TABLE 4—Risk of Fetal Loss, by Occupation and WWTP Exposure Any Time Prior to Conception

Occupation and WWTP Exposure	No. Pregnancies	Rate of Fetal Loss	Relative Risk (RR)	95% Confidence Limits of RR
1a) Exposed Process Operators	10	.100	.85	.11–6.77
b) Un-exposed Process Operators	34	.118		
2a) Exposed Mechanical, Instrument, Electrical	35	.200	4.85	1.51–15.57
b) Un-exposed Mechanical, Instrument, Electrical	97	.041		

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Diet Policies of PKU Clinics in the United States

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Abstract: About two-thirds of 90 clinics treating phenylketonuria (PKU) now recommend indefinite continuation of a low phenylalanine diet as compared to 1978 when fewer than one-fourth had this policy. The percentage of children maintained on diet has increased markedly for six to eight year-olds. Greater conservatism in clinic diet recommendations likely reflects reports of adverse consequences following diet discontinuation and negative individual clinic experiences. (*Am J Public Health* 1984; 74:501–503.)

Introduction

Since 1953, phenylketonuria (PKU) has been treated with a diet restricted in phenylalanine.[1] Although well-treated children have IQs comparable to those of their non-PKU siblings,[2] the age at which the restricted diet can be safely stopped is still unknown.

Reviews of diet discontinuation showed IQ losses[3,4] in about half of the reports. Brown and Warner[3] suggested reasons why real losses in IQ might be obscured in those studies indicating no significant intellectual changes following diet discontinuation.

After four to seven years of follow-up, Seashore[5] reported modest to very significant declines in intellectual performance, attentional and academic problems in school, and electroencephalogram (EEG) changes after diet discontinuation. Pueschel[6] found no changes in eight children six months after discontinuation of diet at age five, in physical, neurological, and psychological assessments, or in somatosensory and visual evoked potentials. The PKU Collaborative Study found lowered school performance after diet discontinuation.[7,8]

This paper describes diet policies of PKU treatment programs in 1982 and compares them with policies found in 1978–79.[9]

Methods

In 1982, a questionnaire was sent to all identified programs involved in the treatment of PKU in the United States.[10,11] Policies for discontinuation or continuation of the phenylalanine-restricted diet were described by each program. We have grouped the policies into three general categories:

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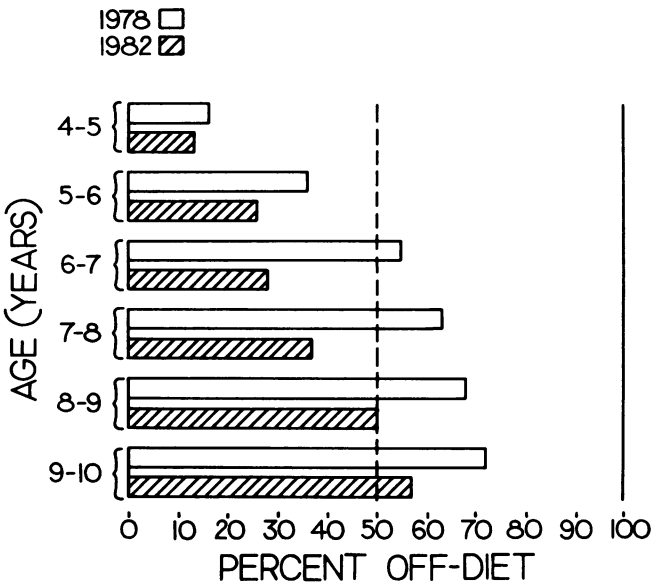

FIGURE 1—Comparison of Per Cent PKU Children Off-Diet (1978 versus 1982)

1) Diet to be continued indefinitely in "strict" or "liberal" form;

2) Diet to be continued until a given age, then discontinuation of diet to be allowed as an option after discussing the pros and cons with the affected individual and/or parents;

3) Diet to be continued until a given age and then completely discontinued.

Clinics defined the terms "strict" and "liberal." Options were allowed for choosing a different diet policy for males and females.

"PKU ON-DIET" was defined to mean any individual on a diet to reduce blood phenylalanine and for whom a PKU formula provides the major dietary protein source, independent of blood levels achieved. This group does not include those on "slightly" modified diets, for whom formula provides only a small percentage of dietary protein restrictions, or but who are not consuming formula. "PKU OFF-DIET" was defined to mean only those who were once but are no longer on a phenylalanine-restricted diet.

Diet policies data are from 90 out of 93 identified PKU follow-up programs. Three clinics had no established diet policy.

Results

Figure 1 shows that children are staying on diet longer in 1982 than in 1978. Table 1 shows that policies of the clinics as a group have become stricter since 1978. Indefinite continuation of diet was recommended by 64 per cent of clinics for males and 72 per cent of clinics for females.

Most clinics indicated that a "strict diet" constitutes mean serum phenylalanine levels maintained at 10 mg/dl or less (72 of the 85 clinics responding). Others suggest 10–15 mg/dl (12 clinics), and one clinic considers levels up to 20 mg/dl to constitute strict control.

A "liberalized diet," for 34 clinics which allow it, is defined as mean serum phenylalanine levels maintained at 10–15 mg/dl (16 clinics), 16–20 mg/dl (14 clinics), 8–10 mg/dl (three clinics), or 20–25 mg/dl (one clinic). Most of these clinics allowed the liberal diet at five to eight years of age.

TABLE 1—Number of Clinics with Various Policies for Diet Discontinuation in PKU

Survey Year	Sex	Policy 1 Indefinite Continuation	Policy 2 Family Choice	Policy 3 Clinic Recommends Age to Discontinue
1978	Both	16	26	30
1982	Males	58	31	1
1982	Females	65	24	1

The number of clinics preferring each policy in 1982 was compared with the number expected if the proportions were the same as in 1978.
$\chi^2 = 107$ for males and 139 for females.
$p < 0.0001$ for both sexes.

For clinics which allow diet discontinuation and included a discontinuation age, this is permitted at five to eight years of age (18 clinics), "as late as possible" (seven clinics), or at three to four years of age (one clinic).

Several clinics ask that children going off-diet continue drinking formula, in an effort to reduce blood phenylalanine levels or to make a return to diet feasible later on.

Seventeen of the 93 clinics now have a more conservative diet policy for females than for males, indicating awareness of the problem of maternal PKU.[12,13]

Discussion

The decision of a majority of PKU treatment programs not to recommend dietary discontinuation for PKU is probably due in part to reports indicating unfavorable results of discontinuation, and to personal clinic experience with adverse consequences. If a family wishes to make the choice to discontinue diet, the burden of the decision is now more commonly placed on the family.

Diet policies chosen by some clinics appear to represent their ideal goal, while others seem to be reflecting what realistically has occurred with diet control for children followed by their clinic. Many comments indicated the difficulties of maintaining a strict diet for older children. Some clinics have, however, indicated considerable success in maintaining a strict diet for older children, teenagers, and young adults.[9]

The trend toward later discontinuation of diet or indefinite continuation of diet comes at a time when state support of formula costs for families is diminishing. In 1978, 85 per cent of PKU programs received financing for some or all of the cost of formula.[10] This survey revealed that only 66 per cent of PKU programs were receiving financing for formula from state health departments and many clinics indicated that there were plans by the state health department to soon withdraw all or the majority of support. The burden of formula costs, which can be $5,000 to 7,000/year or more for a teenager or young adult, is increasingly being borne by health insurance, with families frequently paying for some portion of the total cost.

It will now be important to assess the possible financial, nutritional, social, and psychological problems that may be encountered in trying to maintain the phenylalanine-restricted diet for older children, adolescents, and adults.

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Intradermal Immunization with Human Diploid Cell Rabies Vaccine: Serological and Clinical Responses of Immunized Persons to Intradermal Booster Vaccination

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Abstract: Rabies antibody titers ranged from 0–9.3 IU/mL in 117 human volunteers one year after intradermal vaccination with one or two doses of human diploid cell rabies vaccine (HDCV). At that time, each volunteer received one 0.1-mL booster dose of HDCV intradermally. All 117 volunteers showed good anamnestic responses, with antibody titers rising to 0.5–54.3 IU/mL within seven days of booster injection. Vaccine safety was good; only minor reactions were experienced, all of which resolved spontaneously. (*Am J Public Health* 1984; 74:503–505.)

Nine studies[1–9] have demonstrated that human diploid cell rabies vaccine (HDCV), when given intradermally, provides a safe, effective, and economical method for human pre-exposure prophylaxis against rabies. However, a complete schedule for use of intradermal HDCV in rabies preexposure prophylaxis will require information on the effectiveness of intradermal booster vaccinations.

The study described in this article is a continuation of an investigation initially reported in a previous publication.[7] It describes the serological and clinical responses of human volunteers immunized with intradermal HDCV to an intradermal booster dose of HDCV.

Methods

The 117 subjects were volunteers from the faculty, hospital staff, and student body of the University of Florida College of Veterinary Medicine, Gainesville. They were members of the initial group of 240 volunteers immunized with intradermal HDCV[7] who were available for follow-up study. Informed consent was obtained in writing from each volunteer after the nature of the study protocols had been fully explained. The volunteers were divided into three groups based on their previous exposure to rabies vaccines.[7] The 41 volunteers who had only received two 0.1-mL doses of HDCV intradermally 28 days apart were assigned to group A; 19 volunteers who had previously been vaccinated with duck embryo rabies vaccine (DEV), followed by two 0.1-mL doses of HDCV intradermally 28 days apart, were assigned to group B; and 57 volunteers who had previously received DEV, followed by one 0.1-mL dose of HDCV intradermally, were assigned to group C.

Blood was drawn from each volunteer for serum collection immediately before vaccination and at days 28 (one month), 56 (two months), 182 (six months), 273 (nine months), and 364 (12 months) after initial intradermal vaccination with HDCV. Immediately after the day-364 bleeding, each volunteer received one 0.1-mL booster dose of HDCV intradermally. The HDCV (manufacturered by Institut Merieux of Lyon, France) contained the Pitman-Moore rabies virus strain grown in human diploid cells and inactivated with β-propiolactone; the vaccine used for booster vaccinations in this study was commercial lot No. V-1222 with an antigenic value of 6.59. Each volunteers was again bled seven days after the booster injection to test for an anamnestic response to revaccination.

All intradermal injections were given in the anterior aspect of the forearm, using tuberculin syringes. All serum samples were tested quantitatively for antibodies to rabies virus, using the rapid fluorescent focus inhibition test.[10] Antibody to rabies virus in each serum sample was expressed in international units per milliliter (IU/mL) by comparison of the antibody titers with those of the United States Standard Rabies Immune Globulin reference serum. Serological responses were analyzed statistically to examine for differences between study groups, using the one-way analysis of variance.

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