostat neurons Lipid and sensors of Adipose tissue hormones and signals

B] Centre in hypothalamus

I.e. satiety and

Feeding centre

C] Efferent mechanism mainly by two mechanisms

1] By decreasing or increasing food intake

2] By increasing or decreasing food utilization

Afferent Mechanism

1] Glucostat neuron:

These neurons are present in satiety centre and the activities of these neurons are depending on glucose utilization by brain and the neurons. When the glucose utilized by brain is low that the cerebral /hypothalamic arterio/venous deference for glucose is low. This phenomenon keeps the activity of Glucostat neuron low and inhibits the feeding centre.

But if the AV difference for glucose is very high suggesting increase utilization of glucose by neurons ,the glucostat neuron are activated and stimulate the feeding centre leading to hunger and feeding behaviors .

2] Gut afferents and hormones

Food in the gut leads to release large number of messengers for hypothalamus including Gut hormones i.e.

GRP, Glucagons , Somatostatin , CCK/Cholicystokine

Out of them the CCK play significant role in food regulation.

Gut hormones after release reach brain by blood through blood brain barrier.

Since decades we are aware of existence of gut hormones in brain but there role was not known or rather mysterious.

Recently we begin to learn their role as neuro transmitter.

They also act as afferent feedback mechanism for food intake.

Gut stretching /distension and gut hormones inhibit feeding centre and suppress the eating behaviors for a long time as long as food is present in gut. They also serve as supplementary homeostatic mechanism for protecting gut from indigestion and over distension.

The anorectic mechanism of CCK is mediated by two types of receptors i.e. CCK A and CCK B receptors.

CCK A receptors are peripheral while receptor CCK B Central and peripheral. Central receptor is more important. We hope for selective CCK receptor antagonists for management of Obesity. Anorectic action of CCK is decreased by vagotomy. Distension / relaxation of gut also inhibit the feeding center.

Contraction Hunger contraction increase appetite by stimulating the feeding centre.

3] Some other factors play roles in food intake regulation are

Temperature

Past experiences

Conditioned reflexes

Social factor

Religion and culture factor

Environment Geography

Higher centers and cerebral cortex

4] Afferent information from adipose tissue:

Adipose tissue respond actively to controls energy homeostasis, neuro endocrine and other systems by secreting hormones that act in the central nervous system and peripheral tissues

Adipokines and hormones secreted by adipose tissue.

Leptin, the product of the *leptin* gene, and other adipose-secreted proteins are known as 'adipokines.' They have profound effects on metabolism.

Kennedy et al in 1953, first proposed the existence of a circulating 'adipostatic' factor, based on the tendency of mammals to maintain a constant body weight despite daily fluctuations in food intake and energy expenditure. Harvey et al published in a link between adipose tissue and the brain parabiosis /cross circulation study in rats. Three decade later genes were identified i.e. *leptin* gene give rise to leptin an adipokine. There was further evidence that the diabetes gene encodes the leptin receptor. Mutation of leptin receptor gene also leads to obesity in mice. Defective *Ob* gene [*ob/ob*] mice are not satiated and become obese and diabetic. Garg interestingly observed that Certain lipodystrophies are associated with increase appetite, steatosis, amenorrhea .These abnormalities are reversed by leptin treatment. Leptin is produced mainly by adipocytes, BUT low levels of expression is observed in placenta, skeletal muscle, stomach and intestine .Leptin is increased in obesity and reduced by fasting and in lean individuals. With the discovery of leptin it was hoped that the administration of leptin will revert the changes associated with obesity. But soon it was found that obesity is associated with increase level of endogenous leptin. This was suggestive of leptin resistance and therapeutic administration was not associated with clinical response. The situation is very similar to the type two [NIDDM] diabetes mellitus. This suggests leptin resistance. This finding was confirmed after demonstrating the leptin receptor on various tissues .Gene

responsible for leptin receptor is located experimentally .Obesity developed after Knock-out of gene responsible for leptin receptor. While various leptin receptor isoforms have been discovered, most of the effects of leptin on energy balance and hormone levels occur in the brain through the long leptin receptor isoforms (LRb) and JAK-STAT signal transduction. Leptin is transported across the blood-brain barrier by a saturable process and activates JAK2 and STAT3 leading to inhibition of orexigenic peptides, e.g. NPY, AGRP and MCH, and increased expression of anorexigenic peptides, e.g. MSH, CHART and CRH. Interestingly rise in leptin inhibits JAK-STAT signaling through induction of SOCS3. But in contrast increased leptin sensitivity and associated prevention of obesity and improved glucose and lipids tolerance was found with specific ablation of SOCS3 in neurons or haploinsufficiency of SOCS3.

Loss of PTP 1B, an enzyme that terminates leptin response, attenuated obesity and related abnormalities. The central effect of leptin also involves interactions with key targets of insulin in the brain, for example IRS1 and 2 and PI 3-kinase.

Central level the leptin interact synergistically with insulin including IRS 1 and 2 and PI 3-kinase.

Signals that increase leptin are

- 1]Glucose,
- 2]Insulin,
- 3] chronic glucocorticoid exposure and estrogens increase leptin,

While Signals that decrease leptin are

- 1] B3-adrenergic activity,
- 2] Androgens,
- 3] Growth hormone and
- 4] Inflammatory cytokines

Congenital absence of leptin or leptin receptor is associated with hyperphagia, impaired thermoregulation, ,early-onset obesity, insulin resistance, Steatosis, Neuroendocrine deficits, i.e.. hypothalamic hypogonadism, and immune suppression.

- 2] TNF alpha

Adipose tissue expresses TNF alpha & IL6, well known cytokines with profound effects on metabolism.

In humans, TNF expression is greater in subcutaneous compared with visceral adipose tissue. Adipose tissue expression of TNF is increased in obese rodents and humans and related to insulin resistance. TNF treatment inhibits appetite, increases energy expenditure and induces cachexia.

3] Inter Leukin 6 IL6

IL6 is expressed by adipose tissue, circulates in multiple glycosylated forms and is associated with obesity and insulin resistance. Systemic administration of IL6 increases glucose and lipids and induces insulin resistance. Deletion of the IL6 gene in mice resulted in obesity is typically associated with infiltration of adipose tissue by macrophages that secrete TNF and IL6, as well MCP-1, a chemokine that mediates the recruitment of monocytes.

3] MCP-1 Monocyte chemoattractant protein 1:

MCP-1 is produced by both adipocytes and stromal vascular cells, increased in the circulation in obesity, and involved in the development of insulin resistance, vascular inflammation and atherosclerosis.

4] Adipsin (complement factor D) :

Adipsin is produced by adipose tissue and mediates the production of acylation stimulating protein (ASP) through complement factor-3. ASP inhibits fatty acid oxidation, reduces insulin resistance and enhances insulin secretion.

5] Adiponectin:

Adiponectin was identified by various laboratories, and hence the multiple names, i.e. adipoQ, adipocyte complement-related protein of 30 kDa (Acrp30), adipose most abundant gene transcript 1 (apM1), and gelatin-binding protein of 28 kDa (GBP28). Human adiponectin is a 30-kDa protein and consists of 247 amino acids, resulting in multiple isoforms, monomers, trimers, hexamers and higher order oligomeric structures.

Adiponectin is the most abundant protein secreted by adipose tissue and accounts for as much 0.01% of total plasma protein concentration. Adiponectin is subject to nutritional and hormonal regulation but often in an opposite direction to leptin. In contrast to leptin, the levels of adiponectin produced by adipose tissue and in the circulation are reduced in obesity and type 2 diabetes, weight reduction increases plasma adiponectin concentration. The level is dependent on the degree of hyperinsulinemia and insulin resistance than to

adipose tissue mass. Both adiponectin and leptin exhibit ultradian pulsatility as well as a diurnal variation. As is the case with leptin, adiponectin levels are significantly higher in women than men, and this sexual dimorphism may be related to inhibition of adiponectin production by testosterone. Adiponectin mRNA and protein levels are increased by IGF-1, and decreased by TNF, glucocorticoids, B-adrenergic agonists and dibutyryl cAMP. Genome-wide scans have mapped a susceptibility locus for the metabolic syndrome and diabetes to chromosome 3q27, where the adiponectin gene is located. Plasma adiponectin is inversely related to insulin sensitivity and type 2 diabetes. Moreover, elevated levels of adiponectin in the circulation have been associated with a reduction in the risk for type 2 diabetes. In humans, adiponectin concentrations also appear to correlate negatively with plasma triglycerides and risk for atherosclerosis.

Peripheral injection of adiponectin rapidly phosphorylates AMPK, leading to activation and stimulation of fatty acid oxidation in liver and muscle, and reduction in hepatic gluconeogenesis. Likewise, direct treatment of myocytes and hepatocytes with adiponectin activates AMPK and stimulates lipid catabolism. Leptin regulates lipid metabolism through activation of AMPK, raising the possibility of a common signaling mechanism for these adipocyte hormones. Adiponectin also binds to T-cadherin, a protein that is produced in the vascular beds in the brain and peripheral tissues, and could potentially sequester and modulate the bioavailability of adiponectin.

6] Resistin

It is a unique cysteine-rich protein. Holcomb et. al originally named resistin as FIZZ2 based on its homology to FIZZ1 (found in inflammatory zone 1), a protein induced during lung inflammation. The name 'resistin' (resist insulin) was based on the ability of this novel protein to inhibit insulin-stimulated glucose uptake in vitro in rodents. Resistin-like molecules (RELMs) are expressed in the intestine and various tissues. Kim et. al. identified resistin as an 'adipose specific secretory factor' (ADSF) which inhibited adipocyte differentiation. Similar to leptin, resistin is reduced by fasting and increased in response to refeeding. Studies have also demonstrated the ability of glucocorticoids and TNF to stimulate resistin expression. Resistin expression is extremely low in human adipose tissue, and derived from stromal tissue, i.e., preadipocytes and endothelial and vascular smooth muscle cells.

Earlier on, Kim et al. had suggested that resistin inhibited in vitro adipogenesis by generating transgenic mice. Role of resistin in humans is unsettled. Unlike leptin and adiponectin, the extent of homology between rodent and human resistin is relatively small. At present, there are no known diseases attributable to resistin deficiency or excess to facilitate functional studies.

7] Acylation stimulatory protein: ASP

Very little is known about Acylation stimulatory protein an adipokine. The main physiological actions are decreases in energy expenditure, increases weight, reduces insulin sensitivity, reduces lipid oxidation.

8] Miscellaneous;

Adipose tissue secretes various proteins involved with the coagulation cascade and vascular function.

PAI-1 is elevated in obesity and associated with greater risk for type 2 diabetes and cardiovascular disease.

Various components of the classic rennin-angiotensin system (RAS) are expressed by adipose tissue, and studies have associated the adipose RAS with cardiovascular morbidity in obesity. In support of this idea, targeted ablation of angiotensinogen reduced blood pressure and obesity in mice, while transgenic over expression of angiotensinogen in adipose tissue increased blood pressure and obesity.

Summary:

Effects of adipocyte hormones:

1] Leptin = Thinning. /slimming hormone

Inhibits feeding

Increases energy expenditure

Decreases body fat

Lowers glucose,

Insulin and lipids Stimulates lipid oxidation

Stimulates reproductive and thyroid axes

Stimulates immunity

2]

Adiponectin

Chronic or central treatment

reduces body weight

Reduce fat

Stimulates thermogenesis

Reduces glucose

Improves insulin sensitivity

Reduces lipids by enhancing oxidation

Anti-atherogenic

Anti-inflammatory

3]

Resistin

Inhibits adipogenesis

Induces insulin resistance in rodents

4]

TNFalpha

Inhibits feeding

Cachexia

Induces insulin resistance,

Hyperglycemia and dyslipidemia

5]

IL6

Inhibits feeding

Increases energy expenditure

Decreases weight

Induces insulin resistance,

Hyperglycemia and dyslipidemia

6]

ASP Acylation stimulatory protein

Decreases energy expenditure

Increases weight

Reduces insulin sensitivity

Reduces lipid oxidation

SUMMARY AND CONCLUSION:

Leptin inhibits feeding by binding to long LRB receptor in brain, leading to activation of the JAK-STAT pathway. The leptin signal is terminated by induction of SOCS3 and PTP1B activity. Importance of these molecules have been confirmed in knockout mice. Ablation of LRB and STAT3 in neurons causes hyperphagia, obesity and neuroendocrine deficits, while the loss of SOCS3 or PTP1B prevent obesity. Adiponectin is associated with improvement in insulin sensitivity, decrease lipids by enhancing oxidation and protection against atherosclerosis. Adiponectin is increased by thiazolidinediones and likely mediates the anti diabetic effects of these drugs. Resistin exerts an opposite effect to adiponectin by inhibiting insulin action in rodents, but their role in human is uncertain. The recent breakthroughs in our understanding of energy balance, especially the discovery of adipocyte hormones, into the role of adipose tissue in health and disease. Adipose tissue is a versatile organ system necessary for survival. However, dysregulation of adipose signaling in the brain and peripheral organs clearly leads to major metabolic abnormalities, particularly obesity, insulin resistance, diabetes and dyslipidemia. Leptin, adiponectin and to some extent resistin offer potential mechanisms to explain how adipose tissue is able to modulate glucose and lipid metabolism under various physiologic and pathologic states. While rodents have provided useful models for studying these processes, it is essential to examine the effects of adipocyte hormones by direct administration in humans where possible. Adipocyte hormones could become important markers of disease prevention as well as potential therapeutic targets for obesity and related diseases.

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NEWBORN SCREENING FOR INBORN METABOLIC DISORDERS

Dr.C.Chakrabarti, Dr.Dhanalakshmi Sankar,Dr.Usha Patel &Dr.Nasima Department of Biochemistry. Smt NHL Municipal Medical college.Ahmedabad

India is often portrayed as an underdeveloped country where the primary health care need among children is the provision of water, food and sanitation facilities and prevention of death from infectious diseases and morbidity from nutritional deficiencies, it is unfortunate that there is no place for Inborn Metabolic Disease because of its rarity and lack of facility for proper diagnosis. However, there is also a large number of children, probably more than in any other Asian or Western country, for whom basic facility like food, shelter etc are not the need and whose parents can afford what ever a parent in any other country aspires for their child. It is these parent and their babies who will form the bulk of the newborn in centers in the city or district capital level. Therefore, the need of the hour is to spread more awareness about metabolic errors and have testing facility at every neonatal centre. Considering the ethnic diversity in a city like Ahmedabad, we have enough number of IMDs probably even more provided we look for it. Inborn Metabolic disease screening is an uninspiring endeavour particularly in terms of its occurrence rate and the consequent economical non viability but their needs cannot be neglected because of the needs of the most deprived group.

All of us need to be aware that apparently every healthy newborn has a significant risk of being maimed or killed by an inborn error of metabolism and that is adverse outcome could be reduced or in some instances, eliminated through early diagnosis achieved through newborn screening.

In the host institute we have started basic screening for Inborn metabolic disorder by some chemical methods.

Organic Acidurias and Amino Acidurias are considerably well-known Inborn Metabolic

Disorders. Although each of these diseases is quite rare as a group, separate Inborn Metabolic Diseases have been identified throughout the world, they affect about 1-2 % of

Newborns and therefore pose a significant health problem. Organic acidemias are heterogeneous group of inherited metabolic disorders due to defects in the degradative pathways of amino acid, carbohydrate and fatty acids. Their prevalence is probably underestimated since a substantial proportion of cases remain underdiagnosed

In a study over a period of 20 years at the hospital des Enfants-Malades 366 patients with inborn metabolic disease, organic acidemias accounted for 27% of Cases, Hyperlacticidemias including respiratory chain disorders in 12%. Fatty acid oxidation defects in 8.3%. Methyl Malonic Acidemia was the commonest organic acidemias followed by propionic acidemias.

Many works have been published on congenital hypothyroidism and identified as commonest Inborn Metabolic Disease. Histidinemia, Hyperprolinemia are also reported from India and abroad. The Phenylketonuria register supported by medical research council has collected information on virtually all known females with PKU born in the United Kingdom since 1978.

Date back in early 1960, Homocystinuria, an autosomal recessive disorder was identified by Carson in Northern Ireland and Gerristen in USA, he described a simple biochemical test to identify the disorder from urine sample.

All Inborn Metabolic Disorders may not be treatable but many a cases management involves dietary manipulation means of enhances of toxic metabolites and vitamin supplement and formulas that are devoid of metabolites that cannot be broken down properly.

We are screening Urine sample for clinically suspected cases for Inborn Metabolic disease by a simple, economical and effective technique like thin layer chromatography with different stain for amino acids and organic acids in the same plate and by some other chemical methods.

TECHNICAL ASPECTS OF THE STUDY :

TLC PLATES Precoated aluminium sheets
MIGRATIONS – 2 Unidimensional Ascending
SEQUENTIAL REAGENT SPRAY –

- i) Bromocresol green- Organic acids
- ii) Ortho Dianisidine - Methyl Malonic acid
- Iii) Ninhydrin – Amino acids

SPECIFIC REAGENT SPRAY- Ehrlich's reagent
Citrulline, Proline & Homocitrulline

TLC method for amino acids / organic acids is being performed on precoated cellulose plates (E Merck cat No 1.5552) with suitable solvent system for amino acid as well as organic acid.

Samples are run for about 12 cms and upper part will be stained by BCG for Organic acids next O-Dianisidine for Methyl malonic acid and lower part will be for amino acids by Ninhydrin stain .Stained spots in the sample lanes would be observed corresponding to the Rf values of reference standard.

However, it is not reasonable to make firm decision on the basis of screening test . HPLC is an acceptable technique to analyze and quantification of amino acids from biological fluids. Tandem mass spectrometry or GC/MS are the final answer for diagnosing organic acidurias as IMDs but few centers are equipped with such sophisticated instruments. Lack of laboratory facility may be quoted as limited factor in screening IMDs including aminoacidurias and Organic acidurias at this institute. Considering these facts we have undertaken an easy adaptable technique for urinary mass screening. But we hope to get some modern instrument at our hospital to be better equipped.

In the ongoing study detection of organic acidurias and amino acidurias is a part of our screening programme for inherited metabolic diseases. Adapted procedure is to differentiated and involves several steps: 1) thin-layer chromatography (TLC) in the case of an abnormal finding that is followed at the present study with BCG stain , Ortho Dianisidine stain for organic acids and Ninhydrin stain for Aminoacids followed by 2) gas chromatography (GC) at other centre as this facility is not available at our centre. The next step of the investigation, using 3) gas chromatography mass-spectrometry (GS-MS)

is reserved for more complicated and dubious analyses but it is cost effective and for this sample has to cross the miles even some times the sample need to send abroad . In acutely sick patients and in the case of discrepancies between TLC results on the one hand, and clinical symptoms, supported by other laboratory findings on the other. One case of Methyl Malonic Aciduria screened by this procedure very recently.

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GENE THERAPY IN CANCER

Abhay P. Vakil , Dr. Dinesh A. Rathod (Jr. Lecturer- Pathology)
Dep. Of Pathology NHL Mun Medical college Ahmedabad 380006

All cancers are genetic, in that they develop because of an accumulation of mutations in genes, but most are not inherited. The percentage of cancers that result from a single inherited factor varies depending on the type of tumor. For the more common cancer types, like breast and colon cancer, less than 10 percent are inherited.

Specific recurring mutations have been found in individuals of Ashkenazi Jewish descent, and persons from the Netherlands, Iceland, and Sweden. Mutations recur in these groups because of a founder's effect. "Founders" are a small group of people who, due to geographic or religious isolation, interbred. When a small group of people interbreeds

over generations, specific rare mutations can recur and become more common in the population. This is called a founder's effect.

Gene therapy is defined as the transfer of new genetic material into a cell for therapeutic benefit. This can be accomplished by: 1) replacing or inactivating a dysfunctional gene, 2) replacing or adding a functional gene, or 3) inserting a gene into a cell to make it function normally.

Cancer cells require three genetically controlled components for survival and growth: 1) cancer cells have an abnormally rapid growth rate, 2) cancer cells do not die when the body tells them to and 3) cancer cells resist removal by the body's immune system. The growth advantage of cancer cells allows them to continually grow ultimately resulting in detection. Gene therapy for the treatment of cancer tries to correct the growth rate, the death rate or make the immune system kill cancer cells.

Correction of rapid growth of cancer cells: One approach involves the use of "antisense oligonucleotides". Antisense oligonucleotides are small mirror images of specific growth regulatory gene products (oncogenes i.e. *ras*, *PKC- α* , *raf*, *c-myc*). When antisense oligonucleotides bind to the oncogene products of the cancer, they inhibit function resulting in decreased cancer growth and prolonged survival. The administration of antisense oligonucleotides to patients has resulted in some complete or partial remissions with stabilization of cancer progression in others. The effectiveness of antisense oligonucleotides appears to be enhanced by combining with chemotherapy which is the current area of research.

Control of cancer cell death: In normal cells DNA can become abnormal for a variety of reasons and the body has mechanisms for correcting this or eliminating the entire cell. In normal cells the p53 gene is responsible for repairing abnormal DNA. If the DNA cannot be repaired by the p53 gene it tells the cell containing the abnormal DNA to die by a form of death called apoptosis. In cancer cells the p53 gene can become abnormal and not cause apoptosis in abnormal cells leading to uncontrolled growth. Genetic control of cancer cell death focuses on manipulation of the abnormal p53 gene present in some cancers. One way to do this is to transfer the normal p53 gene with an adenovirus (that cannot multiply) into the cancer cell containing the abnormal p53 gene. This transfer across the tumor cell membrane to the nucleus can re-establish normal genetic control. Clinical trials exploring activity of the adenovirus-p53 approach, have involved treatment of a variety of patients, most notably patients with head and neck cancer, ovarian cancer and non-small cell lung cancer. This approach is well tolerated, and a small but significant proportion of patients have shown clinical benefit. Thus, Phase III trials comparing the role of Adenovirus-p53 gene therapy in combination with standard treatment in head and neck cancer and ovarian cancer are underway.

Another treatment that targets the p53 gene, but in a different manner, involves the use of a replicating virus called ONYX-015. This virus does not replace the gene which induces apoptosis, however, it has been modified so that its growth is selective within the cancer cells that do not have normal p53 function. This promotes death of the

cancer cells taking up the virus and does not appear to adversely effect normal cells which have normal p53 function. Trials with ONYX-015 are also moving forward with Phase III investigations comparing this approach to standard therapy in patients with head and neck cancer.

Efforts to make the immune system kill cancer cells: There are a number of cytokines that have immune activity against cancer when administered into a vein or subcutaneously including; interleukin-2, interleukin-12, alfa interferon, gamma interferon and granulocyte macrophage-colony stimulating factor. These cytokines can also be effective when directly injected into the cancer.

The genes for most of these cytokines have been isolated and when injected into cancers the cell produces the cytokine. Injection of immune-enhancing cytokine genes into cancer cells has been shown to increase antigen expression at the surface of the cancer cell. This enables the immune system to recognize the cancer leading to responses to local cancers as well as distant metastasis. This approach has been well tolerated and shown efficacy compared to historical controls in Phase I/II trials. In Phase III trials injection of interleukin-2 or gamma interferon genes directly into cancer is expected to produce response rates of 15-20% (based on phase I-II trials) which would be similar to that observed after systemic treatment with the respective cytokine. However, injection of the gene for a cytokine directly into the cancer is not associated with the side effects seen after systemic administration of the cytokine itself.

Many of the immune treatments attempt to enhance lymphocyte activity at the area of the cancer. One approach involves injection of a gene which facilitates lymphocyte binding to cancer cells (HLA-B7 plasmid) directly into the cancer. This allows immune lymphocytes to identify and destroy the cancer. This approach has been well tolerated and shown to be effective in Phase I-II trials. Thus, Phase III trials are now underway investigating the role of Allovectin-7 (HLA-B7 plasmid) to enhance immunity against cancer in patients with melanoma and head and neck cancer.

In conclusion, gene therapy approaches to the treatment of cancer are investigational, but thus far, appear to be well tolerated and promise to be effective for some cancers. For patients who have cancers unresponsive to conventional treatments clinical trials of gene therapy should be considered.

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PLACEBO'S IN PAIN – ENDORPHIN'S SEEM TO BE THE KEY.

Purav B. Gandhi. Dr. Falguni R. Shah, Asso. Prof. Of Pathology. Dr. Jayshree M. Shah, Asso. Prof. Of Pathology.NHL Mun.Medical college Ahmedabad 380006

Why pain occurs? It's an unpleasurable experience, but yet a desired one. This is because it signals an ongoing pathology or an abnormality in the body. But your individual experience of pain also depends on psychological and environmental factors also. We divide pain here into two categories – Acute and Chronic.

Acute pain occurs almost instantaneously & here between the point of injury and the perception of pain, a complex system of electrical and chemical exchanges goes into action. A- δ fibers are the sensory nerve fibers that carry the message from the nociceptors, glutamate is the dominant neurotransmitter. This is "good pain" because it warns you to do something to take care of the problems, and passes away on treating the condition.

Chronic pain is the pain that extends beyond the time taken for an injury to heal or an illness to end, and no longer this pain is viewed as a symptom of a disease but rather a disease itself. Non-myelinated C fibers carry these sensations which are perceived as dull and diffuse, substance-P being the chief neurotransmitter. This is "bad pain" because it cannot be alleviated simply by removing the stimulus. It is pain generated by such things as damaged tissue and cancer.

Management of chronic pain must be done effectively as to relieve it quickly and effectively, so as to not compensate with patients quality of life. At present pharmacological management remains the mainstay to relieve pain. NSAID's work by inhibiting the cyclooxygenase pathway and thus inhibit the PG mediated pain, but this seems mainly useful in situations of inflammations. Opioids are extremely effective pain killers but are also addictive so their use is surrounded with controversy and regulation.

In this scenario application of various non-pharmacological means always interests us. Various mental healing modalities and placebo products ensuring pain relief are available today and seem to even work out in many cases. Lots of studies are carried out all around the world to understand its mechanisms and very interesting results found – Endorphins emerge out to be the key.

Endorphins belong to a class of bio-chemicals commonly referred to as neurohormones that act by modifying the way in which nerve cells respond to transmitters. The discovery of this class of bio-chemicals has an unusual and interesting history. In the 1960s, biomedical researchers studying the causes and effects of opium addiction had detected what they suspected were "opiate receptors" in brain tissue. Since it seemed quite unlikely that humans (or other vertebrates) would contain a specific receptor designed for a chemical derived from the poppy plant, the researchers focused their attention on bio-chemicals that might be synthesized in the brain itself. Finally in 1975 a class of bio-peptides was discovered which acts on these receptors and coined as *Endorphins*.

The [placebo](#) effect has been linked to endorphins. In one study, a volunteer received pain by a compression cuff on his arm. In the first trial, no drug was administered and the patient showed signs of pain including facial grimace, increased blood pressure, and sweating. During the next trial, the physician informed the volunteer that he would be injected with morphine and that he would feel no pain. The morphine

was injected, the pain compression repeated, and this time the volunteer showed and reported no pain. The morphine and compression was repeated several times. Then, the volunteer was unknowingly injected with a saline placebo, but still reported no sign of pain, though the last time he was unmedicated the signs of pain were obvious. In a last test, the patients' 'morphine' was actually an injection of naloxone, an opioid antagonist. Even though the volunteer believed the shot was morphine and expected relief, the endorphins' effect was blocked by the naloxone injection and the volunteer displayed the same signs of pain as the first unmedicated trial.

In 1999, clinical researchers reported that inserting [acupuncture](#) needles into specific body points triggers the production of endorphins. In another study, higher levels of endorphins were found in [cerebrospinal fluid](#) after patients underwent acupuncture. In addition, naloxone appeared to block acupuncture's pain-relieving effects. However, skeptics say that not all studies point to that conclusion.

Apart from pain relieving endorphins are also produced on strenuous exercise when the threshold is crossed and produce a state of euphoria known popularly as "Runner's High". The good feeling one gets from an orgasm is partially attributed to the release of endorphins.

Thus understanding the physiology behind endorphin's gives us a wide scope in the field of management of pain. Surely a lot of advancement can be made in this field, and studies and research should be undertaken to *develop specific modules to counteract pain by stimulating deliberate endorphin release*. At present one fails to deal with this in an efficient manner due to lack of belief and high individual variations in pain perception and thresholds. But in coming years surely the mystery of placebo's in pain relief will be completely unveiled. The benefits of this modality to the patient as well as clinician will be unimaginable, as on one side it will relieve the patient from agony of pain and on other hand it will largely cut down the cost of management and cumbersome side-effects related to long term pharmaco-therapies.

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STEM CELL THERAPY AHEAD

Verma AP*, Patel JP**, Nirvan AB ***, Mod HS +

* M.D. (Physiology)

Asso.Prof.in Physiology, N.H.L.Municipal Medical College, Ahmedabad.

** M.S.(Anatomy)

Asst. Prof. in Physiology, N.H.L.Municipal Medical College, Ahmedabad.

*** M.S.(Anatomy),DNB(Anatomy)

Asst.Prof. in Anatomy, P.D.U. Medical College, Rajkot.

- + M.D.(Physiology)
Asst. Prof. in Physiology,N.H.L.Municipal Medical College, Ahmedabad

STEM CELL THERAPY AHEAD

Abstract: The goal of any stem cell therapy is to repair a damaged tissue that can't heal itself .This might be accomplished by transplanting stem cells into the damaged area and directing them to grow new, healthy tissue. It may also be possible to coax stem cells already in the body to work overtime and produce new tissue. To date, researchers have found more success with the first method, stem cell transplants.

Introduction

Why don't we live forever?

Because we get sick?

Because we get old?

Because we get hurt & can't heal?

All these are correct. Each one results from a failure of the body's ability to grow, maintain or repair itself-functions that depend on our stem cells. For decades, researchers have been studying the biology of stem cells to figure out how development works and to find new ways of treating health problems.

Research has shown that cells originating in one organ can travel to another and assume the identity of cells at there new locations. This phenomena, called plasticity has been demonstrated in model organisms such as mice & rats as well as in humans.

Hierarchy of pleuripotency of stem cells:

Zygote: Totipotent, potential to generate all cells of different tissue to make whole organism.

Inner cell mass of blastocyst: Pleuripotent, ability to form all cell types present in the organism but cannot form whole organism.

Adult stem cells : Pleuripotent, usually differentiate along one lineage can show trans-differentiation (or heterokaryon formation)

Human cloning

2 major aspects of human cloning

1. Reproductive cloning :cloning for babies:-Banned by international treaty drafted by United Nations.
2. Therapeutic cloning to form stem cells from blastocyst inner cell mass for cell regeneration therapy

ETHICAL ISSUES RELATED TO THERAPEUTIC CLONING

Stem cells : Exciting to physicians ,scientist & patients

Challenge for Ethicists & Policy makers

Objections:

1. When does life begin?
2. Cloning –Creating of genetic replica?

3. Can blastocyst derived from SCNT be called embryo?
4. Use of oocytes: Issue of mitochondrial inheritance.

THERAPEUTIC CLONING USING STEM CELLS FROM VARIOUS SOURCES

Existing established cell lines of stem cells permitted for research only (Allogenic source).

Adult autologous cells converted into stem cells by oocyte fusion (SCNT) permitted for research with a long term therapeutic goal.

Adult stem cells: Trans-differentiation (Plasticity)

Sources of Stem Cells

1. Embryo's collected during IVF (SPARE embryos)-ESC
2. Embryos created by somatic cell nuclear transfer (cloning) – SCNT derived SC
3. Germ cells or reproductive organs of aborted foetus –GSC
4. Adult blood or umbilical cord blood
5. Bone marrow & other adult tissues –ASC
6. Somatic cells of aborted foetus.
7. Dormant cells obtained from model organisms or human.

MOLECULAR BASIS OF TRANS-DIFFERENTIATION OF ADULT STEM CELLS

1. Trans-differentiation (Metaplasia)-Irreversible switch of adult stem cells of one lineage to differentiated cells of other lineages
2. Associated with change in cellular morphology & reprogramming of gene expression
3. Caused by change in the expression of master regulatory genes, whose function is to distinguish between 2 tissues in normal development (master switch)
4. Master switch genes-mostly transcription factors

Trans-differentiation of BM-SCs

- Two SC populations in BM:
 - 1) Haematopoietic SCs- Give rise to mature lineages of blood
 - 2) Mesenchymal SCs-Give rise to bone, cartilage, fat cells
 Both of them can be induced to produce non- haematopoietic cell types:
 Neurons, pancreatic cells, hepatocytes, muscle cells etc.

Is it a true trans-differentiation?

Is it fusion with target tissue cells to form Heterokaryons

- In this procedure, a nucleus from an adult donor cell is inserted into a recipient egg cell from which the nucleus has been removed. The nucleus provides all of the necessary genetic information, in the form of DNA, for a cell to function and divide. The resulting cell is then stimulated to divide as a zygote and it would result in the growth of embryonic stem cells that are genetically identical to the adult donor cell. Nuclear transfer, the transfer of a post-mitotic somatic cell

nucleus into an enucleated oocyte creates a limitless source of autologous cells that when combined with gene therapy can serve as a powerful therapeutic tool. Therapeutic cloning might be a viable approach to growing an exact tissue match for a patient in need - if the donor nucleus came from the patient, the resulting embryonic stem cell line would be a perfect match.

Researchers and physicians are working to design stem cell therapies that

- Are more effective and
- Reduce the invasiveness and the risk to patients

Today's stem cell therapies usually rely on cells that are donated by another person. This raises the possibility of donor cell rejection by the patient immune system. Now it is possible for a person to use a sample of his or her own stem cells to regenerate tissue, which would reduce or even eliminate the danger of rejection. How might this be done? Some possibilities include. Collecting healthy adult stem cells from a patient and manipulating them in the laboratory to create new tissue. The tissue would be re-transplanted back into the patient's body, where it would work to restore a lost function.

- Therapeutic cloning, as described in Creating Stem Cells for Research, might enable the creation of embryonic stem cells that are genetically identical to the patient.
- One less invasive way to achieve this goal would be to manipulate existing stem cells within the body to perform therapeutic tasks. For example, scientists might design a drug that would direct a certain type of stem cell to restore a lost function inside the patient's body. This approach would eliminate the need for invasive surgical procedures to harvest and transplant stem cells.

On the surface, the possibilities for stem cell therapy seem limitless. Couldn't we use stem cell technologies to replace any diseased or damaged tissue in the body? To answer this question, researchers must figure out the true potential and limitations of stem cells. Some questions currently being addressed include:

- How long will a stem cell therapy last?
 - The reason we age is because our cells do. If adult stem cells are used in therapies, will the tissues created from those cells age and malfunction more quickly? Scientists don't yet know how long different stem cell treatments might last.
- Can we ensure that stem cell therapies won't form tumors in the body?
 - Embryonic stem cells are naturally programmed to divide continuously and remain undifferentiated. To be used successfully in therapies, embryonic stem cells must be directed to differentiate into the desired type of tissue and ultimately stop dividing. Any undifferentiated embryonic

stem cells that are placed in the body might continue to divide in an uncontrolled manner, forming tumors.

- Avoiding tumor growth is crucial to the success of stem cell therapies. **Let's look at this in more detail.**

In both embryonic and adult stem cells, improper regulation of genes can lead to uncontrolled cell division and tumor formation. This is a special concern with cells that have been cultured in the laboratory for a period of time, because they may regulate their genes differently than they would in the body.

Why does this happen? Because most cells in our bodies are not meant to divide indefinitely, and none of them are meant to grow in lab dishes. Many tissues, such as blood and skin, rely on a renewal process that directs cells to stop dividing, differentiate and even die after a period of time. Proper direction comes in the form of signals from neighboring cells and the environment in which the cells live.

To make cells grow indefinitely in lab dishes, this process must somehow be put on hold. This is accomplished by feeding the cells with a liquid medium containing nutrients and growth factor proteins, which cause the cells to activate genes that promote cell division. In most cases, the regular signals provided by the cells' normal environment are not all present.

Not all cells respond well to this new living situation. Some will die, leaving only the ones that are better suited to an environment where indefinite growth is encouraged. After many rounds of division in a lab dish, the surviving cells may have changed so much that they are unable to respond to the signals in the body's normal environment. They may even have permanent changes in their DNA. Putting these cells back into the body is a risky proposal, because they are conditioned to continue growing rather than differentiating, possibly forming tumors.

Simulating the body's normal environments in the laboratory is one of the major challenges in stem cell research, and it is the focus of intensive research efforts around the world. Future therapies will rely on our ability to manipulate stem cells in a way that will be accepted as normal by the body.

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ROLE OF HUMAN CHORIONIC GONADOTROPIN TESTING IN DETECTION OF EARLY PREGNANCY VIABILITY AND Its COMPLICATIONS

DR. DINESH A RATHOD M.D.*, DR. NITA J NINAMA, M.D.**DR. JITENDRA PATEL, M.S.***

HUMAN CHORIONIC GONADOTROPIN (hCG)

HCG is a glycoprotein hormone composed of two dissimilar units, α and β , joined noncovalently. There are multiple forms of hCG in serum and urine samples in early pregnancy, including intact hCG (molecular weight- 36700) and its free subunits free α (molecular weight- 14500) and free β (molecular weight- 10000) free β Unit is degraded by macrophage enzymes and in the kidney to make a β subunit core fragment is the principal hCG-related molecule present in urine during pregnancy⁽¹⁾ intact hCG comprises approximately 70% amino acids and 30% sugar residues. HYPERGLYCOSYLATED HCG(H-hCG) is produced by Invasive cytotrophoblast and it contains significantly larger oligosacharides . H-hCG accounts for more than 80% of different forms of hCG detected in the week following implantation. 61+9% of hCG forms in the week that follows the missing of the menstrual period and 50+4% in the following

weeks. The proportion of H-hCG declines rapidly there, after, accounting for less than 5% hCG in the second and third trimesters of pregnancy ^(1,2,3)

EARLY PREGNANCY DETECTION TESTS

It is important to conform that the manufacture of kit has proven reorganization of intact hCG, H-hCG and free β - subunits. It is not uncommon for a woman to have a negative urinary home pregnancy test result around the time of her missed menstrual period but a positive serum Hcg result when assessed a few weeks later. This discrepancy may be due to the insensitivity of a pregnancy test. A similar situation may occur when a woman has a positive early pregnancy test, but a repeat urine or serum test approximately 1 week later is negative. This is due to early pregnancy loss. ^(3,4)

Old data indicating that serum hCG concentration were the same as urine hCG, but it is proved to be incorrect. Table-I shows that average urine hCG level is, depending on the time of pregnancy and specificity of the test, generally less than one half of the corresponding serum hCG concentration.

ECTOPIC PREGNANCY

In Ectopic pregnancy more than 95% of the time the implantation occurs in the fallopian tube. The incidence of ectopic pregnancy increased after in vitro fertilization (IVF) in which it can be as high as 94%⁽⁵⁾. In screening test that rely on serum hCG levels, abnormally low but persistent hCG level early in pregnancy is the pattern most predictive of ectopic pregnancy. Doubling rate is only indicative and not diagnostic of a failing of pregnancy. A common algorithm of detecting ectopic pregnancies is a transvaginal ultrasound coupled with serial assessment of hCG levels. ^(5,6)

Table-1-Comparison of serum and urine hCG concentration in early pregnancy, in gestation with normal term delivery

Time since last menses	Media	patients	Median concentration	Range of results
4 th complete wk (4 wk-5wk,6d)	Serum	34	253 IU/L	11-3476 IU/l
		33	210 IU/L	12-2548 IU/L
5 th complete wk (5wk-5wk,6d)	Serum	23	3124 IU/L	330-37,290 IU/L
		41	510 IU/L	13-6046 IU/L
6 th complete wk (6wk-6wk,6d)	Serum	21	26,400 IU/L	440-142,230 IU/L
		28	2673 IU/l	142-20,439 IU/L

HETEROPHILIC ANTIBODIES

These are interfering antibodies found in human serum, which causes false elevated hCG.

The finding of positive pregnancy test by serum hCG measurement, along with the absence of the fetal sac as shown by ultrasound, easily can give rise to the false diagnosis of ectopic pregnancy or invasive gestational trophoblastic disease ^(7,8). As heterophilic antibodies are not present in urine samples, urine test can conform the correctness of the serum hCG measurement. Alternatively testing for raised progesterone values that would occur in response to true pregnancy.

HETEROTROPIC PREGNANCY

It is intrauterine pregnancy coexisting with an ectopic pregnancy. The frequency is approximately 1 in 7000 pregnancies in general population but incidence is increase to 1 in 100 pregnancies conceived by IVF. Heterotopic pregnancies are hard to diagnose and 50% cases are identified only after tubal rupture.

SPONTANEOUS ABORTION

In first 8 weeks of pregnancy, serum hCG level should approximately double every 2 days, but it vary greatly at all times during first 8 weeks of gestation. Serum hCG level should plateau as a peak is reached at 8-12 weeks of gestation. Low levels of hCG, non doubling levels of hCG or hCG result that reduce before expected time of hCG peak all are strong indicators of an impending spontaneous abortion

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* Jr Lect., Dept of Pathology, Smt NHL Municipal Medical college, Ahmedabad

** Asst. Professor, Dept of Physiology, Smt NHL Municipal Medical college, Ahmedabad

*** Asst. Professor, Dept of Anatomy, Smt NHL Municipal Medical college, Ahmedabad

PROBIOTICS, PREBIOTICS AND SYNBIOTICS

Dr. Kamlesh P. Patel* & Dr. (Mrs) Varsha J. Patel**

*Associate Professor of Pharmacology, ** Professor & Head of Pharmacology
Smt. N.H.L. Municipal Medical College, Ellisbridge, Ahmedabad-380 006.

Introduction:

Dr. Elias Metchnikoff, a Nobel Laureate, around 100 years ago proposed that “Lactic acid bacteria can render a great service in the fight against intestinal putrefaction” and might “Postpone and ameliorate old age”. This concept was developed further through the decades, and today, the emerging probiotics, prebiotics & synbiotics era is a subject of current debate and intense research.

Probiotics :

The term Probiotic means “for life”, is derived from the Greek language. It is now defined as “live microorganisms which when administered in adequate amounts confer a health benefit on the host”. The most common probiotic organisms clinically useful include members of the bacteria such as *Lactobacillus* and *Bifidobacteria* species & some selected strains of *Streptococcus*, *Lactococcus* & members of yeast & moulds such as *Saccharomyces*, *Aspergillus*, *Acanthosis* & *Candida* species.

Prebiotics :

The term Prebiotic is defined as “ short chained carbohydrates that are indigestible by human enzymes in the GIT and selectively stimulate the growth and activity of specific species of bacteria in the gut, usually bifidobacteria & lactobacilli, with benefits to health”. The most commonly used prebiotics in supplements are Fructooligosaccharides (FOS). Bifidobacteria, due to the presence of beta-fructofuranosidase enzyme are liable to break down and utilize FOS. This helps in stimulation of bifidobacterium growth in the GIT. FOS exhibits nutritional properties on colonic pH and stool bulking. It also increases bioavailability of essential minerals & decreases serum triglycerides. The other types of prebiotics substrates includes Polyols (Xylitol, Sorbitol, Mannitol), Disaccharides (Lactulose, Lactitol), Oligosaccharides (Raffinose, Soybean), Oligo-fructose, other non-digestible Oligosaccharides (Palatinose, Isomalto, Lactosucrose,) and Polysaccharides (Inulin, Resistant starch).

Synbiotics:

The term synbiotic is used when a product contains both probiotics and prebiotics. Since the word alludes to synergism, this term should be reserved for products in which the prebiotic compound selectively favors the probiotic compound, e.g., FOS in combination with strains such as *B. infantis*, *B. longum* etc. Combining probiotics with prebiotics could improve the survival of the bacteria crossing the upper part of the GI tract, thus enhancing their effects in the large bowel. Moreover, the local and the systemic beneficial effects of probiotics and prebiotics might be additive or even synergistic.

Colony Forming Units (CFUs) in Probiotics:

As per probiotics definition the live microorganisms that are administered have to be in adequate amounts to confer a health benefit to the host. Clinical bodies have used probiotic levels of above 1 billion to 10 billion or above. According to Earl Mindell, an internationally recognized expert on nutrition, healthy persons should take 2 to 5 billion Colony Forming Units (CFUs) of probiotics a day and those with GI conditions can take up to 10 billion CFUs per day. In acute diarrhea, lactobacillus is most effective at the dose of 10 billion CFUs per day. For prescription probiotics, the current daily intake recommended by the Natural Health Products Directorate of Canada is 5-10 billion CFUs per day.

The Ideal Properties of Probiotics :

Probiotics supplements are considered ideal, if they fulfill the following important characteristics :

- normal gut inhabitant
- nonpathogenic
- genetically stable
- resistant to acid
- capable of survival, proliferation and metabolic activity at the target site
- high stability

- viability at high populations
- antagonistic towards pathogenic bacteria
- resistant to bile
- immunostimulatory
- able to exert clinically documented health benefits.

The Ideal Properties of Prebiotics :

Prebiotics supplements are considered ideal, if they fulfill the following important characteristics :

- should be a non-digestible food ingredient
- should be principally an oligosaccharide
- neither be hydrolysed nor be absorbed in the upper part of the GI tract
- should reduce the gut pH
- should promote the growth and activity of probiotics
- beneficially affects the host health
- must be selectively fermented so that it is able to alter the colonic microflora towards a healthier composition e.g. by increasing number of saccharolytic species & reducing putrefactive microorganisms
- improves conditions associated with both constipation and diarrhea.

The Ideal Properties of Synbiotics :

Synbiotics supplements are considered ideal, if they fulfill the following important characteristics:

- should be an ideal combination of probiotics with prebiotics
- should exhibit synergistic relationship between viable beneficial bacteria and their selective substrate.
- prebiotic compound should selectively favors the probiotic compound e.g. FOS in combination with probiotics such as *B. infantis*, *B. longum* etc.
- should produce additive or synergistic effect.

Table 1. Mechanisms of action of Probiotics

Target Health Benefit

Postulated Mechanism

Protect the host against intestinal disease

Production of inhibitory substances.

Blocking of adhesion sites.

Degradation of toxin receptors.

Immuno modulation of nonspecific host resistance.

Effects of systemic immunity.

Urogenital infections

Adhesion to urinary & vaginal tract cells.

Colonisation resistance.

Inhibitor production (H_2O_2 , Biosurfactants).

Immune system modulation

Strengthening of non-specific defense against infection & tumours.

Enhancement of secretory IgA production.
Hepatic encephalopathy
Inhibition of urease – producing gut flora.
Anti-colon cancer effect
Mutagen binding.
Carcinogen deactivation.
Inhibition of carcinogenic producing enzymes of colonic microbes.
Improves immune response.
Effects on blood lipids, heart disease
Assimilation of cholesterol within bacterial cell.
Increased excretion of bile salts due to deconjugation by bile salt hydrolase.
Antioxidative effect.
Antihypertensive effect
Peptidase action on milk protein yields tripeptides which inhibit angiotensin-1 converting enzyme.
Cell wall component acts as ACE inhibitors.
Effect on allergic states
Prevention of antigen translocation into blood stream.
Promotion of lactose digestion
Bacterial lactase hydrolyses lactose.
Small bowel bacterial infections
Influence on activity of overgrowth flora, decreasing toxic metabolic production.

Mechanisms of action of Prebiotics :

Prebiotics may stimulate probiotic bacteria not only to grow but also to produce compounds beneficial to the host. Their colonic fermentation produces short chain fatty acids (SCFAs) and lactic acid, which are important factors determining the pH of the colonic lumen. The SCFA have strong effect on the metabolism of the host. Acetate and propionate are gluconeogenic and influence cholesterol production. Butyrate is a major source of energy for colonic epithelial cells, and low concentrations cause differentiation of mammalian cells as well as colon carcinoma cells.

Longer the chains of non-digestible carbohydrates, the slower they are fermented. The longer chains thus allow the stimulation of bacterial metabolism in a more distal part of the colon, whereas the short chains are readily fermented in the proximal part of the colon. Typically, the distal part of the colon is very much energetically depleted. Bacteria are starving, and the proteolysis of dead cells and the subsequent strictly anaerobic fermentation of the released amino acids result in production of (cytotoxic) putrefaction (forming phenolic compounds – skatol, indole and resol) is very important for the prebiotic concept.

Rationale for the concept of synbiotics:

The synbiotics concept combines both the probiotic and the prebiotic approaches. According to this approach, a food or food supplement will include both the live cells of the beneficial bacteria and a selective substrate; the idea being that the beneficial

bacterial cells that survive their transit through the stomach can grow quickly and competitively because of the presence of the selective substrate and establish their predominance.

The increase in metabolic activity of probiotic microorganisms is fundamental to many of the currently proposed mechanisms of health promotion by prebiotics. A further step in this direction is the use of synbiotics, where probiotics and prebiotics are combined. Thus, the living microbial additions would be used in conjunction with a specific substrate for the growth. The results of many researchers point to a synergistic effect of probiotic and prebiotic combination on faecal microflora of experimental animals. This effect was demonstrated by increased total Anaerobes, Aerobes, Lactobacilli, and Bifidobacteria counts as well as by decreased Clostridia, Enterobacteriaceae and E.coli counts.

Results from several landmark clinical trials have shown that, the Probiotics have robust clinical applications in the Gastrointestinal (GI) and Non-Gastrointestinal conditions as shown in Table 2 & 3.

Table 2 : Clinical applications of Probiotics in GI conditions

- ▶ Diarrhoea of various origins
 - Antibiotic - associated diarrhea, Rotavirus diarrhea
 - Traveler's diarrhea, Gastroenteritis
 - Nosocomial diarrhea, Clostridium difficile diarrhea
 - HIV/AIDS diarrhea, Enteral feeding associated diarrhea
- ▶ Irritable Bowel Syndrome (IBS)
- ▶ Inflammatory bowel disease
- ▶ Food allergies and lactose intolerance
- ▶ H. pyloric infection.
- ▶ Colon cancer
- ▶ Pancreatitis
- ▶ Small bowel bacterial overgrowth
- ▶ Alcoholic liver disease

Table 3 : Non – Gastrointestinal applications of Probiotics

-
- ▶ Prevention of vaginitis
 - ▶ Urogenital infections
 - ▶ Enhancement of oral vaccine administration
 - ▶ Atopic eczema
 - ▶ Cystic fibrosis
 - ▶ Dental caries
 - ▶ Various cancers
 - ▶ Hypercholesterolemia
 - ▶ Asthma
 - ▶ Juvenile chronic arthritis
 - ▶ Aphthous ulcers
 - ▶ Halitosis

Safety Profile :

A review outlining the safety of current probiotic compounds has been published. Probiotic have achieved a 'generally regarded as safe' (GRAS) status. Rare reports of infection such as fungemia and bacteremia in immunocompromised patients. Pregnant women and nursing mothers should use probiotic supplements only if recommended by their physicians. Probiotics are contraindicated in those hypertensive to any component of a probiotic-containing product.

Dosage :

Healthy person should take 2-5 billion CFUs (colony stimulating units) of probiotics a day and those with GI conditions can take up to 10 billion CFUs per day. In acute infectious diarrhea, lactobacillus is most effective at a dose of 10 billion CFUs during the first 48 hours, which translates to 5 billion CFUs per day. For prescription probiotics, the current daily intake recommended by the Natural Health Products directorate (NHPD) of Canada is 5-10 billion CFUs per day.

Presentation :

Capsules and Sachets of Probiotic + Prebiotic combination(Pro-wel) and Probiotic alone (Darolac) are commercially available.

Benefits offered by Probiotic & Prebiotic Combination Formula are :-

- Maximum Colony Forming Units (CFUs) :- ensure complete action.
- Fructooligosaccharide (FOS):- offers nutrition to the probiotics & normal intestinal flora.
- Acid – resistant cells :- reach intestine in full force.
- Freezed-dried & nitrogen-flushed cells :- offers excellent stability.
- Vegetable capsules :- ensure universal appeal.

Benefits offered by Probiotic Formula are :-

- L. rhamnosus : inhibits pathogens by producing antibacterial bacteriocins.
- L. acidophilus & B. Longum : enhance phagocytosis & IgA production, also prevent pathogenic attachment to GI epithelium.
- S. bouladii :- digests bacterial toxins.
- L. rhamnosus & L. acidophilus : strengthens epithelium & prevent destruction.

The Future of Probiotics, Prebiotics & Synbiotics :

The alarming increase of inappropriate use of antibiotics and bacterial resistance, along with renewed interest in ecological methods to prevent infections, makes Probiotics, Prebiotics & Synbiotics a very interesting field for research. Evidence is beginning to accumulate describing their beneficial effects in a variety of GI & Non-GI disorders. They offer dietary means to support the balance of the intestinal flora. They may be used to counteract local immunological dysfunction, to stabilize the intestinal barrier function, to prevent infectious succession of pathogenic microorganisms & to influence intestinal

metabolism. Looking ahead, this field holds immense promise for the future in delivering novel therapies in different fields.

Summary :

The advent of probiotics and the discovery that they colonise the human GI tract has thrown light on another symbiotic, man and his gut flora. With research underway there has been tremendous growth in the field of probiotics. They are strengthening their roles in the reduction of antibiotic associated diarrhea, management of rotavirus diarrhea, and diarrhea due to various causes; showing positive effect in the management of lactose intolerance; irritable bowel syndrome, inflammatory bowel disease; and are being researched in various non-gastrointestinal disease. These effects can be seen with a daily intake of 5-10 billion CFUs of probiotics per day. Prebiotics, with their potential to increase the activity of probiotics, are also being increasingly used in preparations containing probiotics. Synbiotics as they are called are metamorphosing from little known entities to well-known agents helpful in the maintenance of good health. It is now become imperative that the clinicians assimilate knowledge about probiotics & prebiotics, and use them for the benefit of their patients.

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CASE REPORTS

ATYPICAL PRESENTATION OF THALASSEMIA MAJOR

DR VINOD BHADUKIYA 3rd Y. RESIDENT
DR SAUKAT PANJWANI 2nd Y.RESIDENT
DR REKHA BHAVSAR PROF.& HEAD
DEPARTMENT OF PEDIATRICS, SMT N.H.L MUN.MEDICAL COLLEGE AHMEDABAD
380006

INTRODUCTION

The thalassemias are heterogenous group of inherited disorders characterized by hypochromic and microscopic anemia caused by deficient synthesis of one or more of polypeptide chain of human hemoglobin. The most important forms of thalassemia from autosomal mutant genes that reduce the rate of synthesis of the alfa and beta thalassemia respectively. Thal.major is a clinically severe disorder due to presence of two identical or

dissimilar beta thal. Mutations one on each chromosome 11. Clinical manifestations of thal. Major usually become apparent during a second 6 months of life and the diagnosis is almost always evident by 2yrs. Of age. The anemia of thal. major is characterised by severe hypochromia, microcytosis with bizarre poikilocytosis, tear drop cells, target cells and leptocytes. Nucleated red cells are found invariably with retic. Count of 2% to 8% is noted. Patient with thal. Intermedia have onset of recognized anemia after 2 years of age maintaining level 6 to 10 gm%. Hb electrophoresis patterns vary with Hb F levels as low 5% to 100% and Hb A from 0 to 100%. In our case age of presentation is 6 years with mild splenomegaly with peripheral smear suggestive of dimorphic anemia.

A 6 yrs old, female patient from Vankar community was admitted with complaints of fever, increasing pallor, respiratory distress, puffiness of face and yellow urine since two days. There was no past history of blood transfusion. There was no past h/o CHRONIC DIARRHOEA, or major operation. There was no family history of blood transfusion but history of death of one elder sib of 10 yrs of age before two yrs, cause of death was not known. On clinical examination: patient febrile 101 f tachycardia (120 pm) marked pallor, icterus and signs of congestive heart failure. She was undernourished (BMI 10.3), height (105/113 cms) with doubtful hemolytic facies, no features suggestive of vitamin deficiency (i.e. conjunctival Xerosis, angular cheilosis) hyperpigmented knuckles and grayish complexion. On systemic examination tender hepatomegaly (span 10 cm) with mild splenomegaly, hemic murmur and other systems were clinically normal. Provisional diagnosis on the basis of history and clinical examination was concluded as acquired hemolytic anaemia with congestive heart failure with probability of malaria. Patient was investigated and treated accordingly.

INVESTIGATIONS:

Hematological: Hb 1.9 gm%, total count, differential count & platelet count were within normal range. On peripheral smear RBCs were hypochromic, microcytic with normochromic and macrocytic with anisopoikilocytosis, few tear drop cells, elliptocytes and occasional macroovalocytes seen. Malarial parasites not seen. Retic count 0.5%. The test was performed on automated Coulter machine.

Blood cells indices: PCV 5.9%, MCV 99.7 fl, MCH 31.9 pg, MCHC 32.1%, RDW 33.7%.

Biochemical investigations: Serum Billirubin total-3.5 mg% with indirect billirubin-2.3 mg% & normal hepatic enzymes.

Radiological Investigations: X-Ray Chest revealed cardiomegaly, osteoporotic ribs, prominent trabeculae suggestive of congenital hemolytic anaemia. So X-ray hand & skull were performed and reported by radiologist as congenital hemolytic anaemia. So the diagnosis was reviewed in the light of clinical findings & investigations as congenital hemolytic anaemia with congestive heart failure.

Again detailed family history was taken. Mother revealed the cause of death of elder sib as thalassemia major. Another 4 yr child was diagnosed as thalassemia major before 3 months. Two sibs not investigated so far (12 yr old female & 2 yr old male)

Further detailed investigations carried out.

Hb Electrophoresis: Hb F 58%, Absent band of HbA on Agar gel electrophoresis, s.ferritin 613 microgm/l. S.Folic Acid & S.B12 levels advised but not carried out because of financial constraints.

Discussion :

The average survival of untreated patient with thalassemia major is < 4yrs & more than 80 % died in first 5 yrs of age. Usual age of presentation of Beta-Thalassemia major and intermedia is 6months to 2 yrs & more than 2 yrs respectively, with hemoglobin at presentation of less than 4gm% in thal.major & 6-10 gm% in thal. intermedia. Both have moderate to gross splenomegaly. Haematological presentation is usually of hypochromic microcytic with tear drop & target cells with anisopoikilocytosis. The thalassaemic patients are expected to have folic acid deficiency but it is not usual to see megaloblastic picture on peripheral smear exam. Our patient presented late (6yrs), mild splenomegaly with severe anaemia (Hb 1.9gm%) with congestive cardiac failure & peripheral smear showing dimorphic anaemia.

Clinical suspicion from haemolytic facies & the radiological reports made us to review the diagnosis. History & further specific investigations proved the diagnosis of thalassemia major.

One should investigate the patient in detail when clinical & hematological features do not match.

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Case report:

A RARE CASE OF ORIGIN OF CYSTIC ARTERY ARISING FROM INFERIOR PANCREATO-DUODENAL ARTERY.

Patel JP*, Nirvan AB**, Shah RK***, Shah GV****, Verma AP⁺, Dave RV***

Corresponding author : Patel JP Assistant Professor in Anatomy, NHL Municipal Medical College, Ahmedabad

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Abstract : Typically cystic artery arises from the right hepatic artery to the right of hepatic duct in the Calot's triangle bounded infero-laterally by cystic duct, medially by hepatic duct and superiorly by inferior surface of liver. On reaching the gall bladder it usually divides into superficial and deep branch. The superficial branch is distributed to the free peritoneal surface of the gall bladder, the deep branch passes behind the gall bladder to become distributed to its attached non-peritoneal surface and to the gall bladder bed.

During the course of routine dissection of celiac trunk and superior mesenteric artery, we found rare anomalous origin of cystic artery, which was taking origin from superior mesenteric artery through its inferior pancreatico-duodenal branch. This kind of

anomalous origin of cystic artery, according to our knowledge is rarely reported in any journal of anatomy. In 70% to 80% of individuals, the cystic artery arises as a branch of right hepatic artery within the hepato-biliary triangle. A double cystic artery has been reported to occur in 15% to 25% subjects.

Keywords:- Variation, Cystic artery, Inferior pancreato-duodenal artery

Introduction

Arterial like other anatomic variations cannot be ignored, for the risks of ligating the wrong vessels or of severing an essential organ-sustaining artery, along with the danger of ischemia and gangrene, of leaking and bleeding from sites of repair and at anastomotic suture lines, are too great, being ubiquitous possibilities. Many years ago Sir Arthur Keith, now in his 80th year, stressed the fact that in the biliary region, variation in anatomic structures were “rampant,” being so numerous and complex as to offer a “defiant challenge to memory.” Cholecystectomy is a dangerous operation was forcefully brought to the attention of surgeons, in 1923, by the admonition of the British surgeon, Flint, to write “Technically, gallbladder surgery is much the most difficult of any abdominal surgery and inadequate appreciation of the abnormalities of this region does not lessen the risk.” A knowledge of the anatomic variations in the biliary region and how they are brought about affords the surgeon guidance and self-confidence and rewards him in most instances with successful operative results, for obviously the best way to avert injuries to blood vessels is to know them.

Normal anatomy

According to Keith L. Moore, the cystic artery supplying the gallbladder and cystic duct commonly arises from the right hepatic artery in the angle between the common hepatic duct and the cystic duct. Typically cystic artery arises from the right hepatic artery to the right of hepatic duct in the Calot’s triangle bounded inferolaterally by cystic duct, medially by hepatic duct and superiorly by inferior surface of liver. On reaching the gall bladder it usually divides in to superficial and deep branch.

According to Gray’s Anatomy the cystic artery arises from the right hepatic artery. It usually passes posterior to common hepatic duct and anterior to the cystic duct to reach

the superior aspect of the neck of the gall bladder, where it divides in to superficial and deep branch to supply inferior and superior surface of gall bladder respectively.

According to Henry Hollinshed, cystic artery, normally arises from the right hepatic artery within the Calot's triangle, passes in the triangle towards the neck of the gall bladder where it typically divides in to two branches, one of which runs on the attached surface of the gall bladder, between it and liver, while the other runs on its peritoneal surface.

Observation

During the course of routine dissection of the arteries supplying supra-mesocolic organs (Liver, Gall bladder, Stomach, Pancreas, Duodenum and Spleen), we found rare anomalous origin of cystic artery arising from inferior pancreateo-duodenal branch of superior mesenteric artery. During dissection of branches of superior mesenteric artery, we traced inferior pancreateo-duodenal artery at the upper border of the third part of duodenum. It was dividing into anterior and posterior branch, which runs on adjacent surface of head of pancreas at the upper border of the duodenum. Before dividing into anterior and posterior branch inferior-pancreateo-duodenal near its origin from superior mesenteric artery give rise to abnormal cystic artery from its superior border. The abnormal cystic artery was running behind the head and uncinata process of pancreas, where it crosses anterior surface of the inferior vena cava. Then, it runs behind the first part of the duodenum, lying on right side of the gastro-duodenal artery. At the upper border of the first part of duodenum it enters in the right free margin of the lesser omentum lying behind portal vein situated between the hepatic artery and the bile duct. At the junction of cystic duct and hepatic duct abnormal cystic artery crosses in front of the bile duct and divides in to superficial and deep branches that supplies respectively to the peritoneal and non-peritoneal surface of the gall bladder.

Discussion

Michels N.A. et al (1951) had observed that the cystic artery was single in 75% and double in 25% of subjects. In 140 of 200 subjects (70 %) the single cystic was a branch of right hepatic artery and only in 5% it arose from some other sources like left hepatic, middle hepatic, common hepatic, retroduodenal, gastroduodenal etc. site of origin of the single cystic artery occurred in Callot's triangle in 57 % of 200 cases, viz., from the

coeliacal right hepatic or its branches, 43 %; from a replace right hepatic, 13% ; from an accessory right hepatic, 1%. Out of these in 10 % cases single cystic artery arise from an abberent hepatic artery derived from the superior mesenteric artery.

They found double cystic artery in 50 subjects out of 200 subjects in which cystic artery arising separately fom the same artery or from the different sources. This percentage of double cystic arteries (25%) is considerably higher than that reported by other author (Lipshutz, 11 % ; Daseler, et al, 13 % ; Flint, 15 % ; Belon, 19 % ;Brewer, 20 % ; Browne, 21 %). A common pattern of the dual cystic is one in which deep cystic arising from a celiacal right hepatic, the superficial from the right hepatic to the left of the hepatic duct which crosses anteriorly. Another fairly common pattern in which the deep cystic arises in single fro the right hepatic artery, the superficial from the gastroduodenal or its retroduodenal branch. The pattern of the superficial cystic or even of the entire cystic arising from the intestinal artery, i.e. from the retroduodenal artery, is very important from a surgical point of view, for ordinarily the surgeon does not look for a cystic artery caudal to the cystic duct.

According to Gray's Anatomy, the cystic artery may arise from the common hepatic artery, sometimes from the left hepatic artery, and rarely from gastro-duodenal or superior mesenteric arteries. In these cases it crosses anterior (or less commonly posterior) to the common bile duct or to common hepatic duct to reach the gall bladder. An accessory cystic artery may arise from the common hepatic artery or one of its branches and the cystic artery often bifurcates near its origin, giving rise to two vessels, which approaches the gall bladder.

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Illustrations



Photo 1. Showing origin of cystic artery (1), inferior pancreaticoduodenal artery (2,3), arising from superior mesenteric artery.



Photo 2. Showing abdominal aorta(1), superior mesenteric artery(2), inferior pancreaticoduodenal artery(3,4) and cystic artery (5).

Case report:

INTERCOSTOBRACHIAL NERVE SUPPLYING THE ENTIRE MEDIAL SIDE OF THE ARM

Patel JP*, Shah RK**, Nirvan AB***, Verma AP⁺

* M.S. (Anatomy)

Corresponding author : DR. Patel JP Assistant Professor in Anatomy, NHL
Municipal Medical College, Ahmedabad

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Abstract

The intercostobrachial nerve is the lateral cutaneous branch of 2nd intercostal nerve which supplies the skin of axilla and upper part of medial side of arm. The medial cutaneous nerve of arm is the branch of medial cord of Brachial Plexus which supplies the rest of medial side of arm. During routine dissection of upper limb of an adult male cadaver, the medial cutaneous nerve of arm was found to be absent on the left side. The intercostobrachial nerve was supplying the entire medial side of the left arm. On the right side the medial cutaneous nerve and intercostobrachial nerve were found normal.

Keywords: variation, intercostobrachial nerve

Introduction

Nervous like other anatomic variations can not be ignored, for the risk of severing the variant nerve unknowingly. In the past many years surgeons have become increasingly aware of the morbidity caused by the division of the intercostobrachial nerve during axillary dissection. Knowledge of such variations is useful during surgery as well as during regional nerve blocks for accurate and adequate anaesthetization.

Normal Anatomy

The intercostobrachial nerve is the lateral cutaneous branch of the 2nd intercostal nerve. It supplies the skin of 2nd intercostal space at the medial wall of axilla, the skin of floor of axilla and medial side of upper part of arm. The nerve enters the axilla by piercing or passing between the digitations of serratus anterior muscle in mid-axillary line. It traverses axilla obliquely lying within the axillary fat, where it gives branches to the floor of the skin of the axilla. It then communicates with the medial cutaneous nerve of arm or with one of its branches or it may communicate with the later in a plexiform manner in the axilla. It then pierces the deep fascia to supply the skin of the medial side of upper arm both anteriorly and posteriorly.

Some authors also describe the intercostobrachial nerve and its axillary branch as anterior and posterior intercostobrachial nerves respectively.

Observation

During the routine course of dissection of upper limb, the variation involving the intercostobrachial nerve was found in the left arm of an adult male cadaver. The nerve was found to enter the axilla by piercing the 2nd digitations of serratus anterior muscle and gave a branch to the skin of the floor of axilla. Another branch was given in the axilla for the medial side of the upper part of arm. As we traced the nerve further it was found to pierce the deep fascia in upper arm and descended along the medial side of the arm, lying beneath the deep fascia. In the arm it gave about four branches at various levels, the last one of them extending towards olecranon fossa of the humerus. Finally it ended by dividing into two branches for the skin over the medial epicondyle of the humerus. The

medial cutaneous nerve of arm was absent and so its entire area of supply was innervated by the intercostobrachial nerve. The lateral cutaneous branch of 3rd intercostal nerve was found normal supplying its area i.e. skin of 3rd intercostals space.

On the right side the medial cutaneous nerve and intercostobrachial nerve were found normal.

Discussion

O'Rourke et al. (1999) had observed intercostobrachial nerve received communication from medial cord of brachial plexus in 36% and in 18% there was connection to the medial cutaneous nerve of arm. Out of total 28 axillary dissections, in one-third cases it reached the level of the elbow joint and in one occasion each there was contribution from first and third intercostals nerves. They also observed that the intercostobrachial nerve was constant in all dissections, but its origin, size, connection to the brachial plexus and medial cutaneous nerve of the arm were variable, as was its ultimate destination in arm. During arm surgeries, the intercostobrachial nerve must be interrupted to provide complete brachial anesthesia. This can be achieved easily by axillary block since the site of entrance of intercostobrachial nerve into the upper arm is the very site of injection of axillary block, where it is blocked by subcutaneous infiltration with the same injection (Captain Ruloph H and De Jong, 1961).

Two other rare variations have been reported by Murakami S et al. where in one case, it penetrated the pectoralis minor muscle and in other it penetrated the pectoralis major muscle but in both of these cases the anomalous nerve supplied the skin of the upper arm (Shinichiro M. et al. 2002). Marios Loukas (2006) reported one case of unilateral innervation of pectoralis minor and major muscles from a branch of the intercostobrachial nerve. Clinical consequences of such variations may include motor losses, in addition to sensory losses resulting from accidental or intentional dissection of intercostobrachial nerve.

According to Gray's Anatomy sometimes, the intercostobrachial nerve is sometimes large and is reinforced by a part of lateral cutaneous branch of 3rd intercostals nerve replacing the medial cutaneous nerve of arm and receiving from the brachial plexus a

connection representing the latter. Occasionally this connection is also absent.

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Illustrations:

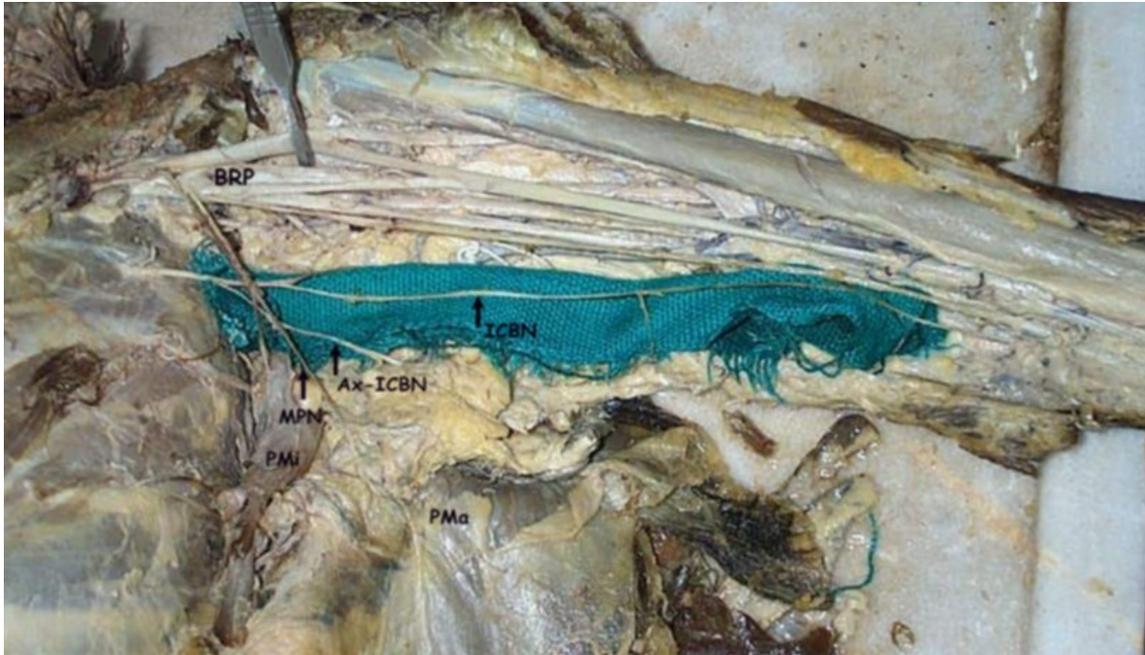


Fig 1: Photo showing variant course of intercostobrachial nerve (ICBN), its axillary branch (Ax-ICBN), medial pectoral nerve (MPN), Pectoralis minor muscle (PMi), Pectoralis major muscle (PMa), and Brachial Plexus (BRP) with its branches.

CORNELIA DE LANGE SYNDROME WITH RAREST PRESENTATION OF RING OF 9th CHROMOSOME.

Dr Aasheeta Shah (Associate professor of paediatrics) Dr. Kirti N. Upadhyay (third year resident) Smt. N. H. L Municipal Medical College, Ahmedabad.

Cornelia de Lange Syndrome (CDLS) is a multiple congenital anomaly syndrome characterized by a distinctive facial appearance, prenatal and postnatal growth deficiency, feeding difficulties, psychomotor delay, behavioral problems, and associated malformations mainly involving the upper and / or lower extremity.

A Male hindu child 8 month old born out of non consanguineous marriage was brought to V. S. HOSPITAL in paediatric department with chief complaint of ,Cough, common cold and fever since 3 days and,Generalized tonic clonic seizure. Patient having complaint of recurrent cough, vomiting and nausea. Past history of taken treatment at orthopedic department for right sided club foot. Patient born out of preterm term normal delivery in hospital setting without any postnatal major complication He is the first and only child of

his parents, the mother age is only 23 yrs., no h/o any antenatal and intranatal complication He is taking his feeds well.

DEVELOPMENT ASSESSMENT :

All form of milestones are delayed.

ON EXAMINATION:

The patient is conscious, active and playful child.

Vitals : normal

Anthropometry : head circum : 36 cm

Length : 55 cm

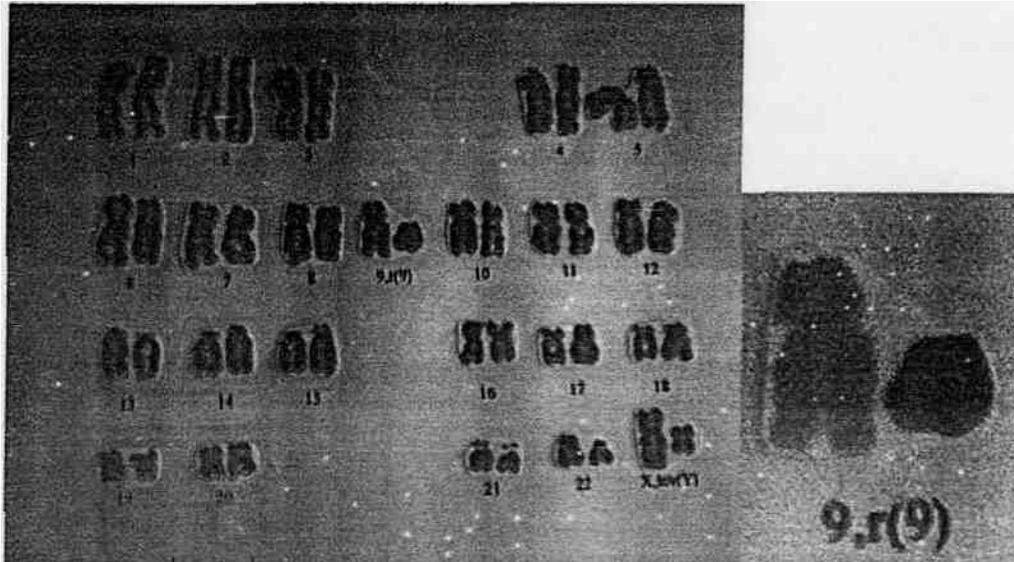
GENERAL Examination :

Coarse facial features :Microcephaly,Brachycephaly,Hirsutism, Long curly eyebrows, Eyebrows merges in midline (synophrosis),Thin downward upper lip,Long philtrum,Micromelia (short limb),Low hair line, Depressed nasal bridge, Low set ears, Abundant hairs over back, Anterior frontanalle open and at level,Skin folds over neck, Generalized hypertrichosis, Intertrigo

SYSTEMIC EX : normal

INVESTIGATION :

1. Hemogram : normal
2. Radiological assessment:
 - i. X-ray skull- microcephaly
 - ii. CT SCAN BRAIN- mild cortical atrophic changes.
3. 2-D ECHO- normal
4. EEG- dysrhythmic changes s/o primary generalized epilepsy.
5. CHROMOSOMAL STUDY : A chromosomal complement having a modal number of 46 chromosomes including ring of 9 chromosome and inversion of Y chromosome. Inversion is normally seen in Asians. The 21 cases have been reported in literature till date.



DIAGNOSIS : CORNELIA DE LANGE SYNDROME

TREATMENT :

Supportive

Genetic counselling

Cornelia de Lange first described it as a distinct syndrome in 1933.

Fortunately, says Dr. Krantz, “the disease has a low recurrence risk (1%) in family.

a large gene on chromosome 5, which they named NIPBL. Mutations giving rise to Cornelia de Lange syndrome occur at different locations within that gene NIPBL stands for Nipped B-like, because the human gene produces proteins similar to those produced by the Nipped-B gene in fruit flies. "The insect gene was called 'Nipped' because a mutation in that gene produces an abnormal fly wing that looks like it had a small bite taken out of it." said Dr. Jackson. Both the fruit fly gene and human gene regulate biological signals that have wide-ranging effects during development, on a variety of organ systems

In rare cases the CDLS may show the ring abnormality on 9 chromosome, very few cases has been reported till date.

Pathophysiology : Etiology and pathogenesis are not clearly known, Most case are sporadic.

Frequency :

- Internationally : Incidence is 1 per 10,000-50,000 live births.

- Race : No differences based on race have been described.
- Sex : No predilection based on sex exists

Prognosis :

- Life expectancy is normal if no major malformations occur. Causes of death include apnea following respiratory aspiration events, cardiac malformations, and complications related to gastrointestinal problems.

Patient Education :

- Teaching methods of conveying pleasure and affection that do not require facial expression can improve acceptance by relatives.

Activity :

The use of sign language can help the patient to overcome frustration caused by excessive speech delay.

PRENATAL DIAGNOSIS:

Deterrence/Prevention :

Genetic counseling and prenatal diagnosis based on ultrasound screening for evidence of manifestations of the syndrome (ie, IUGR, limb defects, diaphragmatic hernia, nuchal translucency)

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WHO 2006 MESSAGE:

7 APRIL 2006 | GENEVA/LUSAKA/LONDON -- A serious shortage of health workers in 57 countries is impairing provision of essential, life-saving interventions such as childhood immunization, safe pregnancy and delivery services for mothers, and access to treatment for HIV/AIDS, malaria and tuberculosis. This shortage, combined with a lack of training and knowledge, is also a major obstacle for health systems as they attempt to respond effectively to chronic diseases, avian influenza and other health challenges, according to The World Health Report 2006 - Working together for health, published today by the World Health Organization (WHO).

More than four million additional doctors, nurses, midwives, managers and public health workers are urgently needed to fill the gap in these 57 countries, 36 of which are in sub-Saharan Africa, says the Report, which is highlighted by events in many cities around the world to mark World Health Day. Every country needs to improve the way it plans for, educates and employs the doctors, nurses and support staff who make up the health workforce and provide them with better working conditions, it concludes.

"The global population is growing, but the number of health workers is stagnating or even falling in many of the places where they are needed most," said WHO Director-General Dr LEE Jong-wook. "Across the developing world, health workers face economic hardship, deteriorating infrastructure and social unrest. In many countries, the HIV/AIDS epidemic has also destroyed the health and lives of health workers."

The World Health Report sets out a 10-year plan to address the crisis. It calls for national leadership to urgently formulate and implement country strategies for the health workforce. These need to be backed by international donor assistance.

Infectious diseases and complications of pregnancy and delivery cause at least 10 million deaths each year. Better access to health workers could prevent many of those deaths. There is clear evidence that as the ratio of health workers to population increases, so in turn does infant, child and maternal survival.

"Not enough health workers are being trained or recruited where they are most needed, and increasing numbers are joining a brain drain of qualified professionals who are migrating to better-paid jobs in richer countries, whether those countries are near neighbours or wealthy industrialized nations. Such countries are likely to attract even more foreign staff because of their ageing populations, who will need more long-term, chronic care," said WHO Assistant Director-General Dr Timothy Evans.

To tackle this crisis, more direct investment in the training and support of health workers is needed now. Initial costs will be for the training of more health workers. As they graduate and enter the workforce, funds will be needed to pay their salaries. Health budgets will have to increase by at least US\$10 per person per year in the 57 countries with severe shortages to educate and pay the salaries of the four million health workers

needed to fill the gap. To meet that target within 20 years is an ambitious but reasonable goal, the Report concludes.

Financing this gap will require significant, dedicated and predictable funding from national sources, as well as from international development partners. The Report recommends that of all new donor funds for health, 50% should be dedicated to strengthening health systems, of which 50% should be dedicated specifically to training, retaining and sustaining the health workforce.

At least 1.3 billion people worldwide lack access to the most basic healthcare, often because there is no health worker. The shortage is global, but the burden is greatest in countries overwhelmed by poverty and disease where these health workers are needed most. Shortages are most severe in sub-Saharan Africa, which has 11% of the world's population and 24% of the global burden of disease but only 3% of the world's health workers.

The Report calls for prompt and innovative initiatives to improve efficiency. For example, HIV/AIDS, TB and other priority disease programmes have implemented ways for health workers with limited formal training to successfully carry out specific health tasks. These experiences should be drawn upon to develop national health workforce strategies.

The World Health Report recommends that in order to achieve the goal of getting "the right workers with the right skills in the right place doing the right things," countries should develop plans that include the following:

- Acting now for workforce productivity: better working conditions for health workers, improved safety, better access to treatment and care;
- Anticipating what lies ahead: a well-developed plan to train the health workforce of the future;
- Acquiring critical capacity: workforce planning; development of leadership and management; standard setting, accreditation and licensing as drivers for quality improvement.

Beyond the national strategies the report urges global cooperation:

- Joint investment in research and information systems;
- Agreements on ethical recruitment of and working conditions for migrant health workers and international planning on the health workforce for humanitarian emergencies or global health threats such as an influenza pandemic;
- Commitment from donor countries to assist crisis countries with their efforts to improve and support the health workforce.
- Courtesy Editor :WHO web site.

CASE REPORT

PULMONARY ALVEOLAR PROTEINOSIS WITH AGAMMAGLOBULINEMIA, A RARE PRESENTATION.

DR. AASHEETA SHAH

DR. RITESH SHAH

DR. KIRTI UPADHYAY Dep. Of Ped. Smt NHL Mun Medical College Ahmedabad
380006

Pulmonary alveolar proteinosis is a rare disease of lung characterized by alveolar and interstitial accumulation of Periodic acid schiff stain positive lipoproteinous material produced by surfactant, which is more common in immunocompromised children

A Muslim patient aged 18 months old, weight 8 kg, born out of non-consanguinous marriage was presented to VS hospital with chief complains of cough, fever and breathlessness since 15 days.

The patient is having complaints of recurrent lower respiratory infections since 6 months of age.

The patient was give many of antibiotics plenty times to cure the consolidation recurring on and off.

The patient was treated with steroids number of times in past for recurring symptoms. Later he was diagnosed as having pulmonary tuberculosis with mesenteric adenitis and was put of anti tuberculous therapy empirically, patient responds poorly to anti tuberculous therapy.

No h/o Koch's contact.

He is only child of his parents, h/o one abortion

He consumes normal family diet.

O/E

Lymphoid hypoplasia.

R/R 84/min

With increase in work of breathing in form of SCR, spo₂- 76%

RS-bilateral air entry present, fine crackles over right lower zone.

CVS-normal

Investigations:

Hemogram leucocytosis with anemia

Abga chronic respiratory acidosis

Serum HIV negative

MT negative

Gastric aspirate for AFB- negative

Gastric aspirate of fungus- negative

Serum LDH 21600

Serum IgG 3.2 mg/dl

Serum IgM 80 mg/dl

Serum IgA 75 mg/dl

CXR s/o soft tissue opacity in right base suggesting segmental pneumonic patch

HRCT Chest s/o ground glass density areas in both lungs predominantly on both lower lobes and posterior segment of right upper lobe s/o consolidation. ? PULMONARY ALVEOLAR PROTEINOSIS

Bronchoscopy- whitish material in droplets and distributed all over the distal alveoli.

Bal fluid culture- negative

Bal periodic acid schiff test- negative

Trans bronchial lung biopsy- section reveals pulmonary parenchyma with alveoli containing PAS positive material, alveolar macrophages contain similar material.

DIAGNOSIS:

PULMONARY ALVEOLAR PROTIENOSIS WITH AGAMMAGLOBULINEMIA

TREATMENT:

Supportive

Iv ig

Brochoalveolar lavage

INTRODUCTION:

Two forms are recognized

1. primary idiopathic
2. secondary due to lung infections, hematologic malignancies and inhalation of mineral dusts such as silica, titanium oxide and insecticides

It has been proposed that defect in macrophage function more specifically an impaired ability to process surfactant may play a role in pathogenesis of PAP. An inherited deficiency in surfactant protein B has been described. A deficiency in expression of beta subunit of gm-csf receptor occurred in 4 patients till date. PAP has been reported in children with lysinuric protein intolerance. Alveolar proteinosis occurs in association with infection particularly in immunocompromised individuals. Late onset alveolar proteinosis caused by IgG1 and IgG2 autoantibody directed against GM-CSF(2,3,5)

INCIDENCE

Internationally an incidence of 1-2 cases per million has been suggested by Shah et al.

SEX

No sex predilection in congenital form but male predominance (2-4:1) in infants and children.

These patients generally present as having dyspnoea, fatigue, cough, weight loss, chest pain and hemoptysis. Later on they develop cyanosis and digital clubbing, PFT shows restrictive pattern and ABGA shows marked hypoxemia and chronic

respiratory acidosis. Diagnosis is confirmed by HRCT, lung biopsy and BAL fluid for PAS positive material and surfactant components. Treatment is form of repeated bronchoalveolar lavage, lung transplantation and subcutaneous administration of recombinant GM-CSF(3)

DIFFENTIALS(4)

Acute respiratory distress syndrome
Pneumonia typical bacterial
Pneumonia pneumocystic carinii
Pulmonary edema-noncardiogenic
Pulmonary haemorrhage

PROGNOSIS:

The overall prognosis for pulmonary PAP is fair, with achievement of complete remissions in many patients(1)

Whole lung lavage most often results in a dramatic response

Some patients require repeated lavages and these patients usually progress to pulmonary fibrosis and have a poor outcome.

Congenital PAP responds favorably to lung transplantation.

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(All the authors were involved in management of the case, writing the case report and approval of the final session)